The Role of the Cervical Spine in Sports Concussion and Post Traumatic Headache: Physiological and Anatomical Correlates

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Introduction

Sports related concussion has quickly become the most widely publicized neurological disorder with estimates ranging from 1.6 to 3.8 million affected individuals annually. The cervical spine plays a major role in concussion biomechanics. The cervical spine has also been implicated as playing a major role in triggering and maintaining migraine headache. Patients with migraine especially chronic migraine, often experience neck pain as part of their symptomatology. Post traumatic headache (which in most individuals meets the International Headache Society (IHS) criteria for migraine) is the most common symptom of sports related concussion with a prevalence approaching 90%. In addition, both concussion and migraine share a common underlying physiological process i.e. the hyper-excitatable brain. Despite their similarities and common physiological entity i.e. the cervical spine, there are no published reports linking the cervical spine with the underlying anatomic, physiological and biomechanical processes of sports concussion and post traumatic migraine headache.

Sports Concussion Biomechanics

A number of studies have attempted to identify possible biomechanical mechanisms. Headshots or helmet hits were the most common mechanism with shots to the lower side of the helmet and oblique portion of the face mask which induce translational and rotational forces on the head. Hits to the vertex or anterior to the vertex of the head will also increase the risk of injury to the cervical spine. Hits to this region do not allow the neck to flex sufficiently to move the head out of the way of the increased force of the torso resulting in damage to underlying cervical structures (see below). Lateral rotation of the head also decreases the extension range of the cervical spine by fifty percent and increases the likelihood of extension injury. The player’s padding can also play a role in damage to the cervical spine. Although the helmets offer some protection their padding allows for the impact forces to be transmitted over a greater amount of area and time. However, this creates an increase in axial compression as the padding creates a pocket for the head to be held in one position and as a result increases in exposure time to compressive force for the cervical spine. Blindside hits to the body which can induce lateral flexion of the neck and rotation of the head have also been demonstrated to induce concussion. Blindside hits are quite common and result in a whiplash type injury to the cervical spine. Although in many cases the player being hit will undergo extreme flexion and extension of the cervical spine (as well as rotation), they will also experience an increase in compressive forces from below i.e. the torso which results in an increase in axial loading of the cervical spine (see below). When the head is not supported the degree of neck extension is determined by acceleration of the head with respect to the torso, i.e. acceleration is directly proportional to the player doing the hitting (see below). It is also dependent on the underlying resistance of the cervical muscles and ligaments of the player being hit. In addition, the upward forces combined with forward displacement of the trunk causes the head to rotate backward into extension which results in tension and buckling as the lower cervical segments extend and the upper cervical segments flex (Figure 1). The aforementioned forces cause the vertebra to abnormally rotate into extension causing extreme...
compression on and damage to the facet joints in particular. Hyperflexion produces tensile stress on the posterior cervical muscles and ligaments resulting in damage to these structures. 7,8

In addition to the acute effects of high impact collisions, there also appears to be chronic effects of repeated lower impact collisions. 10 Much of the biomechanical research has looked at the threshold to sustain concussion. Broglio et al looking at data from the head impact telemetry system (HITS) on college and high school athletes estimated the threshold for concussion to be approximately 959g when looking at linear acceleration and approximately 5500 rad/s/s for angular acceleration.11 The NFL has found that concussion in professional football players involves a mean impact velocity of 9.3 meters/sec or 20.8 mph. In comparison if a car hits pillar or structure the impact duration in less than 6 meters per second. 4

There are several theories as to the possible mechanism of concussion, however none are universally accepted. 12,13 The mechanism is felt to be similar in sports, falls and motor vehicle accidents. 9,4 Characteristics needed to sustain a concussion include rotational, angular, and/or lateral forces on the head, or transferred to the head by other parts of the body, this in turn causes rotation of the cerebral hemispheres around the upper brainstem (Figure 1). 14 Employing basic physics, Newton's second law (F = ma) applies to the linear acceleration component and outlines the basics of head impacts. Any impact to the head will transmit force to the brain. Furthermore, the magnitude of the impulse applied to the head is a product of the force applied during the impact times its duration. 11 As the magnitude of impact force (delivered by the striking player) increases, the greater the acceleration of the head in the struck player represented here by ‘m’. 11,5 When looking at rotational/angular acceleration situation the formula T = I x alpha applies.11,15 τ (Tourque) is a rotation-producing quantity, the moment of inertia I is a measure of an object's resistance to a change in rotational motion, and α is the angular acceleration. 11 To what extent each linear versus angular acceleration plays a role in concussion remains to be seen.

Another variable to consider is the transfer of momentum between the two athletes. The equation v1m1 + v2(m2 + m3) = m1v3 + m2v4 + m3v5 + momentum lost from energy transfer applies, with the left side = pre-collision, right side = post-collision conditions. V1m1 represent the velocity and respective mass of the athlete doing the hitting and v2(m2 + m3) represent the velocity of the athlete being hit (v2) and the effective mass of the body (m2) and head (m3). Following impact (i.e., the right side of the equation), the velocity of athlete one will decrease as momentum transfers to the struck athlete. Momentum is then transferred to the head and body of the striking athlete Principles of conservation of momentum only apply to rigid objects, with the momentum of a collision remaining constant as long as no other external forces apply.

An example of which would be the athlete’s head or body striking the turf as they are hit or hit by the other athlete. 11 Finally, where the athlete is hit also plays a factor. If an athlete is struck in the chest then more momentum is transferred to the body. However the athlete sustains a helmet to helmet hit, post impact velocity of the head is significantly higher as less momentum is transferred to the body.

Given that the body is not a rigid object, but a series of linked rigid objects the law of conservation of momentum does not fully apply, with force being equal to the effective mass times the acceleration (F=me(a), with (meffective =P(FiDt)/vi). Effective mass is dependent on the force being applied during impact, the time of the force application, and the speed at which the collision occurs. 11 As such effective mass can be increased or decreased based on how tightly coupled the rigid objects (i.e. neck and body) are at the time of impact. If the athlete being hit pre-contracts his neck the effective mass increases as the head and torso are more rigidly coupled. 11 Conversely, the athlete doing the hitting can deliver a greater force of impact by pre-contracting their neck musculature and creating a single rigid unit of their head and body (i.e. leading with their helmet). The resulting increase in transfer of momentum is a result of a change in the effective mass of the hitting athlete. As part of the NFL’s investigations on concussions, Viano et al. reported that increasing neck tension resulted in a 35% decline in concussion risk. The authors reported that neck contraction resulted in a lower injury risk because the head and torso were coupled. 15 There has been a recent push among concussion experts for studies looking at isometric and isokinetic muscle
exercises and cervical muscle strengthening as a way to prevent concussion especially in younger and adolescent athletes.

Unfortunately, increasing neck tension can also result in damage to the underlying cervical structures (i.e. facets, ligaments and muscles). Pre-contraction and flexion of the cervical musculature, as in a head first tackle results in increased axial loading. As a result the player initiating the hit will experience a disappearance of their normal cervical lordosis thus removing the energy absorbing component of the neck. Often times in anticipation of the hit the player receiving the hit will also contract their cervical muscles. In high impact sports such as football and ice hockey the player being hit often times will be looking down slightly i.e. at the puck or in the case of a wide receiver at the ball. Running backs also tend to instinctively lower their heads just prior to impact with the tackler. If contact is applied to the helmet, especially to the crown, the player’s cervical spine will experience a compressive load from the torso. As the helmets padding reaches its absorptive limits there is a second increase in compressive load on the cervical spine which is compressed between the head and torso. When the compressive load exceeds the cervical spines absorptive capabilities i.e. 3340 to 4450 N, soft tissue and hard tissue damage will occur. 

![Figure 1. Head and neck biomechanics in concussion. Angular and lateral forces (pictured on the left) result in rotation of the cerebral hemispheres around the upper brainstem. Blindside hits and body blows can result in hyperflexion and hyperextension of the cervical spine (pictured on the right).](image)

**Concussion Pathophysiology**

The pathophysiology of concussion (Figure 2) is poorly understood, what is known is based on rat percussion models and a few neuroimaging studies. There are three phases of concussion, the acute, intermediate and late phases. Post concussive deficits are based on temporary neuronal dysfunction and not cell death. Alterations in cerebral blood flow (CBF) also likely play a factor. The acute phase is characterized by metabolic and ion derangements, disruption of neural membranes and axonal stretching. The later results in abrupt and indiscriminant release of neurotransmitters and unchecked ion fluxes. Excitatory neurotransmitters such as NMDA and glutamate trigger neuronal depolarization with an efflux of potassium and influx of calcium. Increased extracellular calcium triggers further neuronal depolarization and further release of excitatory neurotransmitters and still further release of potassium into the extracellular space. Normally excessive extracellular calcium is taken up by surrounding glial cells;
however this mechanism is overcome in concussion. The massive excitation is followed by a wave of neuronal suppression (i.e. Spreading Depression). Early LOC, amnesia and other cognitive deficits may be a result of post traumatic Spreading Depression. Membrane pumps become activated in an effort to restore homeostasis which results in increase glucose utilization. Increased glycolysis leads to increased lactate production which results in neuronal dysfunction through processes such as metabolic acidosis, membrane damage, alterations in blood brain barrier permeability, and cerebral edema. The intermediate phase is characterized by uncoupling of glucose metabolism and cerebral blood flow. Calcium influx, mitochondrial dysfunction and delayed glucose hypo-metabolism also occur. There is a biphasic recovery of oxidative metabolism with a reduction on day 1, recovery by day 2, bottom out by day 5 and complete recovery by day 10. Calcium accumulation can persist for 2-4 days and the excess calcium is sequestered in mitochondria resulting in impaired metabolism and energy failure. Cerebral glucose use is diminished by 24 hours and can last up to 2-4 weeks post injury with the average recovery at 10 days. Cerebral glucose metabolism and oxidative metabolism correlate with the average concussion recovery time of 10 days. Intracellular Magnesium levels are immediately reduced and remain for up to 4 days, and magnesium level recovery is correlated with improvement in motor function. The hallmarks of the late phase are delayed cell death, persistent calcium accumulation and neurotransmitter alteration. Persistent elevations in intracellular calcium can lead to over activation of enzymes and free radical production resulting in cell death. Post concussion alterations in NMDA, adrenergic, cholinergic, and GABA neurotransmission can result in long term deficits in memory and cognition, even in the setting of minimal anatomic damage. Loss of forebrain cholinergic neurons can lead to learning and spatial memory deficits. Loss of GABA can result in disinhibition of hippocampal structures (i.e. easy distractibility) and increase the risk of seizures. Repeat Concussions during the post injury period, when the cell is most vulnerable can have catastrophic consequences. In the first 30 minutes when the system is stretched to its maximum, the brain may be unable to respond to a second stimulus induced increase in cerebral glucose metabolism. An increase in intracellular calcium after a second physiological stimulus can lead to protease activation and programmed cell death. Alterations in NMDA receptor composition can persist for one week post injury and a second injury in this period can lead to further impairment of excitatory neurotransmission. In addition to ion fluctuations and neurotransmitter dysfunction CBF is known to decrease immediately following both TBI and mTBI and can remain lowered for extended periods of time. It has been hypothesized that alterations in CO2 levels may play a significant role in the regulation of CBF. Following severe TBI cerebral auto-regulation is either lost or impaired and younger patients may have issues in cerebral reactivity which in itself is likely mediation by alterations in the brains metabolic activity. Furthermore, cerebral oxygenation is significantly reduced (up to a 35% decrease) on day one following mTBI, and appears to be unresolved up to 7 days following the injury. Finally, it has been proposed that there may be neuro-autonomic cardiovascular dysregulation, i.e. an uncoupling between the autonomic nervous system and the cardiovascular system, following mTBI, which in turn could result in alterations in CBF.
Figure 2. Concussion Pathophysiology (Giza and Hovda).

Functional Cervical Anatomy

There are a number of anatomic sites in the cervical spine including the facet joints, spinal ligaments, intervertebral discs, vertebral arteries, dorsal root ganglia, peripheral nerves and neck muscles that could be damaged or compromised when an athlete sustains a concussion. These sites could then act as a possible trigger or be involved in the triggering and even chronicity of post traumatic headache.

Cervical Kinetics

Normal cervical range of motion is approximately 80-90 degrees in flexion, 70 degrees in extension, 20 to 45 degrees in side bending and 90 degrees in rotation. Movement of the cervical spine is complex and multi-planer. For example motion in one plane of one segment of the cervical spine usually results in complementary (and sometimes opposite) motion of another segment. In addition, movement of the head (which occurs in all concussions) is not a reliable indicator of spinal injury. However and as stated above, the interaction of the head and upper cervical spine is essential in understanding mechanism of injury in
concussion. The weight of the head is transferred to the cervical spine through the lateral atlanto-axial articulations of C2 (i.e. the axis). C1 (atlas) articulates with the occipital condyles, acting as a cradle. Its primary motions are flexion and extension, rotation and lateral flexion are not possible between the above structures.  

The odontoid process of C2 extends into and rests within the facet of C1 and allows the atlanto-occipital complex (A-O) (i.e. C1, C2 and occiput) to rotate from side to side as one unit (this movement is accompanied by extension and lateral flexion of the C spine). Rotation of the A-O complex is aided by the stabilizing properties of the upper cervical ligaments (see below). Furthermore, cervical spine flexion results in extension of C1 and cervical spine extension results in flexion of C1. Finally, the remaining cervical vertebrae (C3-7) are resistant to lateral flexion. During concussion the normal kinetics of the cervical spine are often compromised resulting in injury to underlying cervical structures.

**Facets**

Each cervical vertebrae (C2-7) contains two facet joints enclosed by a thin, loose ligament known as the facet capsule (Figure 3). The capsule is a loose structure which tends to follow the movements of the bony structures it surrounds. The facets contain mechanoreceptors and unmyelinated nociceptors and receive their innervation from dorsal rami from the two levels surrounding the joint. The capsule contains Aδ- and C-fibers, along with nociceptors reactive for substance P and calcitonin gene-related peptide (CGRP). Aδ fibers (mechanoreceptors) are small myelinated fibers which are involved in hyperalgesia and quick intense acute pain. C fibers (nociceptors) are small unmyelinated fibers involved in throbbing, burning, and chronic pain. Stimulation of the slower C fibers results in a "wind up" of nociceptive activity which can contribute to spinal sensitization. CGRP and substance P are neuropeptides which are neurotransmitters and nociceptive neuromodulators and can play a role in pain modulation as well. Injury to the facets is via two mechanisms; from excessive rotation of the cervical vertebrae resulting in pinning of the synovial fluid and/or excessive strain on the capsule (i.e. via cervical hyperflexion or hyperextension), resulting in activation of afferent pain fibers. Damage to C1-2, C2-3, C3-4 can result in referred pain to the vertex and frontal regions, neck and occiput, whereas damage to C1-2 and C2-3 can result in referred pain to the orbit.

![Figure 3. Cervical facet joint and capsule.](image-url)
Ligaments

Ligaments have a number of functions including; joining/stabilizing cervical vertebrae, they provide joint position sense and absorb energy during high-velocity, high impact movements of the spine. 1, 20 The cervical vertebrae are joined by multiple ligaments including the anterior and posterior longitudinal (thin sheets of tissue that span the anterior and posterior portions of the vertebral bodies), capsular (encase the facets), interspinous (joins adjacent spinous processes and are not present in all adults), supraspinous ligaments and ligamentum flavum (joins adjacent laminae). The upper cervical ligaments i.e. Alar and Transverse ligaments (Figure 4) provide significant stability of the two upper cervical vertebrae as they lack intervertebral discs. 1, 20 The alar ligaments prevent excessive rotation and lateral flexion and the transverse ligament prevents anterior dislocation of atlas on axis during flexion. 24 Due to their high collagen and low elastin content they are easily ruptured at low strains and high speed elongation, especially with head rotation, both of which can occur when a player sustains a concussion. 1, 20 The resulting upper cervical instability can result in suboccipital muscle spasm and pinching on the facets.

![Figure 4. Upper cervical ligaments.](image)

Vertebral Arteries

The vertebral arteries enter the spine at the C6 transverse processes bilaterally ascending through the transverse foramen of each cervical vertebra, exiting at C1, where they then travel along the C1 posterior arch and enter the foramen magnum of the skull (Figure 5). 20 The arteries can be injured with over extension and/or over axial rotation of the upper cervical spine. The mechanism injury appears to be either arterial stretching or pitting. The resultant decrease in vertebral artery blood flow can cause hypo-perfusion of brainstem structures leading to symptoms such as headache, disequilibrium, blurred vision, tinnitus, and vertigo. 30
Dorsal Root Ganglia

The dorsal root ganglia are relay centers for the major afferent pain pathways and contain cell bodies of peripheral sensory nerves. After exiting spinal canal from the dorsal horns dorsal nerve roots gives rise to the dorsal root ganglion which sends projections to dorsal rami which in turn contribute to peripheral nerves including the greater and lesser occipital nerves (see figure 6). The roots of the upper four cervical nerves are small, while those of the lower four are large. The dorsal roots are on average about three times larger than the ventral roots, except for the dorsal root of C1 which is smaller. The roots of the first and second cervical nerves are short, and run nearly horizontally to their points of exit from the vertebral canal. The second to the eighth cervical nerves become progressively longer i.e. C8 is much longer than C2 and positioned downward. The C2 DRG is the only ganglion located outside the dura and is located between the posterior arch of the atlas and lamina of C2, i.e. posterior and medial to the atlanto-occipital joint where it fills approximately 75% of the space. It contains cell bodies that innervate a large portion of the neck and scalp. It is vulnerable to compression (especially with neck hyperextension) and can cause pain similar to that associated with the occipital nerve. (See below) In addition, the nerve endings of dorsal root ganglion neurons have a variety of sensory receptors that are activated by mechanical, thermal, chemical, and noxious stimuli and are quite sensitive to mechanical loading.
Compression of the dorsal root ganglion by a mechanical stimulus lowers the voltage threshold needed to evoke a response and causes action potentials to be fired. This firing may even persist after the removal of the stimulus. The dorsal roots which lack the thick epineural sheath of peripheral nerves are also quite sensitive to injury. For example, during extreme neck motions the neural foramina change shape and decrease their diameter and compress the nerve root within the intervertebral foramen.

Figure 6. Dorsal and ventral horns, dorsal root and dorsal root ganglia.

**Spinal and Peripheral Nerves**

There are eight cervical spinal nerves which form immediately after the ganglion and emerge through the intervertebral foramen. Each spinal nerve contains sympathetic and somatic fibers, along with fibers connecting these systems with each other. Somatic fibers contain efferent and afferent inputs. The efferent fibers convey impulses to the voluntary muscles, and are continuous from their origin to their peripheral distribution. The afferent fibers convey impressions inward from the skin, etc., and originate in the unipolar nerve cells of the spinal ganglia. Sympathetic fibers also contain afferent and efferent connections with blood vessels and visceral structures. After emerging from the intervertebral foramen, each spinal nerve gives off a small meningeal branch which reenters the vertebral canal through the intervertebral foramen and supplies the vertebrae and their ligaments. The spinal nerve then splits into a posterior or dorsal, and anterior or ventral division (Figure 7).
The posterior division of the first cervical or suboccipital nerve emerges above the posterior arch of the atlas and beneath the vertebral artery. It enters the suboccipital triangle and supplies the following muscles; Rectus capitis posterior major, Obliqui superior and inferior; and gives branches to the Rectus capitis posterior minor and the Semispinalis capitis. The nerve will occasionally give off a cutaneous branch which accompanies the occipital artery to the scalp, and communicates with the greater and lesser occipital nerves (Figure 8). The C2 spinal nerve emerges between the posterior arch of the atlas and the lamina of the axis. It branches into dorsal and ventral rami just posterior to the atlanto-occipital joint (A-A joint). The dorsal rami of C2 then loops around the Obliquus Capitis Inferior muscle where it gives off a branch to supply the muscle. The dorsal rami then divides into medial, lateral, superior communicating and inferior communicating branches. The medial branch forms the greater occipital nerve (GON) (see below). The lateral branch supplies motor input to the splenius capitis, longissimus capitis, and semispinalis capitis, and is often joined by the corresponding branch of the third cervical nerve. The third cervical nerve branches into dorsal and ventral rami within the intravertebral foramen. The dorsal rami of C3 divides into the lateral branch, medial branch and a communicating branch with the dorsal rami of C2. The lateral branch supplies the longissimus, splenius and semispinalis muscles. The medial branch is also called the third occipital nerve, it pierces the semispinalis, splenius and trapezius muscles and then provides sensory innervation along with the GON to the suboccipital region and ends in the skin of the lower part of the back of the head (Figure 8). The third occipital nerve also supplies the C2 and C3 vertebral region. The nerve can be compressed after trauma by the suboccipital muscles and trapezius where it is felt to be a source of headache. Furthermore, injury to any of the structures of the upper cervical spine can result in headaches referred to the distribution of the upper three cervical nerves. It can also cause headache which is in a pattern of the first division of the trigeminal nerve as central process of the upper three cervical sensory nerves enter the spinal cord and converge on the trigeminal cervical nucleus in the cord which has projections to the trigeminal nerve (see below).
The posterior divisions of the lower five cervical nerves divide into medial and lateral branches. C4 and C5 also divide into superficial and deep branches. The superficial branches of the fourth and fifth rami supply the cervical portions of the splenius and semispinalis and the skin on the back of the neck. Deep branches supply muscles attached to the spinous process one level lower i.e C5 supplies C4. The lateral branches of the lower five nerves supply the iliocostalis cervicis, Longissimus cervicis, and Longissimus capitis. The ventral rami innervate the anterior muscles of the spine (i.e. longus capitis and rectus capitis), supply sensory innervation to the vertebral bodies and go on to form the cervical and brachial plexuses. The A-A joint and atlanto-occipital joints are innervated by the C1 and C2 ventral rami. Ventral rami are easily damaged by flexion extension injuries of the neck and therefore are a potential source of neck pain.

Figure 8. Upper cervical region including the suboccipital muscles, greater occipital and third occipital nerves.

The greater occipital nerve originates from the medial branch of the dorsal ramus of the C2 spinal nerve and may intercommunicate with branches from the dorsal branch of the C3 spinal nerve. A number of studies have attempted to trace the course of the GON. Bovium et al demonstrated that the nerve pierced the semispinalis most often, followed by the trapezius and rarely the inferior oblique. It is possible that after cervical trauma any one or a combination of these muscular investments could serve as a source of compression or irritation of the nerve. Guyron et al found the nerve rarely pierced the trapezius which was an unlikely site of compression. The only consistent transmuscular course was in the region of the semispinalis, which they felt was the most likely point of compression or irritation. After traveling through the semispinalis muscle, the nerve runs with the occipital artery, which usually lies just medial to this nerve. The GON terminates in the subcutaneous tissue above the superior nuchal line where it
provides cutaneous innervation to most of the posterior scalp (Figure 8). The nerve can also be damaged by direct trauma to the occiput and can be irritated by pulsations of the occipital artery which itself can be damaged by cervical trauma.

The lesser occipital nerve (LON) originates from the ventral rami of spinal nerves C2 and C3. It pierces the deep fascia and runs superiorly above the occiput to supply the skin of this area (see figure 8). Pain in the region supplied by the nerve often manifests as cervicogenic headaches. The nerve can also be damaged by direct trauma to the occiput and can be irritated by pulsations of the occipital artery which itself can be damaged by cervical trauma.

The recurrent meningeal nerves also originate from the ventral rami and course medially through the intraventricular foramen usually supplying somatic afferent input (including nociceptive fibers) to the posterior longitudinal ligament, uncovertebral joints and spinal dura matter. The upper cervical (C1-3) recurrent meningeal nerves have large branches and ascend into the posterior cranial fossa supplying the A-A joint and components of the cruciform and alar ligaments. After entering the posterior cranial fossa they supply the cranial dura matter. The recurrent meningeal nerves play a role in referred pain/occipital headache from the upper cervical ligaments and AA joints.

Cervical Muscles

The cervical muscles (see figure 9) may play both a direct and indirect role in modulating pain. The superficial muscles i.e. sternocleidomastoid or trapezius attach to the skull, shoulder girdle, and ligamentum nuchae but do not attach directly to the cervical vertebrae. Deeper muscles, such as splenius, semispinalis, and longissimus attach directly to the facet and can indirectly affect other anatomical structures. The scalenes, and longus, attach on multiple cervical vertebrae and the deepest neck muscles, the multifidus muscles, insert directly on the facet capsule of cervical vertebrae and can be affected by injury to the capsular ligaments. When an athlete sustains a head shot or body shot the anterior and posterior neck muscles can experience active lengthening causing sprain/strain injury. The cervical muscles also tend to have a complex architecture (i.e. tendons and spindles) and injury can result in significant pain. Activation results in increased intervertebral compression and altered intervertebral physiology. The cervical muscles are oriented primarily vertically and activation produces axial compression of the cervical spine, resulting in increased loads on the discs and facet joints. Spasm of the cervical muscles may be a protective response to trauma and, the interaction between muscles and the nervous system may result in chronic pain. Patients with chronic pain demonstrate altered neuromuscular patterns and pain and increased muscle activity may reinforce one another. Finally, nociceptive inputs from the cervical muscles can trigger migraine in susceptible individuals.
Post Traumatic Headache and Migraine Pathophysiology

Post traumatic headache is by far and away the most common symptom of sports related concussion with an incidence of approximately ninety percent. Although there are no specific studies on headache phenotype in athletes, when the International Headache Society classification criteria for primary headache disorders is used to characterize civilian PTH migraine or probable migraine is the most common headache phenotype.

Migraine pathophysiology has evolved considerably since Wolff proposed the “vascular theory” in the 1940’s. Moskowitz suggests that migraine represents a highly choreographed interaction between major inputs from both the peripheral and central nervous systems in genetically susceptible individuals. However, the specific mechanisms underlying the development of migraine remain to be fully elucidated.

Current consensus is the headache phase of migraine begins with the activation and sensitization of trigeminovascular meningeal nociceptors, which lead to sequential activation (and sensitization) of second and third-order trigeminovascular neurons. Activation and sensitization in turn activate different areas of the brainstem and forebrain, resulting in pain and other accompanying migrainous symptoms.
pathophysiology is similar to concussion pathophysiology as both conditions render the cerebral cortex hyper-excitatory through abnormal excitatory/inhibitory balance i.e. Cortical Spreading Depression (CSD) or similar process. There is a large body of evidence that supports the role of CSD as a key event in migraine with aura, however further research is needed to determine if CSD-like events occur in migraine without aura. Recently the concept of the "hyper-excitable interictal brain" has been proposed by Moskowitz and others. According to the theory the migraineurs cortex is in a hyper-excitable state between attacks. This could result from either enhanced excitation or reduced inhibition, is hypo-excitable, and/or has a lower pre-activation threshold. Recent transcranial magnetic stimulation (TMS) studies point to an imbalance in excitatory and inhibitory neurotransmission. Possible mechanisms include alterations in circuits that maintain excitatory and inhibitory balance, and/or alterations of cortical neuro-modulation by serotonergic, noradrenergic or cholinergic inputs originating in the brainstem, both resulting facilitation and propagation of CSD. The later concept provides a possible direct link to the physiology of concussion as the late phase of concussion also involves abnormalities in cholinergic, adrenergic, as well as NMDA and GABA neurotransmission. Moreover, familial hemiplegic migraine (FMH) mouse models provide further evidence for the hyper-excitatory brain concept as well as links to possible concussion pathophysiology. FMH is a heterogeneous disorder involving mutations in genes that encode for neuronal voltage gated P/Q calcium channels (Cav2.1), sodium channels and sodium-potassium ATPase. In certain knockout mice excitatory neurotransmission was enhanced and was thought to result from increased glutamate release at pyramidal cell synapses as a result of increased calcium influx. Interestingly this phenomenon also occurs in the concussed brain and alterations in calcium are seen throughout the concussion process. Whether or not migraine is truly a disorder of glutamatergic neurotransmission and/or excitatory inhibitory imbalance remains to be ascertained. It's possible however that certain migraine triggers i.e. prolonged sensory stimulation or even trauma could disrupt the excitatory/inhibitory balance (possibly through increases in extracellular potassium) resulting in the initiation of CSD.

The headache phase depends on the activation and sensitization of trigeminal sensory afferents that innervate cranial tissues, in particular, the meninges and their large blood vessels. The origin of nociception i.e. from pial, dural, or extracranial structure remains unclear. Recent evidence suggests that vasodilatation may not be necessary to trigger a migraine attack. The innervation of intracranial vasculature and the meninges is via nonmyelinated (C-fibers) and thinly myelinated (Ad fibers) axons containing vasoactive neuropeptides such as substance P (SP) and calcitonin gene-related peptide (CGRP). These fibers originate in the trigeminal ganglion and reach the dura primarily through the ophthalmic branch of the trigeminal nerve (V1), with additional innervation provided by neurons in the upper cervical dorsal root ganglia. Central projections from trigeminal sensory afferents terminate in the so-called trigeminocervical complex (TCC) comprising the C1 and C2 dorsal horns of the cervical spinal cord and the caudal division of the spinal trigeminal nucleus (TNC). The spinal trigeminal nucleus also receives input from adjacent skin and muscles which likely contribute to referred pain. Almost all dural afferents are mechanoreceptors which are sensitive to changes in vascular diameter and which may provide a mechanism for the throbbing character of migraine pain. As is the case with other pain syndromes the pathophysiology of migraine involves both ascending and descending pathways (Figures 10 and 11). The trigeminal nucleus complex has ascending connections with the brainstem, thalamus and hypothalamus which may be related to migraine symptoms such as fatigue, loss of appetite, memory loss, irritability, and certain autonomic symptoms, interestingly many are also involved in concussion. Projections from the ventral posterior medial nucleus (VPM) of the thalamus project to primary secondary somatosensory and insula cortices which are involved in location, quality and intensity of pain. Other thalamic i.e. dural sensitive Po neurons project to visual, auditory and partial association cortices, contributing to associated migraine symptoms such as visual and memory loss, motor and limbic abnormalities. In addition, photosensitivty appears to be mediated at various levels of the thalamus.
The TCC also receives descending (inhibitory) input from the cortex, brainstem and hypothalamus. There is increasing evidence that alterations in cortical excitability play a significant role in migraine pathophysiology. There are direct portico-trigeminal projections from the contralateral primary somatosensory and insula cortices to the TCC. The periventricular hypothalamic nucleus (PVN) projects to the TCC and the midbrain periaqueductal gray sends projects to both the TCC and rostral ventral medulla. The PAG could either enhance or inhibit the activity of neurons that facilitate pain or suppress activity of neurons that inhibit pain. Whereas the PVN may act to modulate pain and contribute to the development of central sensitization (see below).
hyper-excitability of the trigeminovascular pathways. Another more plausible migraine trigger and one that directly relates to concussion is cortical spreading depression (CSD). CSD is a slowly propagating wave of neuronal and glial depolarization followed by a prolonged inhibition of cortical activity. CSD plays a significant role in migraine with aura in genetically susceptible individuals, and many have proposed it as a possible trigger of migraine without aura. In a typical migraine patient CSD arises spontaneously in response to specific triggers that overwhelm the regulatory mechanisms controlling cortical extracellular potassium. It is known that intense electrophysiological activity such as that seen in epilepsy can activate overlying meningeal nociceptors and generate ipsilateral headache. There is now evidence that cortical spreading depression (CSD) can trigger headache by activating dural nociceptors and central trigeminovascular neurons in the TCC. With that said the concept is still not widely accepted and remains controversial. As is the case in the physiology of concussion CSD is triggered by increases in extracellular potassium. In migraine this is felt to be mediated by nociceptors (peptide) with axons extending to the pia. The resultant wave leads to the release of nitric oxide, glutamate and serotonin which in turn through somewhat poorly understood mechanisms activate meningeal afferents and release of inflammatory neuropeptides such as CGRP and Substance P which promote neurogenic inflammation in the dura resulting in sustained activation and sensitization of meningeal nociceptors. CSD can also result in gene activation in the TCC, as well as dilatation and increased blood flow in the middle meningeal artery which may act as a “driver” of headache pain. The real controversy remains as to whether CSD can actually trigger the perception of headache. This concept is supported by the observation that electrical activity seen in temporal lobe epilepsy is sufficient to activate meningeal nociceptors resulting in ipsilateral headache, and in rat studies where the electrical stimulation threshold for induction of CSD increases after treatment with migraine preventative medications. Finally, familial hemiplegic migraine knockin mice show lower electrical stimulation thresholds for CSD providing support that CSD as a potential migraine trigger.

The maintenance of a migraine attack appears to involve both peripheral and central sensitization. Peripheral sensitization mediates the throbbing perception of headache and involves an increase in sensitivity to noxious or non-noxious sensory stimuli caused by hyper responsiveness within primary afferent fibers. It appears to be mediated by meningeal inflammation caused by the release of proinflammatory neuropeptides such as CGRP and Substance P and resulting extravasation of plasma proteins and mast cells and ultimately the release of cytokines i.e. neurogenic inflammation (NI). The maintenance of peripheral sensitization is not fully understood however cortical spreading depression has been proposed as being a major factor. This raises the question of whether the biomechanics of concussion could cause peripheral sensitization via dural stretching or changes in dural blood flow? Central sensitization is the increased sensitivity to noxious or non-noxious sensory stimulation (aka allodynia) and is caused by hyper responsiveness of neurons in the TCC and thalamus. It appears to be mediated by activation of the descending pathways, more specifically the PAG and nucleus cuneiformis appear to be involved in the maintenance of central sensitization. Approximately two thirds of migraine patients experience allodynia in the periorbital and extracephalic regions. Facial allodynia likely results from sensitization of neurons in the TCC via meningeal nociceptors, whereas extracephalic allodynia reflects sensitization of thalamic neurons receiving input from the cranial meninges and extracephalic skin. Moreover, the initiation of central sensitization depends on afferent input from previously sensitized meningeal nociceptors and once established central sensitization becomes independent of afferent input.
Figure 11. Descending migraine pathways
Discussion

The biomechanics of sports related concussion are both directly and indirectly related to the cervical spine and its associated structures. In addition to the lateral and rotational forces the player experiences on their head, they also experience axial loading on the spine itself as well as flexion, extension and rotation of the neck which is almost identical to what is seen in whiplash injuries. This results in damage to underlying structures including the facets, ligaments, dorsal root ganglion, cervical muscles, spinal/peripheral nerves and stretching of the vertebral artery. All of the aforementioned cervical structures can play a role in triggering and/or maintaining migraine headache. Migraine and sports concussion are linked by the concept of a hyper-excitible brain. In addition, they share a number of common pathophysiological processes including abnormalities in cholinergic adrenergic and GABA neurotransmission, alterations in cortical blood flow, calcium and potassium ion dysfunction, release of excitatory neurotransmitters such as glutamate and possibly CSD. Despite their underlying similarities there are still questions that need to be answered including: How does post traumatic migraine develop after concussion? And what is the specific role of the cervical spine in triggering, maintaining and chronification of the athlete’s headache?

It is unlikely that a single mechanism is involved and multiple interrelated processes are likely occurring simultaneously (Figure 12). After sustaining a blow to the head or body a cascade of events including brain activation and cervical dysfunction are triggered. Focusing on the later, injury to the upper cervical structures could result in sensitization of the TNC and/or referred pain to the head. Damage to the facets (especially C1-4) from capsular strain and or pinning of the synovial fluid could result in activation of afferent pain fibers via the corresponding dorsal rami with referred pain to the occiput and orbit. Activation of the dorsal rami of C2-4 could also result in GON activation and subsequent activation of the TNC. The Alar and Transverse ligaments can stretch or even rupture causing instability of the atlas/axis, further pinning of the facets (and subsequent activation of mechanoreceptors and nociceptors) and sub-occipital muscles spam which can indirectly trigger migraine (see below). Arterial stretching or pitting of the vertebral arteries can result in decreased blood flow and brainstem hypo-perfusion which can directly activate the TNC, RMV, PAG, thalamus, and hypothalamus (i.e. ascending fibers) and/or deactivate brainstem structures involved in the descending pathways. Compression of the DRG (especially C2) can result in activate afferent pain fibers that project to the neck and scalp as well as spinal and peripheral nerves, especially the third occipital and GON which play a direct role in transmitting migraine pain (see below). Furthermore, there is likely lowering of the voltage threshold resulting in prolonged and persistent hyper-sensitization of the DRG which in turn can contribute to the development of chronic cervical pain and chronic post traumatic headache.
Figure 12. Possible mechanisms of peripheral and central activation of post traumatic migraine in concussed athletes.

Perhaps more important are the direct and indirect effects on the upper spinal nerves especially C2 and the GON which receive a high convergence of input from the deep cervical muscles and skin and mediate afferent flow from the deep paraspinal neck muscles zygapophyseal joints and ligaments. Nociceptive afferents from the C1, 2 and 3 spinal and the GON converge onto second-order neurons that also receive afferents from adjacent cervical nerves and from the first division of the trigeminal nerve via the trigeminal nerve spinal tract (Figure 13). Furthermore, trigeminocervical neurones can also receive convergent input from the supratentorial dura mater and contralateral GON. In a recent study by Johnson et al including six patients diagnosed with either migraine with or without aura or chronic migraine, radiofrequency stimulation of C1 spinal nerve evoked peri-orbital and frontal pain, whereas stimulation of the C2 nerve evoked pain in an occipital and parietal distribution and stimulation of the C3 nerve evoked pain in occipital, peri-auricular, submental, and/or lateral cervical distributions. The authors concluded that C1 may play a role in migraine possibly secondary to activation of the TNC. The study also provided further evidence for the convergence of both trigeminal and cervical nerves on the TCC. The concussed athlete can experience damage and/or activation (i.e. secondary to biomechanical forces on the cervical spine) to the upper spinal nerves. For example damage/irritation to the C1,C2 and C3 cervical nerves result from sub-occipital muscle spasm (i.e. obiquis capitis inferior, splenius capitis, longissiumus capitis and semispinalis capitis muscles) or via directed compression from the upper cervical bony structures (i.e. A-O joint and foramen). The GON and to some extent the lesser occipital nerve, can be directly compressed by trauma (i.e. helmet to helmet) or via irritation or compression from the semispinalis muscle and/or occipital
artery pulsations (GON). Activation of either the GON or upper spinal nerve afferents can trigger migraine through their projections to the TCC (see above) and can result in referred pain to the cervical, occipital and supraorbital regions. Blockade and neurostimulation of the GON and supraorbital nerves and injection of onabotulinum toxin A in concussed athletes (unpublished data and anecdotal experience) with both acute and chronic post traumatic migraine headaches has resulted in both temporary and even permanent resolution of their headaches, further supporting a major role of the cervical spine and more specifically the GON in post-traumatic migraine headache. Finally, damage/irritation to either the third occipital nerve (via compression/irritation from the trapezius and splenius muscles) or recurrent meningeal nerve (at the level of the intravertebral foramen) could result in referred pain to the occiput and in theory could also activate their respective upper spinal nerves and subsequently the TCC. Finally, active lengthening and resultant sprain/strain and spasm of the cervical muscles can trigger migraine and along with localized cervical pain. The hypothesis is supported by a recent study by Le Doare et al who demonstrated activation of trigeminocervical neurons in the TCC after afferent stimulation of the cervical muscles in a rat model.  

![Diagram of afferent inputs from the cervical spine nerves and trigeminal nerve to the trigeminal cervical complex.](image)

In addition to peripheral triggers from cervical dysfunction, direct activation of cortical and brainstem structures is another plausible mechanism for triggering post traumatic migraine headache in concussed athletes (Figure 12). Alterations in cerebral blood flow (i.e. meningeal arteries) and stretching of meningeal arteries (secondary to lateral and rotational forces) can result in activation of meningeal mechanoreceptors and nociceptors respectively, which in turn can trigger sequential activation (and sensitization) of second and third-order trigeminovascular neurons. Significant damage to the meningeal arteries in theory could result in the development of peripheral sensitization and prolongation/chronification of the athlete’s
headache. Rotational forces also cause the cerebrum to rotate around the upper brainstem which could result in microscopic damage/dysfunction to structures in the upper brainstem and diencephalon. Direct activation of neurons in the PAG, thalamus, and hypothalamus could result and can trigger migraine, especially in genetically susceptible individuals. Furthermore, damage/dysfunction of the PAG and paraventricular hypothalamic nucleus (PVN) could deactivate descending inhibition of the RVM and subsequently TCC resulting in post-traumatic migraine headache. Prolonged activation/deactivation could result in central sensitization and the development of chronic post traumatic migraine. Employing controlled cortical impact in rats Elliott and Oshinsky were able to support the role of central sensitization in the development of chronic post traumatic headache. Their results demonstrated persistent bilateral peri-orbital mechanical hypersensitivity that intensified over time, and which correlated with persistent increases in brainstem CGRP. Increased glial activation persisting for up to 14 days (which is also the average concussion recovery time) was also found, with increases in CGRP actually outlasting glial activation. The latter is suggestive of central sensitization and headache chronification.  

Immediate post concussive ion fluxes (Ca++ and K+) and resultant activation of excitatory neurotransmission i.e. CSD as well as late phase abnormalities of cholinergic, adrenergic, NMDA and GABA neurotransmission could trigger headache by activating dural nociceptors and central trigeminovascular neurons in the TCC. Central activation of the insula and somatosensory cortex from the aforementioned process is another possible trigger. The hypothesis that excitatory neurotransmitters play a role in post-traumatic headache (PTH) is supported by a study by Goryunova et al, who looked at Glutamate receptor autoantibodies (at 6 and12 months) in children with PTH, mTBI and TBI. They hypothesized that antibodies to AMPA and NMDA glutamate receptors play a role in the long term outcome of mTBI and chronic PTH. Their data showed increased antibodies to NMDA in a single concussion and PTH, and increased antibodies to AMPA in repeated concussions and PTH. They concluded that antibodies to AMPA and NMDA glutamate receptors play a role in the long term outcome of mTBI and chronic PTH.  

It is not unreasonable to hypothesize that the cervicogenic, vascular, mechanical and electrophysiological process described above are more likely to trigger post traumatic migraine in genetically susceptible individuals i.e. those with a prior history of migraine or family history of migraine. Although there are very few studies pertaining to headache in concussed athletes (Conidi, poster International Headache Society meeting 2011), recent evidence suggests that individuals with a prior history of migraine and early post traumatic headache have a higher risk for prolonged post concussion symptomatology. Future studies focusing concussed athletes with acute and chronic post traumatic headache are desperately needed to further delineate the underlying cervical mechanisms and neurophysiological processes.

References


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