

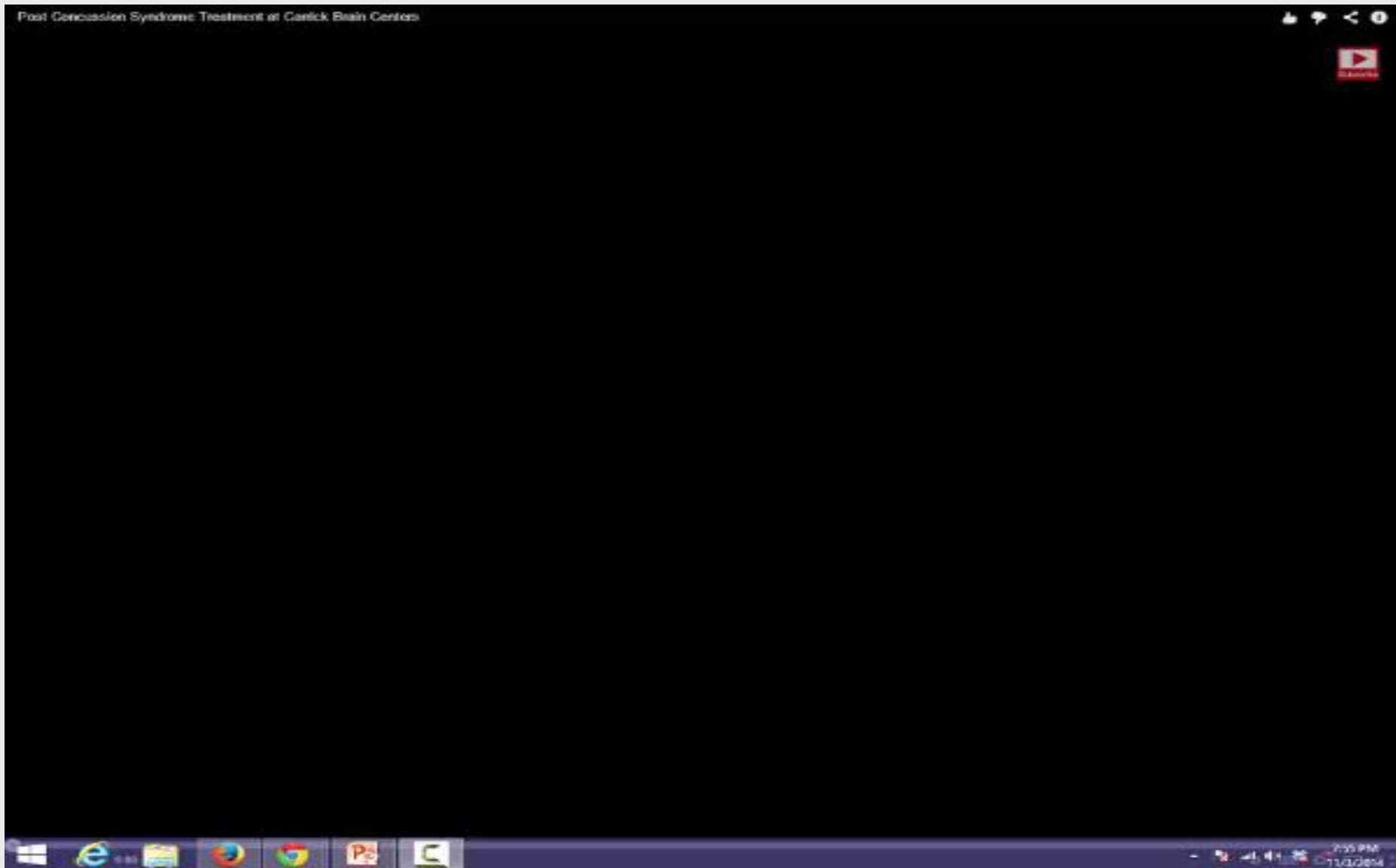


Dr David Jay Traster DC
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CONCUSSION



Carrick Brain Centers Concussion Rehabilitation



Dr Carrick on ABC Nightline



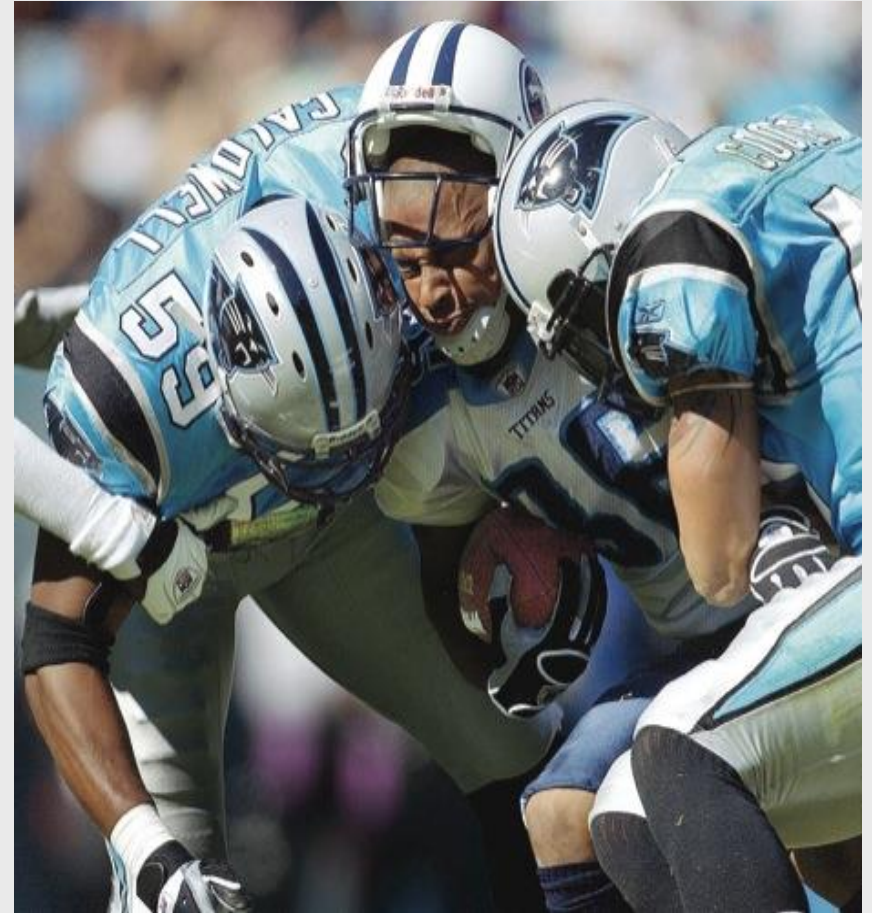
Concussion (Mild Traumatic Brain Injury) and the Team Physician: A Consensus Statement. *Medicine & Science in Sports & Exercise*. 2011.

- Concussion or mild traumatic brain injury (MTBI) is a pathophysiological process affecting the brain induced by direct or indirect biomechanical forces.
- Concussions occur as a result of imparted linear and rotational accelerations to the brain. Because of modifying factors, there is currently no known threshold for concussive injury.



The Epidemiology of Sport-Related Concussion. *Clinical Sports Medicine*. Jan 2011.

- 38 million children and adolescents participate in organized sports in the United States.
- 170 million adults participate in physical activities, including sports.
- 1.6 to 3.8 million concussions occur in sports and recreational activities annually. These numbers are vastly underestimated due to underreporting.



Concussions Among United States High School and Collegiate Athletes. *Journal of Athletic Training*. 2007.

- Sports are second only to motor vehicle crashes as the leading cause of traumatic brain injury among people aged 15 to 24 years.
- Participation in high school and collegiate sports continues to increase, with more than 7 million high school students participating in 2005–2006 and almost 385,000 collegiate students participating in 2004–2005.
- In the 9 high school sports studied over the course of the 2005–2006 school year, 4,431 injuries were reported, 396 (8.9%) of which were concussions. This included 137 concussions (34.6%) that occurred in practice and 259 (65.4%) that occurred during competition.
- The weighted national estimate for the number of concussions sustained in all sports was 135,901. Based on the national estimate, the majority of concussions resulted from participation in football (40.5%, n = 55,007), followed by girls' soccer (21.5%, n = 29,167), boys' soccer (15.4%, n = 20,929), and girls' basketball (9.5%, n = 12,923).

Table 2. National Estimates of Activity Associated With Concussion Injury by Sport, High School Sports-Related Injury Surveillance Study, United States, 2005–2006 School Year

Sport*	Activity	Proportion	
Football		(n = 55 007)**	
	Blocking drill	2225	4.1%
	General play	1866	3.4%
	Kick-off coverage/return	3238	5.9%
	Passing play (offense/defense)	8928	16.3%
	Punt coverage/return	1497	2.7%
	Running play (offense/defense)	30 418	55.4%
	Tackling drill	2833	5.2%
Wrestling	Other	3895	7.1%
		(n = 5935)	
	Conditioning	608	10.2%
	Escape	377	6.4%
	Fall	200	3.4%
	Riding	153	2.6%
	Sparring	1297	21.9%
	Takedown	2526	42.6%
Soccer	Other	774	13.0%
		Boys (n = 20 929)**	Girls (n = 29 167)
	Attempting a slide tackle	959 4.6%	0
	Ball handling/dribbling	0	1760 6.0%
	Blocking shot	673 3.2%	0
	Chasing loose ball	286 1.4%	3423 11.7%
	Defending	780 3.7%	4408 15.1%
	General play/other	2203 10.6%	2475 8.5%
	Goaltending	4268 20.5%	2440 8.4%
	Heading ball	8433 40.5%	1014 436.7%
	Receiving a slide tackle	0	1482 5.1%
	Receiving pass	2180 10.5%	864 3.0%
	Other	1045 5.0%	1601 5.5%
Basketball		Boys (n = 3823)	Girls (n = 12 923)
	Ball handling/dribbling	399 10.4%	2456 19.0%
	Chasing loose ball	994 26.0%	1367 10.6%
	Defending	513 13.4%	2872 22.2%
	General play/other	0	226 1.8%
	Passing	0	257 2.0%
	Rebounding	1164 30.5%	2151 16.6%
	Receiving pass	259 6.8%	147 1.1%
	Screening	0	690 5.3%
	Shooting	494 12.9%	2069 16.0%
	Other	0	688 5.3%
Baseball and softball		Baseball (n = 1991)	Softball (n = 3558)
	Batting	1008 50.6%	246 6.9%
	Catching	171 8.6%	1057 29.7%
	Fielding	100 5.0%	398 11.2%
	General play	171 8.6%	104 2.9%
	Pitching	100 5.0%	246 6.9%
	Running bases	0	152 4.3%
	Other	441 22.1%	1355 38.1%

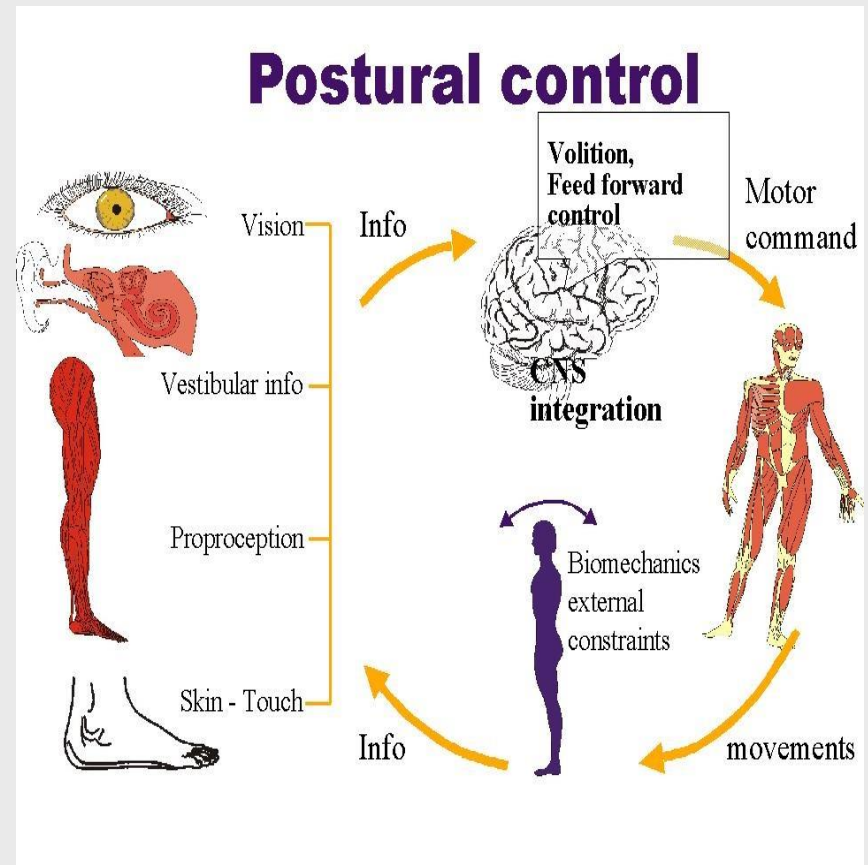
The Epidemiology of Sport-Related Concussion. *Clinical Sports Medicine*. 2011.

- The rate of concussion has been increasing steadily over the past two decades. This trend is likely due to improvement in the detection of concussion, but may also reflect an increase in the true number of concussive impacts occurring.
- As athletes get bigger, stronger, and faster, it is logical that the forces associated with their collisions would also increase in magnitude.
- It is important to realize that there is currently no effective headgear that prevents concussions so, as the number of forceful collisions increase, the number of concussions would be expected to increase.
- Within a given sport, females tend to report higher rates of concussion than males. Within comparable sports, evidence indicates that female athletes may be at a greater risk of concussions than male athletes. The evidence also indicates that, in general, concussions result in cognitive impairment in females more frequently than in males.
- These variations may be due to biomechanical differences, such as differences in body mass, head mass, or neck strength.
- Proper strength and conditioning, especially focused on strengthening the muscles of the neck, is a suitable way to limit the forces experienced by the head.



Previous Mild Traumatic Brain Injury and Postural-Control Dynamics. *Journal of Athletic Training*. 2011.

- In the United States, TBI represents a major medical concern that costs nearly \$60 billion in direct and indirect expenses annually.
- Traditionally, mild traumatic brain injury has been thought to result in short-lived impairment of postural control and neurocognitive functioning.
- However, individuals with a history of mTBI exhibited altered postural dynamics compared with individuals without a history of mTBI. These findings support the notion that changes in cerebral functioning that affect postural control may persist long after acute injury resolution.



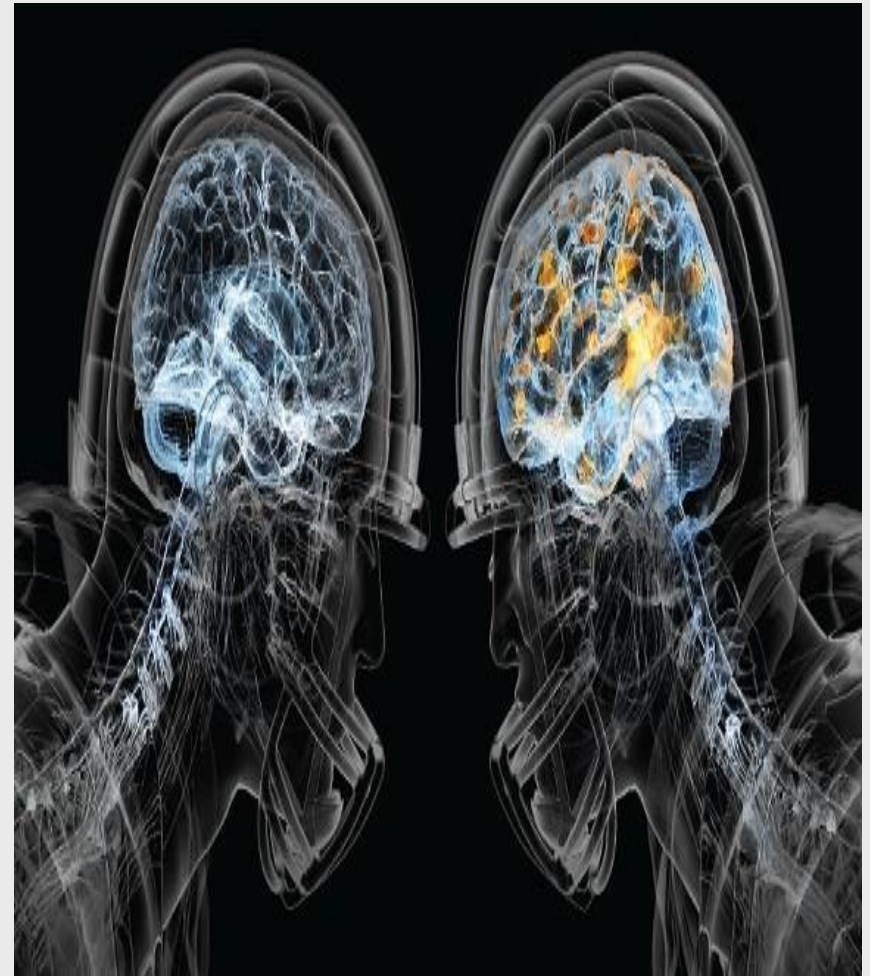
Objectively Assessing Balance Deficits After TBI: Role of Computerized Posturography. *Journal of Rehabilitation Research & Development*. 2007.

- The annual incidence of all severities of traumatic brain injury (TBI) in the United States is estimated to be between 500,000 and 2 million cases. Of these, the approximately 44,000 people with moderate to severe TBI have significant residual physical or neurobehavioral sequelae.
- The National Institutes of Health report that 2.5 million to 6.5 million Americans have TBI-related disabilities.
- Balance impairment, or postural instability, is a common source of residual physical disability after severe traumatic brain injury (TBI).
- There is an association between early balance deficits after TBI and late functional recovery.
- Postural imbalances as long-term sequelae of severe TBI may not be surprising given that balance involves a complex interaction of sensory, motor, and musculoskeletal systems. Even minor impairments in integration of this information could lead to significant long-term disability.
- Computerized Posturography Testing safely and effectively assists the diagnosis of balance impairments and provides quantitative data to track changes over time and/or assess the efficacy of treatment interventions. Similar to findings in mild TBI, vestibular dysfunction appears to underlie postural instability after severe TBI.



Comprehensive Assessment and Management of Athletes with Sport Concussion. *The International Journal of Sports Physical Therapy*. 2012.

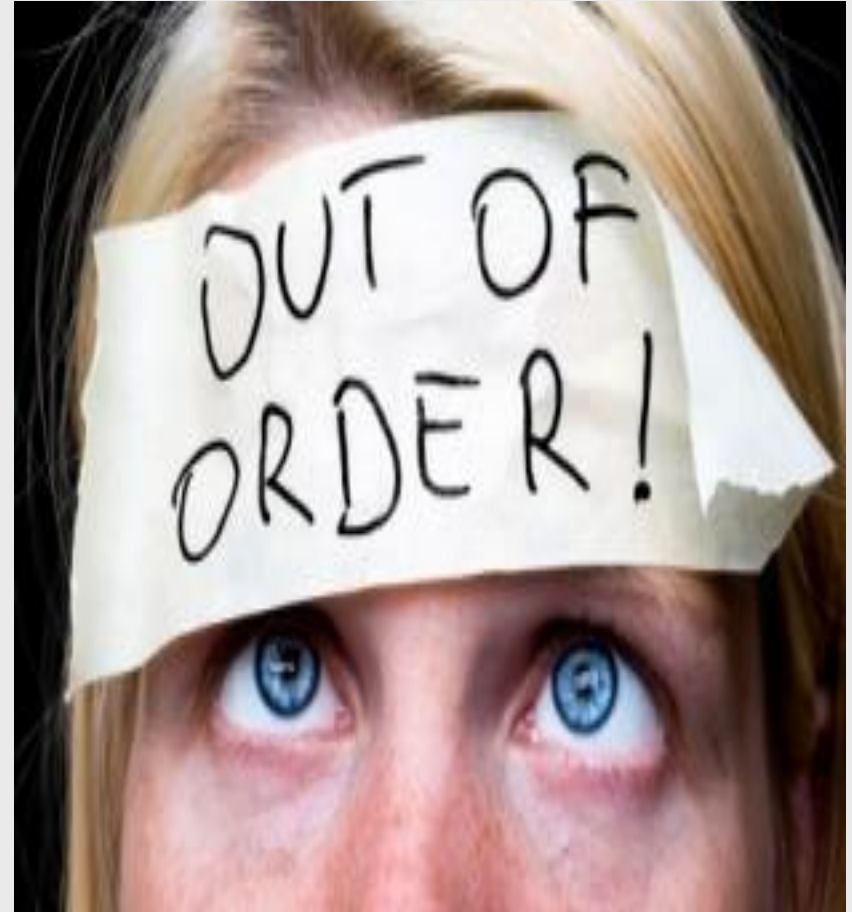
- The brain is a complex and complicated organ. No two mTBIs are the same and, consequently, no two treatment programs can be identical.
- Athletes with concussion rapidly develop short-term impairment of neurologic function; among those, 80 to 90% resolve spontaneously within the first ten days, although the recovery timeframe may be longer in children and adolescents than in their adult counterparts.
- However, a small percentage of patients experience prolonged, physical, behavioral, neuropsychological, and/or personality changes frequently termed post-concussive syndrome (PCS).



The Current Status of Postconcussion Syndrome.

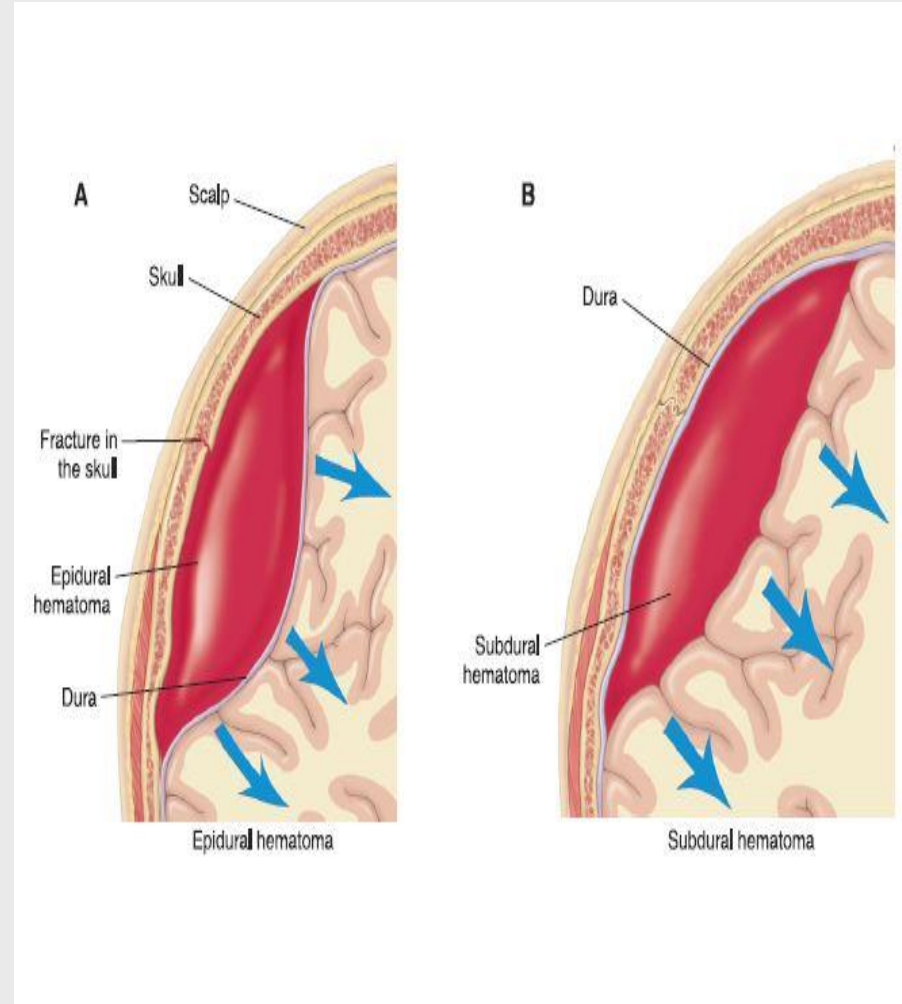
Neuropsychiatry. 2011.

- Concussions are temporary disruptions of brain function that appear to be a very mild form of TBI.
- Cardiovascular disturbances, eye movement disturbances, slowed reaction times, and feeling 'like in a fog' are all compatible with the possibility of brainstem disturbance in some patients.
- The fact that with multiple concussions the individual may not fully recover does suggest that some underlying structural change in brain anatomy may occur, even with concussions.



Classification of Sport-Related Head Trauma: A Spectrum of Mild to Severe Injury. *Journal of Athletic Training*. 2001.

- Epidural hematoma is an accumulation of blood between the dura and skull. The dura becomes detached and dissects to the point of dural attachment to the overlying cranium. Hemorrhage occurs beneath the skull and outside the dura, resulting in the classic computed tomography (CT) appearance of a biconvex or lenticular shape of the hematoma.
- Epidural hematoma is caused by head impact, usually of the acceleration-deceleration type, and can result in inward deformity, leading to dural detachment from the inner table of the skull. Most patients with an epidural hematoma have a skull fracture, which leads to laceration of the middle meningeal artery or vein.
- An acute subdural hematoma is the most common major head injury and is associated with severe neurologic disability and death in many patients. Acute subdural hematoma results from bleeding within the subdural space as a result of stretching and tearing of the subdural veins. These veins drain from the cerebral surface and connect to the dura or dural sinuses.
- A cerebral contusion injury can evolve over hours and days after the injury. Multiple small areas of contusions may coalesce into a large area resembling a lesion, more accurately termed intraparenchymal hemorrhage. Injuries remote from the site of cranial impact may also occur. The direct, or coup, lesion results from injury at the impact site, and the remote, or contrecoup, lesion occurs as the opposite side of the brain rebounds against the skull or because of vacuum phenomena existing within the parenchyma at that location. The contrecoup lesion results in a hemorrhagic lesion in the cerebral tissue directly opposite the impact site, typically at the inferior surfaces of the frontal and temporal lobes. Contusions are often multiple and are frequently associated with other extra-axial and intra-axial hemorrhagic lesions.



Consensus Statement on Concussion in Sport: The 3rd International Conference on Concussion in Sport Held in Zurich, November 2008.

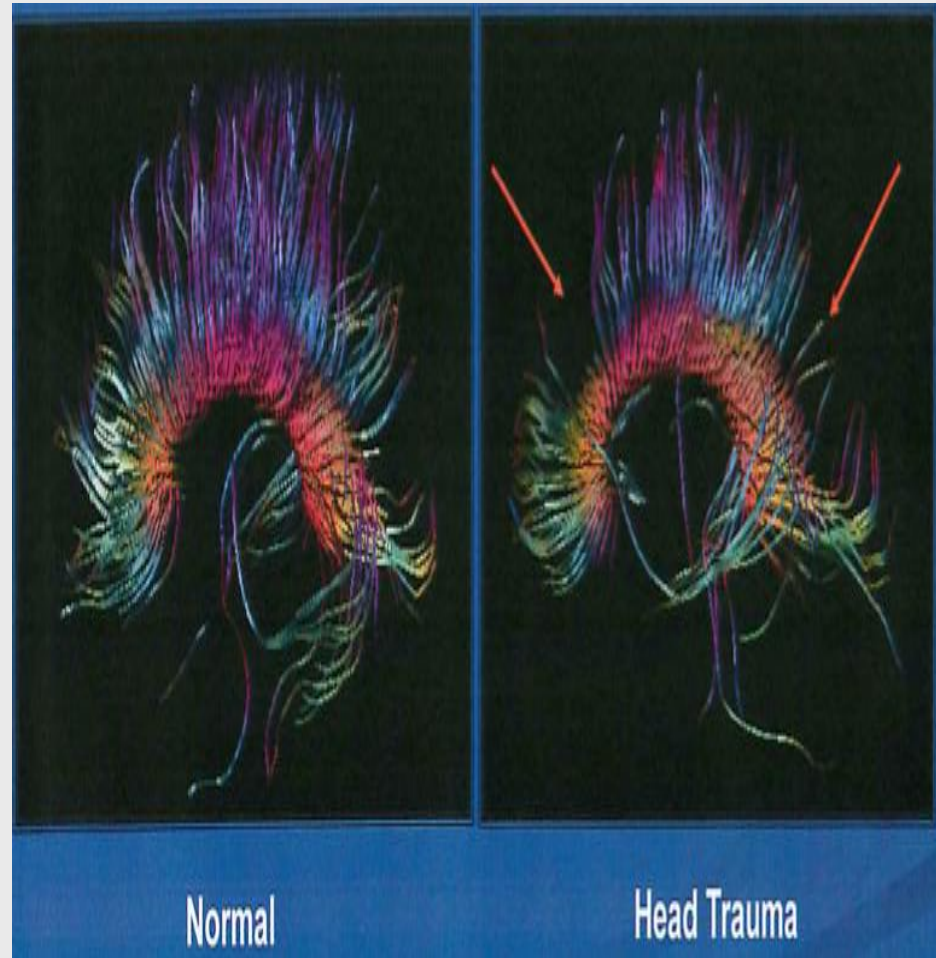
Journal of Athletic Training. 2009.

- It was recognized by the panelists that conventional structural neuroimaging is normal in concussive injury.
- Brain computed tomography (CT) (or, where available, MR brain scan) contributes little to concussion evaluation but should be employed whenever suspicion of an intracerebral structural lesion exists such as prolonged disturbance of conscious state, focal neurologic deficit, or worsening symptoms.
- Published studies using both sophisticated force plate technology as well as those using less sophisticated clinical balance tests (eg, Balance Error Scoring System [BESS]) have identified postural stability deficits lasting approximately 72 hours following sport-related concussion. It appears that postural stability testing provides a useful tool for objectively assessing the motor domain of neurologic functioning and should be considered a reliable and valid addition to the assessment of athletes suffering from concussion.
- The application of neuropsychological (NP) testing in concussion has been shown to be of clinical value and continues to contribute significant information in concussion evaluation. It must be emphasized, however, that NP assessment should not be the sole basis of management decisions; rather, it should be seen as an aid to the clinical decision-making process in conjunction with a range of clinical domains and investigational results.



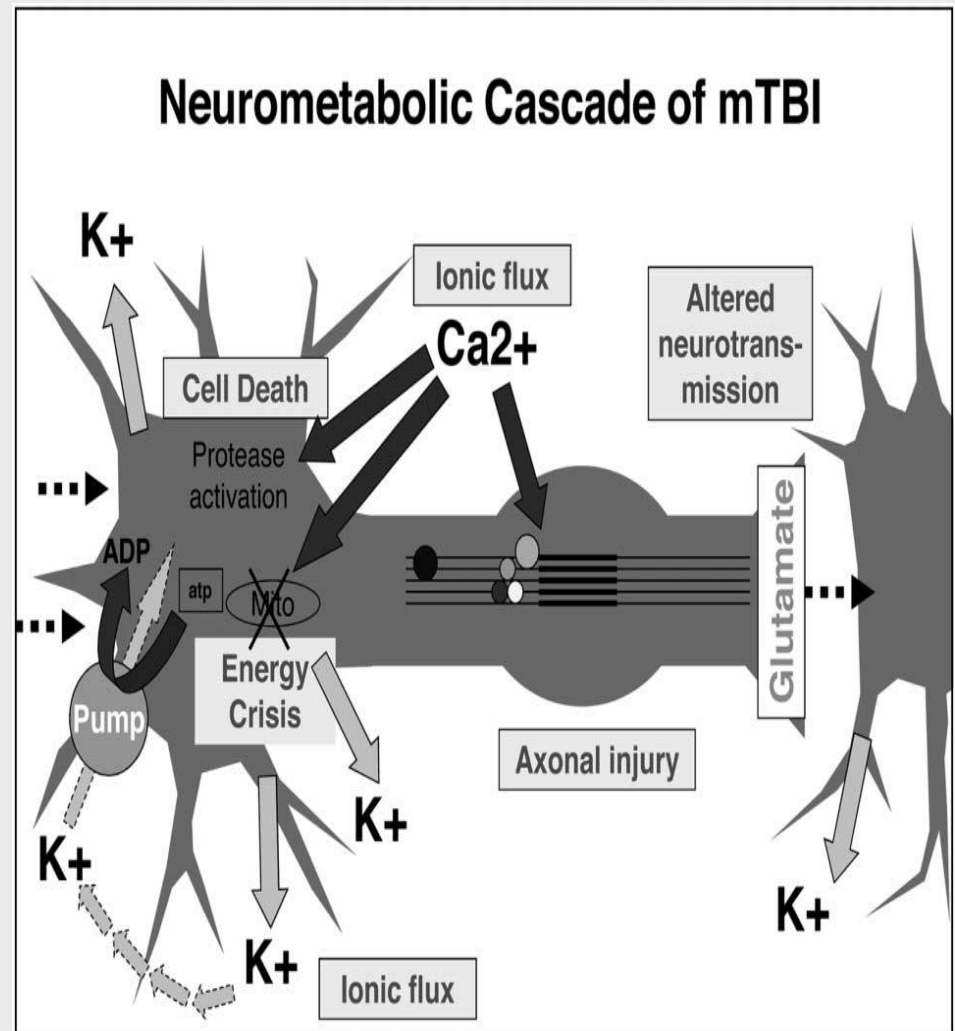
A Unified Science of Concussion. *Annals of the New York Academy of Sciences*. 2010.

- A common pathological feature of TBI includes distributed injuries to the subcortical white matter, or diffuse axonal injury (DAI), that may occur with or without focal injury.
- Magnetic resonance imaging (MRI) technique of diffusion tensor imaging (DTI) can detect microscopic brain white matter tract lesions after concussion, or mild traumatic brain injury (mTBI).
- In blunt closed head injury, these diffuse axonal damages have been attributed to shear strain and tissue deformation caused by the rotational accelerations of the brain as an external force is applied to the head.



The Neurometabolic Cascade of Concussion. *Journal of Athletic Training*. 2001.

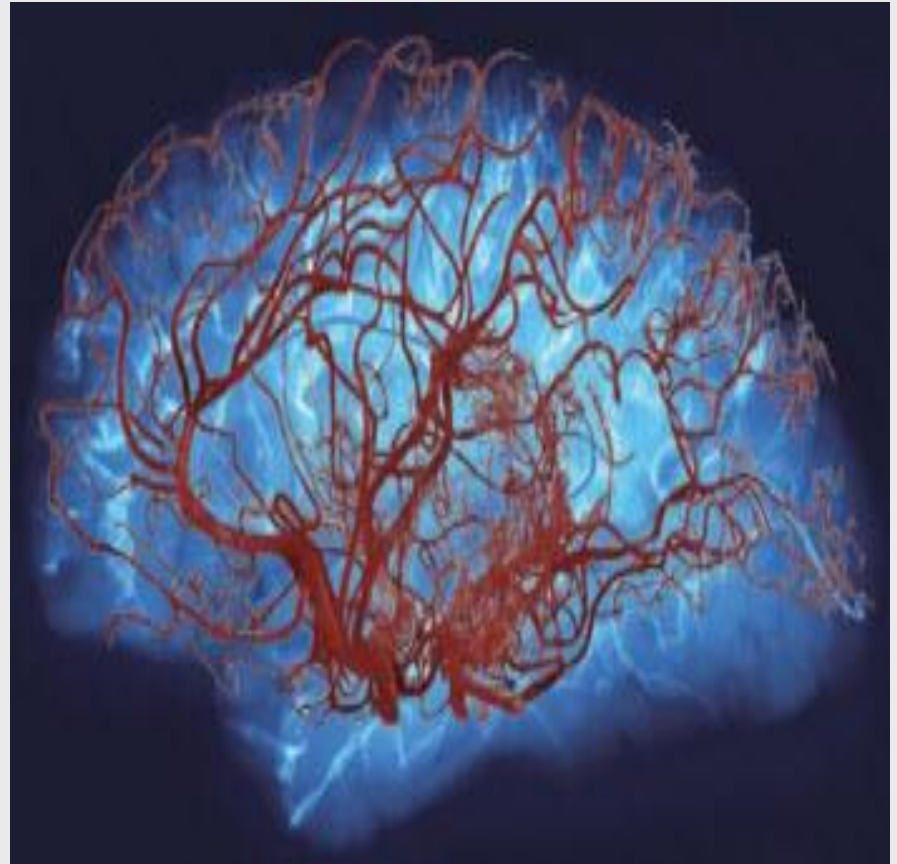
- Neurometabolic Cascade Following mTBI.
 - 1. Nonspecific depolarization and initiation of action potentials.
 - 2. Release of excitatory neurotransmitters.
 - 3. Massive efflux of potassium.
 - 4. Increased activity of membrane ionic pumps to restore homeostasis.
 - 5. Hyperglycolysis to generate more adenosine triphosphate (ATP).
 - 6. Lactate accumulation.
 - 7. Calcium influx and sequestration in mitochondria leading to impaired oxidative metabolism.
 - 8. Decreased ATP production.
 - 9. Calpain activation and initiation of apoptosis.



Rehabilitation of Concussion and Post-Concussion Syndrome.

Sports Health. 2012.

- Data suggest that at least some patients with PCS have measurable pathophysiology.
- Concussed athletes with prolonged depressive symptoms showed reduced functional magnetic resonance imaging activation in the dorsolateral prefrontal cortex and striatum and attenuated deactivation in medial frontal and temporal regions accompanied by gray matter loss in these areas.
- Some PCS patients have persistent abnormalities of brain blood flow on single-photon emission computed tomography scan, neurochemical imbalances (eg, serum S100B), and electrophysiologic indices of impairment.
- Autoregulation, the maintenance of cerebral blood flow at appropriate levels during changes in systemic blood pressure, and cerebral blood flow are also disturbed after concussion, which may explain why symptoms often reappear or worsen with physical and/or mental exertion.
- Impairment of the cerebral vasculature after TBI sensitizes the brain to secondary insults, such as hypotension, intracranial hypertension, and dehydration



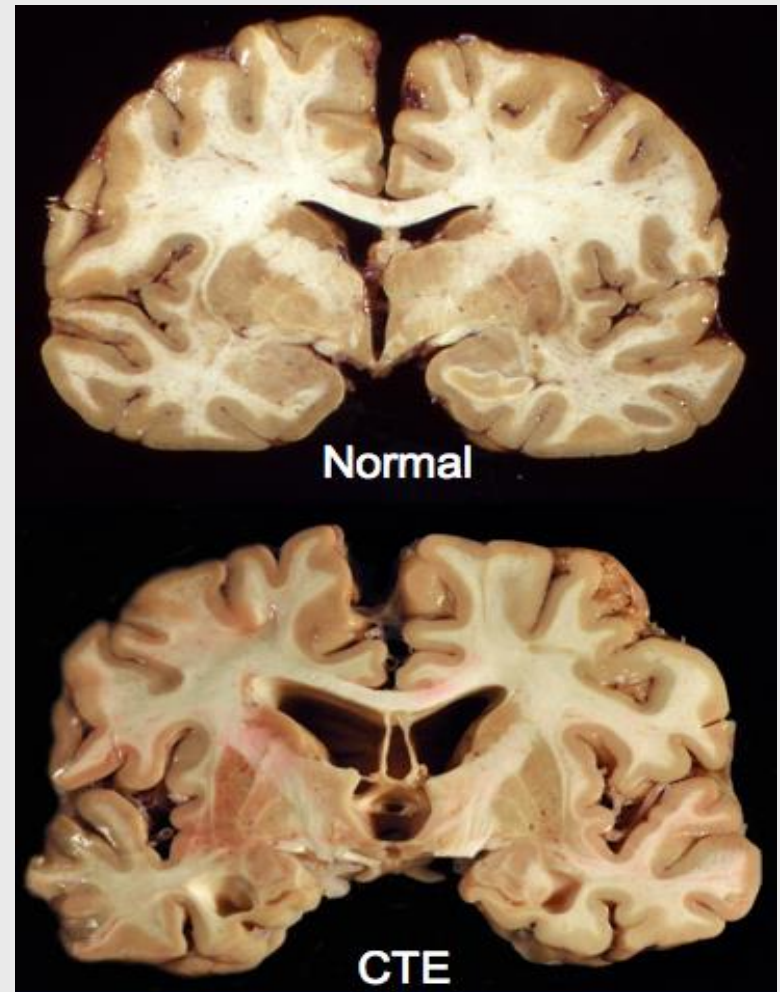
Traumatic Brain Injury and Intestinal Dysfunction: Uncovering the Neuro-Enteric Axis. *Journal of Neurotrauma*. 2009.

- Isolated TBI has systemic consequences for several organs, leading to important clinical sequelae, including pneumonia, cardiovascular disorders, autonomic abnormalities, intestinal dysfunction, and multi-system organ failure.
- Several areas of intestinal dysfunction following TBI have been described, including stomach ulceration and gastritis (Cushing's ulcer), prolonged ileus and other motility problems, and most importantly impairment of gut barrier function.
- TBI significantly decreased the expression of the intestinal tight junction proteins ZO-1 and occludin, which correlates to increased intestinal permeability and distinct changes in intestinal histology.
- We have observed an increase in intestinal permeability and marked changes in intestinal histology 6 hours following TBI. Levels of intestinal tight junction proteins may be an important factor in increased intestinal permeability following TBI.



Chronic Traumatic Encephalopathy in Athletes: Progressive Tauopathy After Repetitive Head Injury. *Journal of Neuropathology & Experimental Neurology*. 2009.

- Since the 1920s, it has been known that the repetitive brain trauma associated with boxing may produce a progressive neurological deterioration, originally termed dementia pugilistica, and more recently, chronic traumatic encephalopathy (CTE).
- CTE is associated with memory disturbances, behavioral and personality changes, parkinsonism, and speech and gait abnormalities.
- CTE is characterized by atrophy of the cerebral hemispheres, medial temporal lobe, thalamic, mammillary bodies, and brainstem, with ventricular dilatation and fenestrated cavum septum pellucidum.
- There are multiple reasons for neuronal loss in acute traumatic injury including neuronal death from direct physical damage, necrosis from the immediate release of excitatory transmitters such as glutamate, and diffuse delayed cell death involving both necrotic and apoptotic death cascades. Other contributing factors include focal ischemia, breakdown of the blood-brain barrier, inflammation, the release of cytokines, and deafferentation.



Traumatic Brain Injury and Amyloid- β Pathology: A Link to Alzheimer's Disease? *Nature Reviews Neuroscience*. 2010.

- There are several possible mechanisms linking an episode of TBI to later development of neurodegenerative disease, such as neuronal loss, persistent inflammation and cytoskeletal pathology.
- However, the pathophysiological link that has received the most attention is the production, accumulation and clearance of amyloid- β (A β) peptides following TBI.
- Compelling data from several studies demonstrate that a history of TBI is one of the strongest epigenetic risk factors for Alzheimer's Disease and may accelerate its onset.

Healthy Brain



Brain with Alzheimer's



Vestibular Loss as a Contributor to Alzheimer's Disease.

Medical Hypotheses. 2013.

- Alzheimer's disease (AD) is the leading cause of dementia and a disease that is increasing rapidly as the elderly population in the industrialized nations continues to rise. It is projected that over 13 million Americans will suffer from it by 2050.
- In contrast to the widespread neural and behavioral failure seen in later stages of disease, the initial symptoms are most salient in the area of memory, particularly topographical memory, and are accompanied by specific degeneration of the hippocampal and parahippocampal regions of the medial-temporal cortex and hypoperfusion of the parietal-temporal and posterior cingulate cortices.
- The vestibular system, more than any other sensory system, diffusely projects to a variety of cortical and subcortical structures. Although the largest vestibular projection zone lies in the posterior Sylvian region containing the parietal-insular and parietal-temporal cortex, there is also an important and specific vestibular projection to the medial-temporal cortex, including the hippocampus and parahippocampal gyrus.
- The hypothesized contribution of vestibular loss to degeneration of the topographical cortical system would be an example of anterograde degeneration, in which destruction of lower structures leads to degeneration of their higher projection zones.
- Anterograde degeneration occurs following damage to many types of sensory organs and can occur transneuronally, with neurons several synapses removed from the end-organ being affected and suffering apoptotic cell death.
- If vestibular loss does, indeed, turn out to be a major contributor to AD, then vestibular prevention and therapeutic strategies may eventually prove crucial in preventing or slowing the progression of this disease.



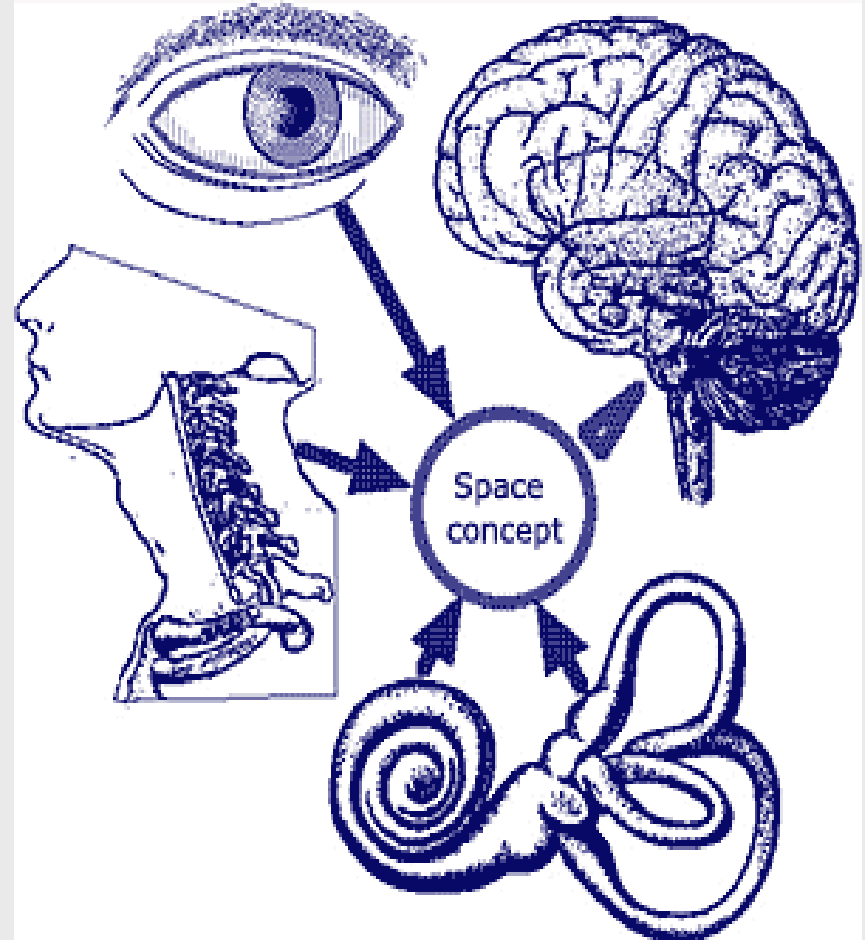
Gravity influences top-down signals in visual processing. *Plos One*. 2014.

- **OBJECTIVE:** Investigate the impact of gravity on visual processing.
- **CONCLUSION:** Visual perception is not only based on incoming visual signals but also on information about a multimodal reference frame that incorporates vestibulo-proprioceptive input and motor signals. These results demonstrate that gravity-related sensory input modulates primary visual cortical areas.



Dizziness after traumatic brain injury: Overview and measurement in the clinical setting. *Brain Injury*. 2006.

- Dizziness has been reported in up to 80% of traumatic brain injury cases within the first few days after injury.
- Dizziness is a very non-specific term and can be placed into four broad categories.
- (1) Vertigo: The illusion of movement. This is clearly related to the vestibular system.
- (2) Pre-syncopal lightheadedness: A sensation of impending faint. This may be due to cerebral ischaemia, e.g. a drop in blood pressure related to postural change.
- (3) Multisensory dizziness: Occurs with pathology involving multiple sensory systems. This diagnosis is said to be more common in older populations and in populations with systemic disorders (e.g. diabetes).
- (4) Psycho-physiologic dizziness: Symptoms include visual vertigo and space phobia.
- Dizziness can be further explained in relation to a definition of vestibular function as the 'neural sensory-motor interaction that leads to the maintenance of balance (motor function) and the perception of motion of objects relative to oneself (sensory function) as part of the larger and global function of orientation'.
- In recent years, vestibular rehabilitation has emerged as an accepted and effective means of treating dizziness and vestibular disorders. It involves exercises and activities designed to enhance central nervous system compensation to vestibular system dysfunction.



An Assessment of Gait and Balance Deficits After Traumatic Brain Injury. *Archives of Physical Medicine and Rehabilitation*. 2003.

- Patients' complaints of instability after TBI may have objective correlates and may be rectifiable. Balance and gait testing in these patients is warranted.
- Subtle complaints of persistent imbalance by patients after a TBI should be investigated.
- Gait analysis and balance and vestibular testing can document subtle changes in gait and balance among those with TBI.
- Imbalance may not be due merely to diffuse brain injury. Comprehensive vestibular testing seems appropriate in all patients with persistent complaints of imbalance and instability after TBI.



The Biomechanical Properties of Concussions in High School Football. *Medicine & Science Sports Exercise*. 2010.

- While an accurate biomechanical diagnostic pathway continues to evade researchers, the clinical examination remains the gold standard for concussion diagnosis.
- Medical organizations recommend that the clinician employ a battery of tests that evaluate a number of cognitive domains known to be affected by concussion.
- An assessment battery that employs measures of concussion related symptoms, neurocognitive functioning, and postural control remains the most sensitive to injury in excess of 90% from which to base the diagnosis.



Concussion In Sports: The Sideline Assessment. *Sports Health*. 2009.

- Questioning the athlete about the injury will provide pertinent information relative to the injury. First, a level of consciousness can be established through dialogue with the athlete. If the athlete is not alert enough to understand the questions or is passing in and out of consciousness, he or she should be transported to a medical facility for further evaluation.
- Second, it is important to determine whether the athlete is suffering from retrograde or anterograde amnesia. To establish the presence or absence of retrograde amnesia, injury history questions should start at the time of impact and work backward. For example, the athlete may be asked the following: “Do you remember getting hit?” “Do you recall the play you were running?” “What team are we playing against?” and “Do you remember arriving at the field before the game?” Conversely, the assessment of anterograde amnesia should begin with questions surrounding events following injury, such as “Who was the first person you saw on the field?” and “Do you recall coming over to the bench?”
- Third, observation and palpation looking for autonomic signs and possible fractures.



Management of Cerebral Concussion in Sports: The Athletic Trainer's Perspective. *Journal of Athletic Training*. 2001.

- Post Concussive Symptoms
 - Testing continues with the presentation of a post-concussion symptom scale, which, in addition to being administered at preseason baseline, time of injury, and 2 to 3 hours post injury, should also be administered daily until the athlete is asymptomatic.
- Cranial Nerve Testing
 - After reviewing the athlete's symptoms, assess the function of the cranial nerves. The cranial nerves can be tested quickly: sense of smell (I), eye tracking and pupil reactivity (III, IV, V), facial expressions (VII), biting down (V), swallowing (X), protrusion of the tongue (XII), and shoulder shrugs (XI).
- Balance Error Scoring System
 - The BESS is a quantifiable version of a modified Romberg test for balance, consisting of 3 tests lasting 20 seconds each, performed on firm and foam surfaces.
- Standardized Assessment of Concussion
 - The SAC measures the immediate neurocognitive effects of concussion and is designed to assess orientation, immediate memory, concentration, and delayed memory. Administration of the SAC takes 5 minutes; orientation, immediate memory, neurologic function, concentration, delayed recall, and symptoms during exertional testing are assessed.

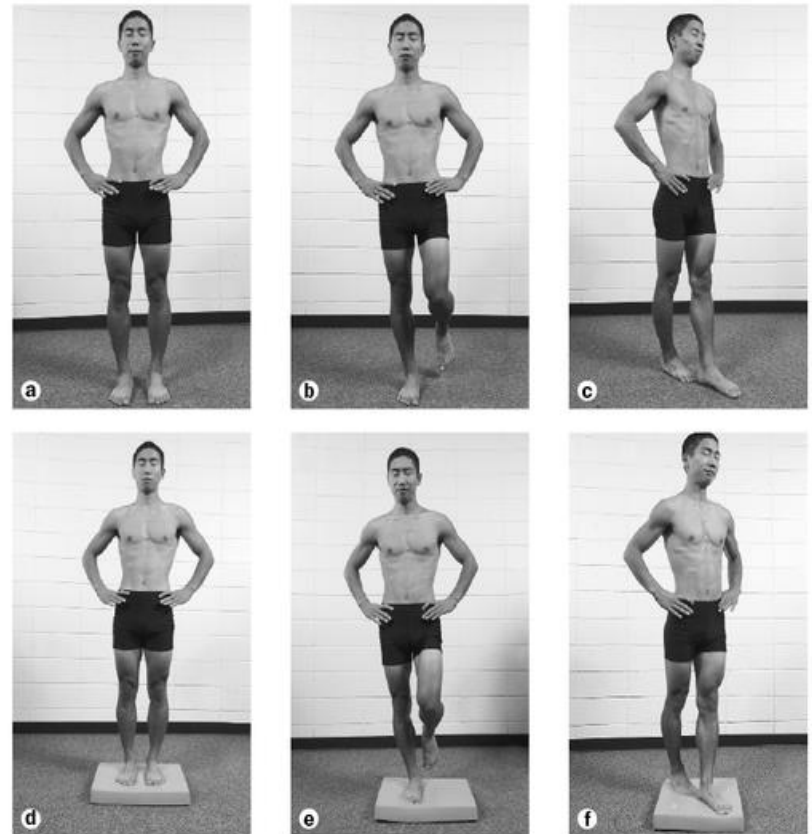


FIGURE 12.3 Balance error scoring system (BESS). Top row, firm surface condition. Bottom row, soft surface condition. Left column, parallel stance. Middle column, single-leg stance. Right column, tandem stance.

Recovery of Static Stability Following a Concussion. *Gait & Posture*. 2013.

- The key finding of this study was that balance control of concussed athletes was not fully recovered upon return to play as indicated by increased velocity of COP. This deficit was evident despite recovery of COP displacement and reduction of reported symptoms.
- Displacement is a first-order variable coding position of the system, whereas velocity and acceleration represent higher order variables coding direction and intensity of movement. As such, displacement is controlled via somatosensory feedback while velocity and acceleration require greater sensory integration from the visual and vestibular systems.
- Without vision, the vestibular and somatosensory inputs must be up-regulated to maintain balance.
- During the acute post-concussion phase, impaired vestibular and visual input to the CNS would likely be reflected by increased COP displacement and velocity compared to healthy controls. In the current study, COP displacement recovers while COP velocity remains elevated when concussed athletes return to play. This would suggest recovery of the somatosensory system, but a persistent impairment in the vestibular system.
- A second key finding was that balance deficits were more pronounced in the A/P direction. During quiet standing, A/P movement is primarily controlled by ankle extensors which receive input from the descending lateral vestibulospinal tract (VST). Following concussion, damage to the vestibular system could result in impairments to the lateral VST.
- Symptom evaluation and possibly subjective balance assessments may not be sensitive enough to detect deficits in balance control that are present in concussed athletes who have returned to play. Therefore, development of objective balance assessment tools is required to ensure that athletes are not returned to play with sensorimotor impairments.



The use of the dual-task paradigm in detecting gait performance deficits following a sports-related concussion: A systematic review and meta-analysis. *Journal of Science and Medicine in Sports*. 2013.

- There has been increasing interest in the fields of human movement science and physical therapy in the ability of persons to perform two tasks simultaneously, which is termed: dual-task (DT) performance.
- Two days following a concussion, participants walked significantly slower and exhibited greater medial-lateral sway than the non-concussed controls, during dual-task conditions.
- When two concurrent tasks compete for common 'central resource capacity', the processing ability of the brain can be compromised, which can manifest as performance decrements in one or both of the concurrently performed tasks. It is speculated that changes in brain function following a concussion^{38,39} exacerbate this situation resulting in the differences observed for gait velocity (GV) and ML-ROM.
- DT related changes for gait speed and medial-lateral sway during walking can distinguish concussed and non-concussed individuals.
- The DT paradigm is a novel assessment procedure for sports related concussion and may possibly detect subtle neurological deficits associated with a concussive brain injury.



Simplest Tasks Have Greatest Dual Task Interference With Balance In Brain Injured Adults. *Human Movement Science*. 2004.

- Attention difficulties and poor balance are both common sequel following a brain injury.
- One of the most frequent motor impairments following a brain injury is difficulty with postural stability particularly under demanding situations.
- Brain injured adults demonstrated greater interference with balance when concurrently performing cognitive tasks than control participants.
- Difficulty in performing two different tasks concurrently (dual tasking) and has been shown in patients following traumatic brain injury using upper limb tasks.
- A disturbance to postural control when concurrently performing cognitive tasks has been reported in several populations with balance and cognitive impairments.



Impaired Eye Movements in Post-Concussion Syndrome Indicate Suboptimal Brain Function Beyond the Influence of Depression, Malingering or Intellectual Ability. *Brain*. 2009.

- Eye movement function is impaired in Post-Concussive Syndrome (PCS), the deficits being unrelated to the influence of depression or estimated intellectual ability, which affected some of the neuropsychological tests.
- Eye movement function in PCS does not follow the normal recovery path of eye movements after mild closed head injuries, marking ongoing cerebral impairment independently of patient self-report and neuropsychological assessment.
- Whilst oculomotor and neuropsychological tests partially overlapped in identifying suboptimal brain function, eye movements provided additional evidence of dysfunction in areas such as decision making under time pressure, response inhibition, short-term spatial memory, motor-sequence programming and execution, visuospatial processing and integration, visual attention and subcortical brain function.
- Indications of poorer subcortical/subconscious oculomotor function in the PCS group support the notion that PCS is not merely a psychological entity but also has a biological substrate.
- Despite the cost intensive nature of eye movement assessment in terms of required equipment, eye movement testing should be feasible in centers, which have easy access to eye tracking technology.



Occurrence of Oculomotor Dysfunctions in Acquired Brain Injury: A Retrospective analysis. *Optometry*. 2007.

- Medical records of 220 individuals with either TBI (n 160) or CVA (n 60) were reviewed retrospectively investigating the frequency of occurrence of oculomotor dysfunctions including accommodation, version, vergence, strabismus, and cranial nerve (CN) palsy.
- The majority of individuals with either TBI (90%) or CVA (86.7%) manifested an oculomotor dysfunction. Accommodative and vergence deficits were most common in the TBI subgroup, whereas strabismus and CN palsy were most common in the CVA subgroup.
- These new findings should alert the clinician to the higher frequency of occurrence of oculomotor dysfunctions in these populations and the associated therapeutic, rehabilitative, and quality-of-life implications.
- Predictive visual tracking shows promise as an attention metric to assess severity of mTBI. Deficits seen during predictive visual tracking correlate with DTI findings and with observed damage to neural pathways known to carry out cognitive and affective functions that are vulnerable to mTBI.



Saccadic Eye Movements in Mild Traumatic Brain Injury: A Pilot Study. *Canadian Journal of Neurological Sciences*. 2014.

- Saccades are rapid eye movements that move the line of sight between successive points of fixation. Their dynamic properties are well understood and easily measured, including reaction time, amplitude, peak velocity, duration, and frequency of errors.
- In our study, there was some correlation between saccadic reaction times and self-reporting symptoms.
- Persistent prolonged saccadic reaction times in mTBI patients may separate patients with persistent mTBI from those with recovering mTBI.



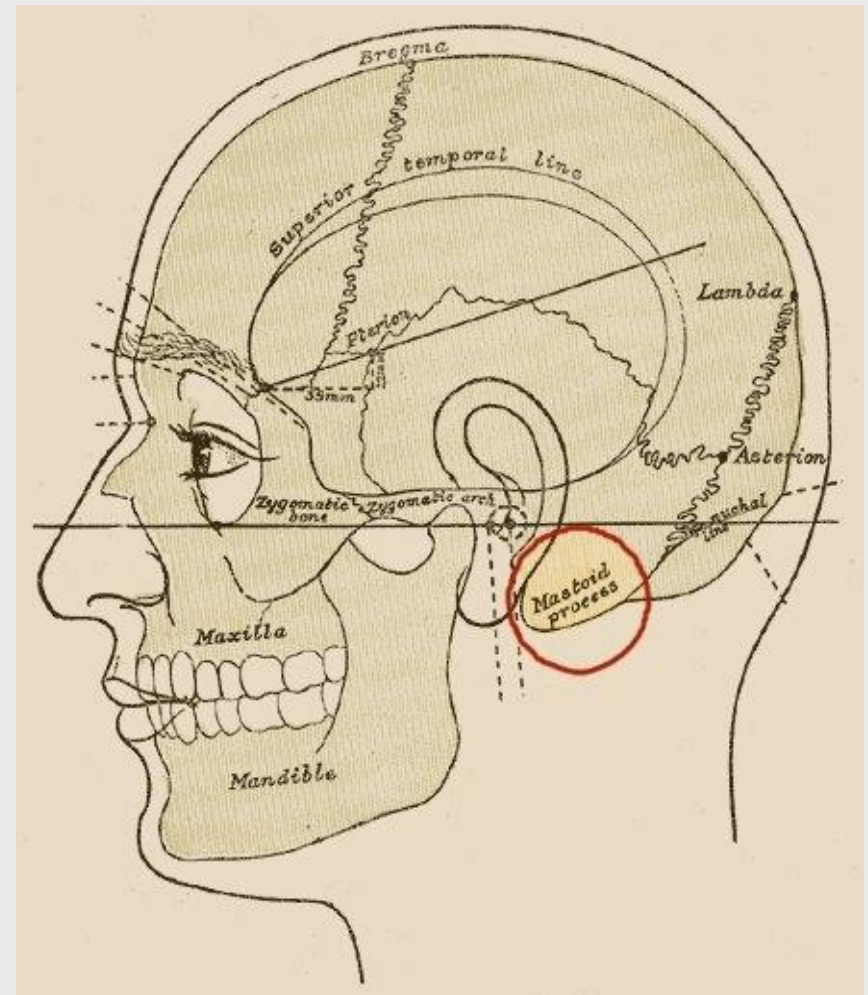
Saccadometry: The Possible Application of Latency Distribution Measurement for Monitoring Concussion. *British Journal of Sports Medicine*. 2007.

- The time taken to look at a suddenly presented visual target, saccadic latency, reflects cortical decision time, and has proved a useful measure of the general level of cerebral function, being affected by conditions ranging from sedative levels of anaesthesia to metabolic disorders. Furthermore, because saccades to the left and right are independently controlled by each hemisphere, it can provide information about lateral functional asymmetry.
- Useful comparisons can be made between an individual's baseline and post-injury saccadic latency distributions, and that large changes are a relatively common outcome of boxing, even in the absence of a period of unconsciousness; those experiencing more head trauma generally showed the largest latency increases.
- This implies that mild traumatic brain injury impairs cortical decision processes, causing a shift in latency distribution.
- Even very mild traumatic brain injury there are obvious alterations in saccadic latency distributions, with increased mean latency, but that they return to pre-fight levels within a small number of days.



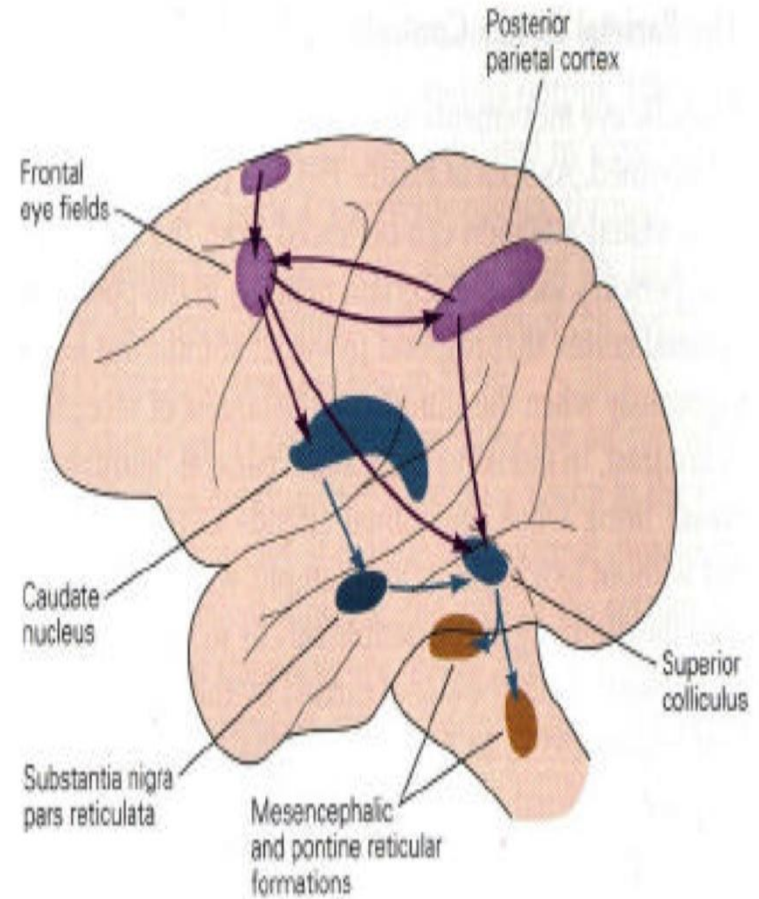
Vestibulo-Ocular Monitoring as a Predictor of Outcome After Severe Traumatic Brain Injury. *Critical Care*. 2009.

- The results indicate that vestibulo-ocular monitoring with galvanic labyrinth polarization performed during the first days after traumatic brain injury helps to predict favourable or unfavourable outcome.
- As an indicator of brainstem function, vestibulo-ocular monitoring provides a useful, complementary approach to the identification of brainstem lesions by imaging techniques



Differential Eye Movements in Mild Traumatic Brain Injury Versus Normal Controls. *The Journal of Head Trauma Rehabilitation*. 2014.

- One method for the objective assessment of the brain after PCE and mTBI that has shown promise as a user friendly, low cost, non-invasive, definitive approach is eye tracking. Eye tracking has been advocated as a rapid, convenient, and portable (ie, field ready) method of evaluation.
- Eye tracking assessment typically involves the examination of saccades, fixation, and smooth pursuit eye movements (SPEM).
- Saccades (rapid, accurate, ballistic shifting of gaze to a new area of interest) are studied because they require the complex coordination and timing of neural circuitry in numerous different brain areas, including primarily the frontal lobe, basal ganglia, superior colliculus, and the cerebellum, and would therefore be likely to be sensitive indicators of injury to one of these areas.
- Temporal associations between injury, symptom presentation, and eye-movement abnormalities may be an important key to use of eye tracking to monitor recovery after mTBI.
- Robust differences were found between responses of subjects with symptomatic mTBI and controls to horizontal and vertical stepwise target displacement tasks, with subjects with symptomatic mTBI having statistically larger position errors, smaller saccadic amplitudes, smaller predicted peak velocities, smaller peak accelerations, and longer durations.
- Differences in responses to smooth pursuit tasks were also found between the 2 groups. The amplitudes were significantly larger for subjects with symptomatic mTBI for the horizontal smooth pursuit task. In comparison to controls, pursuit gain was lower among subjects with symptomatic mTBI.



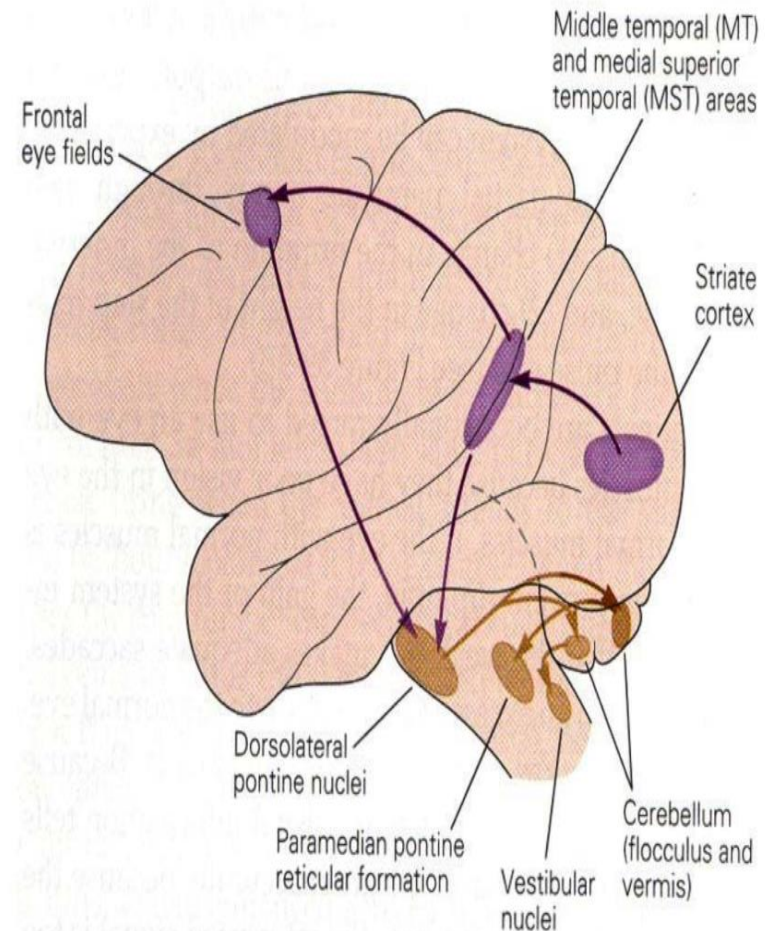
Visual Tracking Synchronization as a Metric for Concussion Screening. *The Journal of Head Trauma Rehabilitation*. 2010.

- Performance variability during predictive visual tracking is a powerful indicator for decreased integrity in frontal white matter tracts vulnerable to mTBI as well as for altered cognitive functioning.
- Visual tracking performance can be monitored precisely and continuously, allowing detection and objective quantification of subtle momentary lapses in attention over a matter of seconds, a significantly shorter time than required for administration of traditional neurocognitive testing.
- Measurement of visual tracking performance is promising as a fast and practical screening tool for mTBI.



A Unified Science of Concussion. *Annals of the New York Academy of Sciences*. 2010.

- Although subjective patient self-report is the leading method of diagnosing mTBI, current scientific evidence suggests that quantitative measures of predictive timing, such as visual tracking, could be a useful adjunct to guide the assessment of attention and to screen for advanced brain imaging.
- Magnetic resonance diffusion tensor imaging (DTI) has demonstrated that mTBI is associated with widespread microstructural changes that include those in the frontal white matter tracts.
- Deficits observed during predictive visual tracking correlate with DTI findings that show lesions localized in neural pathways subserving the cognitive functions often disrupted in mTBI.
- Predictive visual tracking shows promise as an attention metric to assess severity of mTBI. Deficits seen during predictive visual tracking correlate with DTI findings and with observed damage to neural pathways known to carry out cognitive and affective functions that are vulnerable to mTBI.



Physiological, Vestibulo-Ocular and Cervicogenic Post-Concussion Disorders: An Evidence-Based Classification System with Directions for Treatment. *Brain Injury*. 2014.

- At a minimum, the initial examination of patients with acute concussion should include a full neurological exam including testing of cranial nerve, motor, sensory, reflex and cerebellar function. The examination should also include a thorough assessment of balance, gait and cognitive functions such as speech and memory.
- Symptoms and impairments in post-concussion recovery period for symptom “clusters” that point to operational post-concussion disorders that can be identified by salient features of patient history, physical examination and aerobic treadmill testing.
- Physiologic Post Concussion Syndrome
 - It is hypothesized that the pathophysiological basis is characterized by persistent alterations in cell membrane permeability, ion transport regulation, neurotransmitter release, cellular metabolism and cerebral blood flow that have yet to fully recover after the patient’s initial injury.
 - Although patients with Physiologic PCD may report mild persistent symptoms or be asymptomatic at rest, they continue to have exacerbation of symptoms during cognitive activity and/or physical exercise, reflective of a persistent cerebral metabolic energy deficiency.
- Vestibulo-Ocular Post Concussion Syndrome
 - The integration of the vestibular, oculomotor and somatosensory systems is necessary to allow human beings to optimally navigate and function within a complex visuospatial environment. This complex system is compromised of highly specialized neural networks that interact at multiple levels of the craniospinal axis to regulate gait, maintain balance and postural control, as well as coordinate eye movements.
 - Common visual complaints such as blurred vision, diplopia, difficulty reading or motion sensitivity have been found to arise from subtle deficits in accommodation, version (pursuits, saccades and fixation), convergence insufficiency as well as photosensitivity and, rarely, visual defects and cranial nerve palsies.
- Cervicogenic Post Concussion Syndrome
 - The high density and complexity of muscle and joint mechanoreceptors throughout the cervical spine are a rich source of proprioceptive information that is conveyed to multiple levels of the CNS and make the cervical spine important in mediating balance, head orientation and eye movement.
 - Postulated mechanisms include alteration in mechanoreceptor functioning secondary to trauma or inflammation and the central modulatory effect of pain and the sympathetic nervous system on cervical somatosensory integration.

Table I. Summary of pathophysiology, predominant symptoms, pertinent physical examination findings, graded treadmill test results and treatment options in patients with PCDs.

	Physiologic PCD	Vestibulo-ocular PCD	Cerviogenic PCD
Pathophysiology	<ul style="list-style-type: none"> Persistent alterations in neuronal depolarization, cell membrane permeability, mitochondrial function, cellular metabolism, and cerebral blood flow 	<ul style="list-style-type: none"> Dysfunction of the vestibular and oculomotor symptoms 	<ul style="list-style-type: none"> Muscle trauma and inflammation Dysfunction of cervical spine proprioception
Predominant symptoms	<ul style="list-style-type: none"> Headache exacerbated by physical and cognitive activity Nausea, intermittent vomiting, photophobia, phonophobia, dizziness, fatigue, difficulty concentrating, slowed speech 	<ul style="list-style-type: none"> Dizziness, vertigo, nausea, light-headedness, gait instability and postural instability at rest. Blurred or double vision, difficulty tracking objects, motion sensitivity, photophobia, eye strain or brow-ache, and headache exacerbated by activities that worsen vestibulo-ocular symptoms (i.e. reading) 	<ul style="list-style-type: none"> Neck pain, stiffness, and decreased range of motion Occipital headaches exacerbated by head movements and not physical or cognitive activity Lightheadedness and postural imbalance
Physical exam findings	<ul style="list-style-type: none"> No focal neurological findings Elevated resting HR 	<ul style="list-style-type: none"> Impairments on standardized balance and gait testing Impaired VOR, fixation, convergence, horizontal and vertical saccades 	<ul style="list-style-type: none"> Decreased cervical lordosis and range of motion Paraspinal and sub-occipital muscle tenderness Impaired head-neck position sense
Graded treadmill test	<ul style="list-style-type: none"> Graded treadmill tests are often terminated early due to symptom onset or exacerbation 	<ul style="list-style-type: none"> Patients typically reach maximal exertion without exacerbation of vestibulo-ocular symptoms on graded treadmill tests 	<ul style="list-style-type: none"> Patients typically reach maximal exertion without exacerbation of cervicogenic symptoms on graded treadmill tests
Management options	<ul style="list-style-type: none"> Physical and cognitive rest School accommodations Sub-symptom threshold aerobic exercise programs should be considered for adolescent and adult athletes 	<ul style="list-style-type: none"> Vestibular rehabilitation program Vision therapy program School accommodations Sub-symptom threshold aerobic exercise programs should be considered for adolescent athletes 	<ul style="list-style-type: none"> Cervical spine manual therapy Head-neck proprioception re-training Balance and gaze stabilization exercises Sub-symptom threshold aerobic exercise programs should be considered for adolescent and adult athletes

PCD, post-concussion disorder; VOR, vestibulo-ocular reflex.

Sensorimotor disturbances in neck disorders affecting postural stability, head and eye movement control. *Manual Therapy*. 2008.

- **OBJECTIVE:** Present clinical recommendations for assessment and management of sensorimotor control disturbances in neck disorders.
- **CONCLUSION:** Given the importance of the neck for postural stability, head and eye movement control, as well as the nature of the changes in sensorimotor control seen in those with neck disorders, assessment and management of such disturbances should form an important part of the multimodal approach to neck disorders. This should include addressing the causes of the altered cervical somatosensory input such as improving neuromuscular function and decreasing pain and inflammation as well as a tailored sensorimotor exercise program to improve identified deficits in postural stability and head and eye movement control. Dizziness and unsteadiness may be as a result of aberrant cervical proprioception, however it may also be caused by damage to the vertebral artery, vestibular receptors or central nervous system
- **COMMENTS:**
 - The receptors in the cervical spine have important connections to the vestibular and visual apparatus as well as several areas of the central nervous system. The cervical muscles, especially the suboccipital muscles, are involved in relaying and receiving information into the central nervous system
 - Dysfunction of the cervical receptors in neck disorders can alter afferent input subsequently changing the integration, timing and tuning of sensorimotor control.
 - Muscle spindles in the cervical region have high densities of up to 200 muscle spindles per gram of muscle.



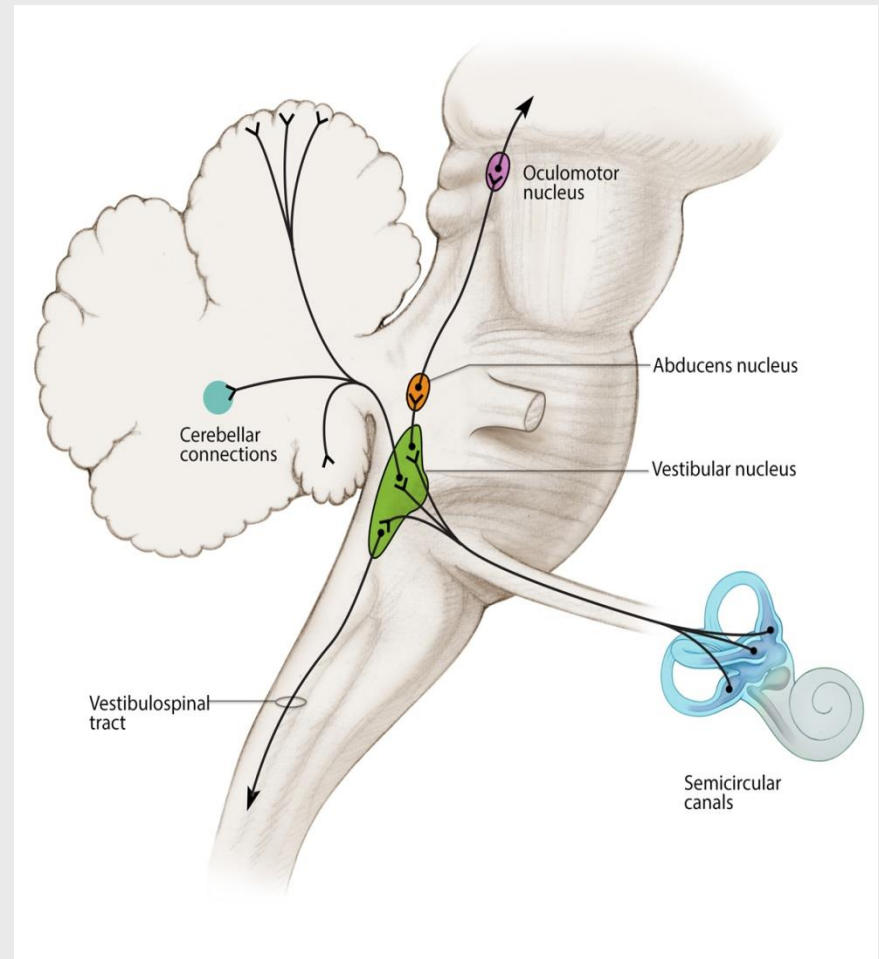
Vestibular Rehabilitation After Mild Traumatic Brain Injury with Vestibular Pathology. *NeuroRehabilitation*. 2011.

- Individuals with mTBI often demonstrate unsteadiness or disequilibrium.
- There is a definitive impact of vestibular physical therapy intervention on dizziness and disequilibrium in mTBI patients whose headaches and vertigo are controlled by medical therapy.
- Vestibular physical therapy is advantageous in improving functional dynamic visual acuity, standing balance and gait in mTBI patients with vestibulopathy.
- Customized exercise programs of gaze stabilization, dynamic visual acuity, static postural stability, dynamic postural stability, desensitization of head motion, aerobic conditioning yield the best results in symptom resolution.
- Using vestibular physical therapy in coordination with a structured multidisciplinary program dramatically improves symptom control and realization of functional self-goals.



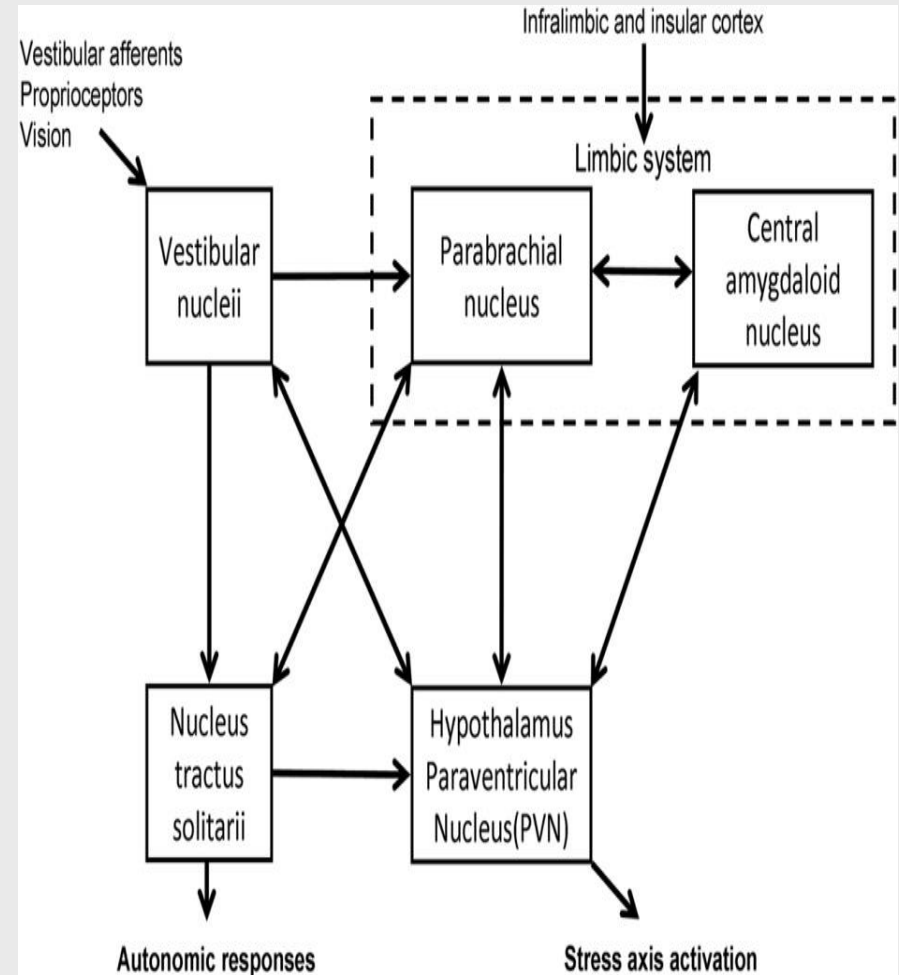
Vision Rehabilitation for Visual-Vestibular Dysfunction: The Role of the Neuro-Optometrist. *NeuroRehabilitation*. 2013.

- Peripheral Component
 - The vestibular apparatus makes up the peripheral component of the vestibular system (the inner ear) that forwards information to the central vestibular system located within the CNS. The vestibular apparatus is located bilaterally within the petrous portion of the temporal bone, comprised of the bony labyrinth and otoliths and is part of the vestibulocochlear complex. The labyrinth has two main subdivisions, which are sensitive to different types of head movements
- Central Component
 - Vestibular Pathways make up the central component of the vestibular system. Vestibular afferent information from receptor hair cells is transmitted via the Vestibulocochlear or VIII Cranial Nerve and arrives at the brainstem and vestibular nuclei. Central axons bifurcate into an ascending branch which extends to the superior vestibular nucleus and the cerebellum and a descending branch which reaches the medial, inferior and lateral vestibular nuclei.



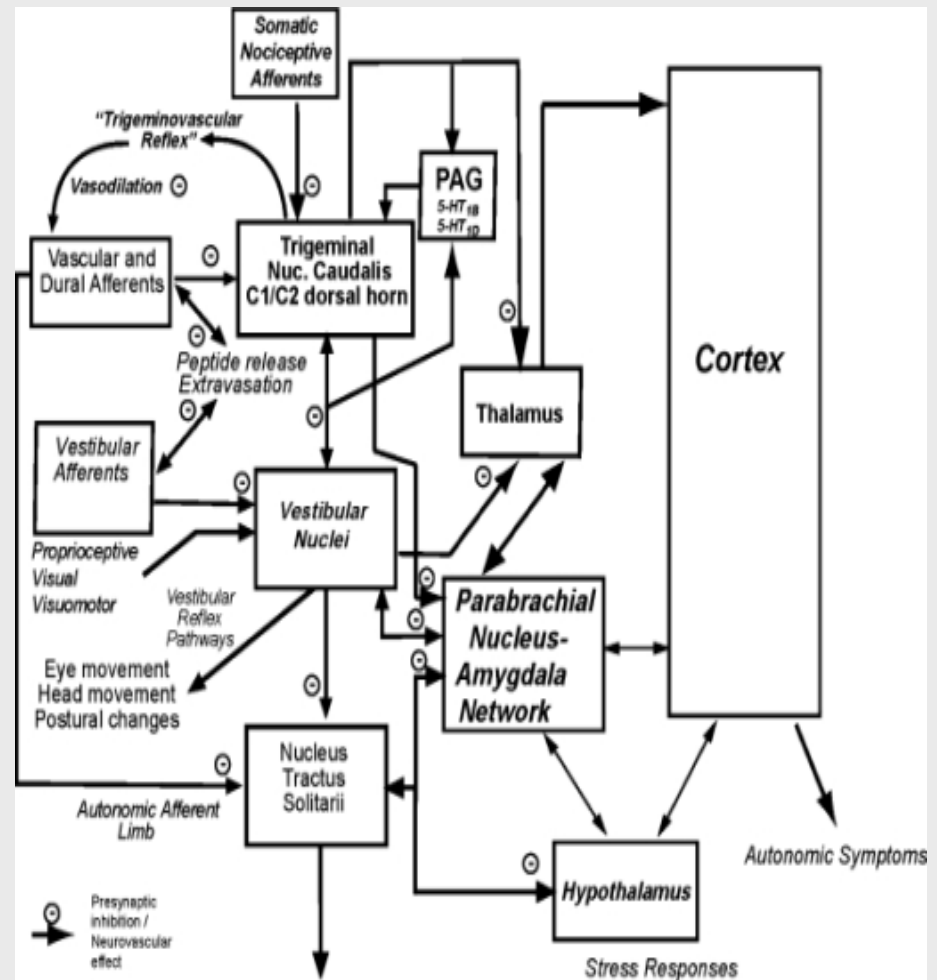
Sensorintegrative Dysfunction Underlying Vestibular Disorders After Traumatic Brain Injury: A Review. *Journal of Rehabilitation Research & Development*. 2012.

- In addition to its role in spatial analysis, the vestibular system is also highly integrated with arousal, autonomic functions, and emotional modulation.
- Vestibular nuclei project to and receive projections from multiple rostral structures implicated in arousal, autonomic function, emotional decisions, fear, and anxiety.
- These structures are the locus coeruleus (the main source of cortical norepinephrine) and, via the parabrachial nucleus, the amygdala, infralimbic cortex, hypothalamus and PIVC.
- The multimodal nature of the vestibular system also offers innovative possibilities for rehabilitation of TBI.
- Stimulation of vestibular periphery has been shown to have therapeutic benefits for cognition and persistent pain.
- Additional possibilities exist for intermodal benefits from peripheral stimulation, such as hearing and vision improvements or anxiety reduction from vestibular training.
- Because of its position at the intersection of higher-level sensory computations and emotions, the central vestibular system is an intriguing access point to better understand the multisensory effects of TBI.



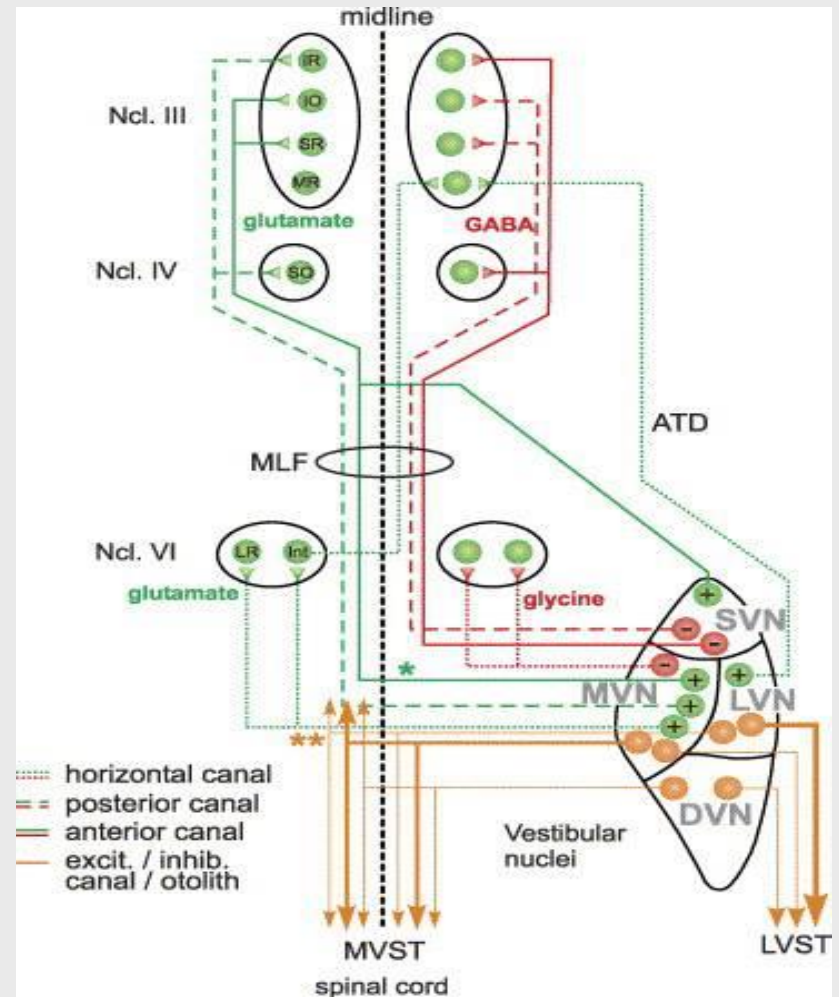
Vestibular Rehabilitation for Dizziness and Balance Disorders After Concussion. *Journal of Neurologic Physical Therapy*. 2010.

- The primary finding of this study is that people who had persistent dizziness and gait and balance dysfunction after having a concussion seem to have improved after vestibular rehabilitation.
- Vestibular rehabilitation may reduce dizziness and improve gait and balance function after concussion.
- For most measures, the improvement did not depend on age, indicating that vestibular rehabilitation may equally benefit both children and adults.
- Vestibular rehabilitation should be considered in the management of individuals post concussion who have dizziness and gait and balance dysfunction that do not resolve with rest.



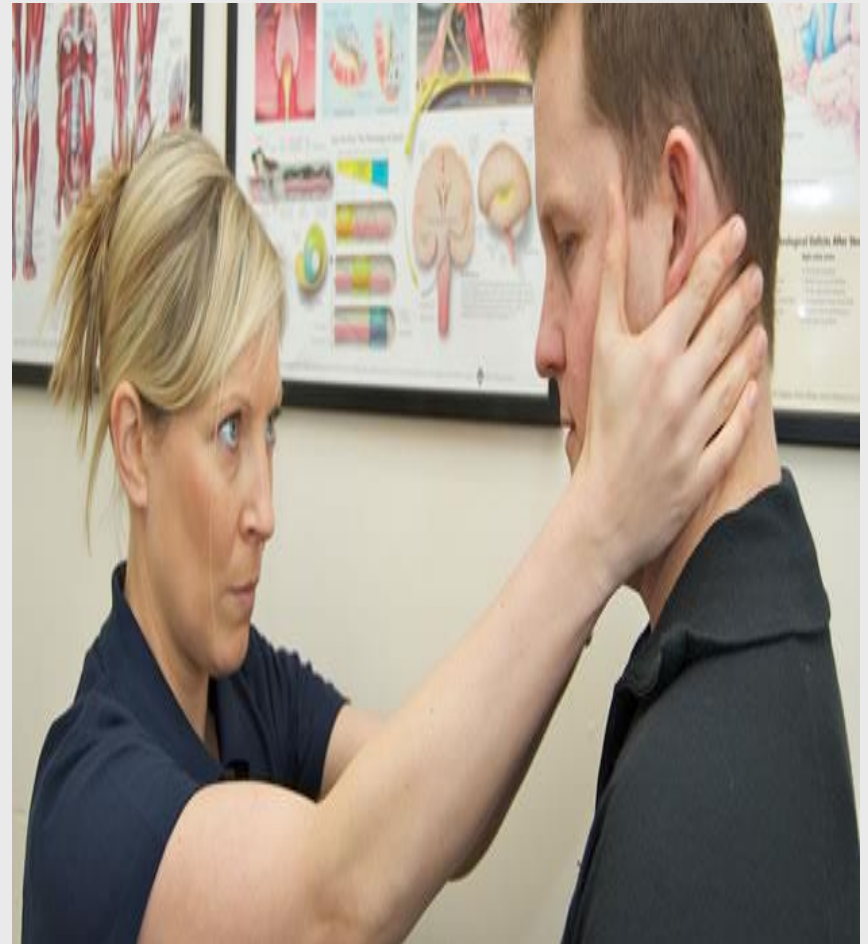
An Update on Vestibular Physical Therapy. *Journal of the Chinese Medical Association. 2013.*

- Vestibular rehabilitation is effective and beneficial for many patients with disequilibrium and balance disorders. Relief of symptoms of vertigo, improved balance and postural control, decreased dizziness, and improvements of quality of life have all been reported after a course of vestibular rehabilitation.
- Vestibular physical therapy is a program of exercises designed to either adapt the vestibuloocular reflex (VOR), i.e. change the gain of the VOR, habituate the person to movement, or to teach sensory substitution plus improve a person's balance/postural control.
- Adaptation of the VOR through head movements has been demonstrated in both primates and humans.
- Habituation is another concept that is used in the rehabilitation of the dizzy patient whereby a person practices a provoking maneuver repetitively in order to be better able to control their symptoms.
- Most commonly, physical therapists use the canalith-repositioning maneuver to treat BPPV.
- Persons with head injuries can experience unilateral or bilateral hypofunction, central vestibular signs and symptoms and also unilateral or bilateral BPPV.
- Vestibular signs and symptoms can be successfully treated with exercise, although the specific exercises used will depend on the patient's complaints.
- Recent evidence suggests that vestibular rehabilitation in young and older persons post concussion may speed recovery.



Exercise Prescription Patterns in Patients Treated with Vestibular Rehabilitation After Concussion. *Physiotherapy Research International*. 2013.

- Vestibular rehabilitation is a key component to the management of dizziness and balance disorders resulting from vestibular system dysfunction, either peripherally or centrally.
- Vestibular rehabilitation reduces dizziness and improves overall balance for individuals with head injury.
- There are five main exercise categories:
 - 1) eye–head coordination
 - 2) sitting balance
 - 3) standing static balance
 - 4) standing dynamic balance
 - 5) ambulation



Vestibular Rehabilitation Therapy: Review of Indications, Mechanisms, and Key Exercises. *Journal of Clinical Neurology*. 2011.

- The exercises for vestibular rehabilitation can be categorized into two types: 1) Physical therapy for vestibular hypofunction and 2) Canalith repositioning therapy for benign paroxysmal positional vertigo (BPPV).
- The goals of VRT are 1) enhancing gaze stability, 2) enhancing postural stability, 3) improving vertigo, and 4) improving daily living activities.
- The overall mechanisms of recovery from vestibular lesions are vestibular adaptation and vestibular substitution.
- Vestibular adaptation involves readjusting the gain of the VOR or vestibulospinal reflex, whereas vestibular substitution employs alternative strategies to replace the lost vestibular function.
- Exercises related to eye and head movements are key to improving gaze stability, whereas exercises performed while standing on a narrow base or a cushion with the eyes closed are key to improving postural stability.
- VRT is applicable to patients with stable vestibular lesions whose vestibular function is poorly compensated, regardless of their age, the cause of their lesion, and symptom duration and intensity. The use of centrally acting medications and visual/somatosensory deprivation should be avoided.

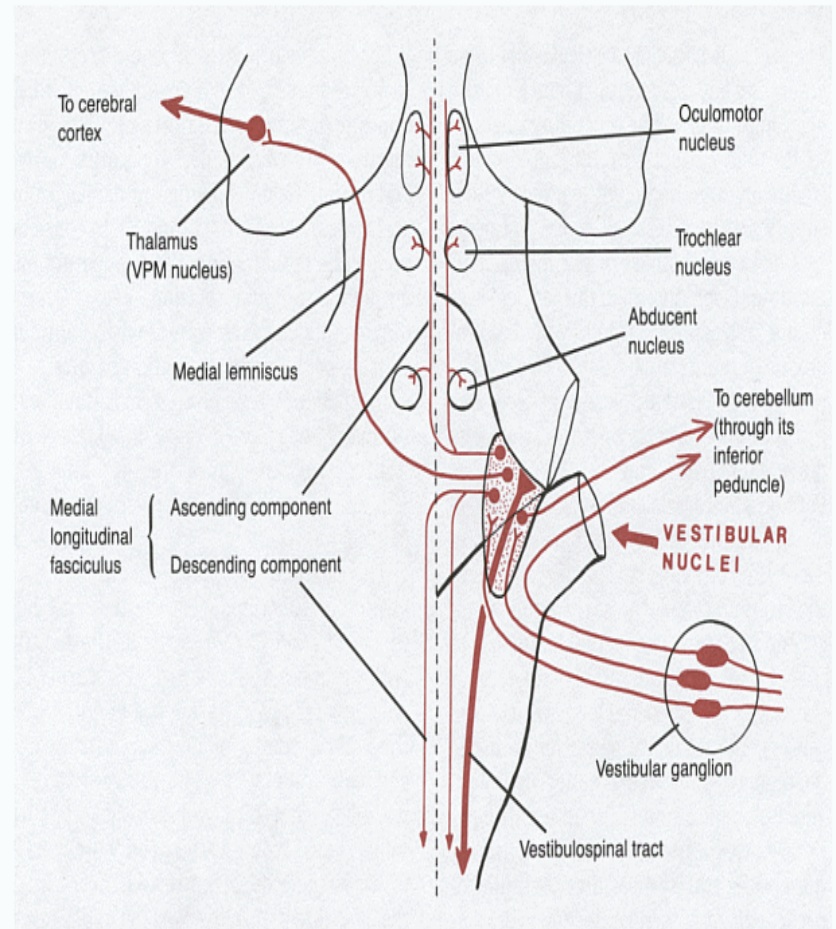


Neurophysiology of Vestibular Rehabilitation.

NeuroRehabilitation. 2011.

- Adaptive plasticity for peripheral vestibular lesions is amazingly competent, even enabling the vestibular system to adapt to peculiar sensory situations requiring a reversal of the VOR.
- Adaptations learned within one sensory context may not work within another. For example, a patient who can stabilize gaze on a target with the head upright may not be able to do so when making the same head movements from a supine posture. Similarly, when the VOR of cats is trained using head movements of low frequency, no training effect is seen at high frequencies.
- Repair of central lesions is much more limited than that available for peripheral lesions; this is the “Achilles’ heel” of the vestibular apparatus. Symptoms due to central lesions last much longer than symptoms due to peripheral vestibular problems.
- When there are cerebellar lesions, or lesions in the pathways to and from the cerebellum, symptoms of vestibular dysfunction can be profound and permanent.

Central connections of the vestibular system



Is It Possible To Restore Function With Two Percent Surviving Neural Tissue. *Journal of Integrative Neuroscience*. 2004.

- **OBJECTIVE:** Discuss how much normal neural tissue is required for functional reorganization after a lesion.
- **CONCLUSION:** Clinical and experimental studies suggest that as little as two percent remaining tissue may be sufficient, at least in some cases, for functional reorganization. Recent sensory substitution studies with persons who have been diagnosed with total vestibular loss suggest that the persisting function after removal of the substitution system may be related to the survival of a small amount of vestibular tissue.



Closing an Open-Loop Control System: Vestibular Substitution Through The Tongue. *Journal of Integrative Neuroscience*. 2003.

- The human postural coordination mechanism is an example of a complex closed-loop control system based on multisensory integration.
- Sensory data from vestibular, visual, tactile and proprioceptive systems are integrated as linearly additive inputs that drive multiple sensory-motor loops to provide effective coordination of body movement, posture and alignment.
- After sensory loss the brain can utilize tactile information from a sensory substitution system for functional compensation.
- Here we have demonstrated that head-body postural coordination can be restored by means of vestibular substitution using a head-mounted accelerometer and a brain-machine interface that employs a unique pattern of electrotactile stimulation on the tongue.
- Moreover, postural stability persists for a period of time after removing the vestibular substitution, after which the open-loop instability reappears.
- The results presented here support the concept of developing practical tactile sensory substitution and augmentation systems based on brain plasticity.



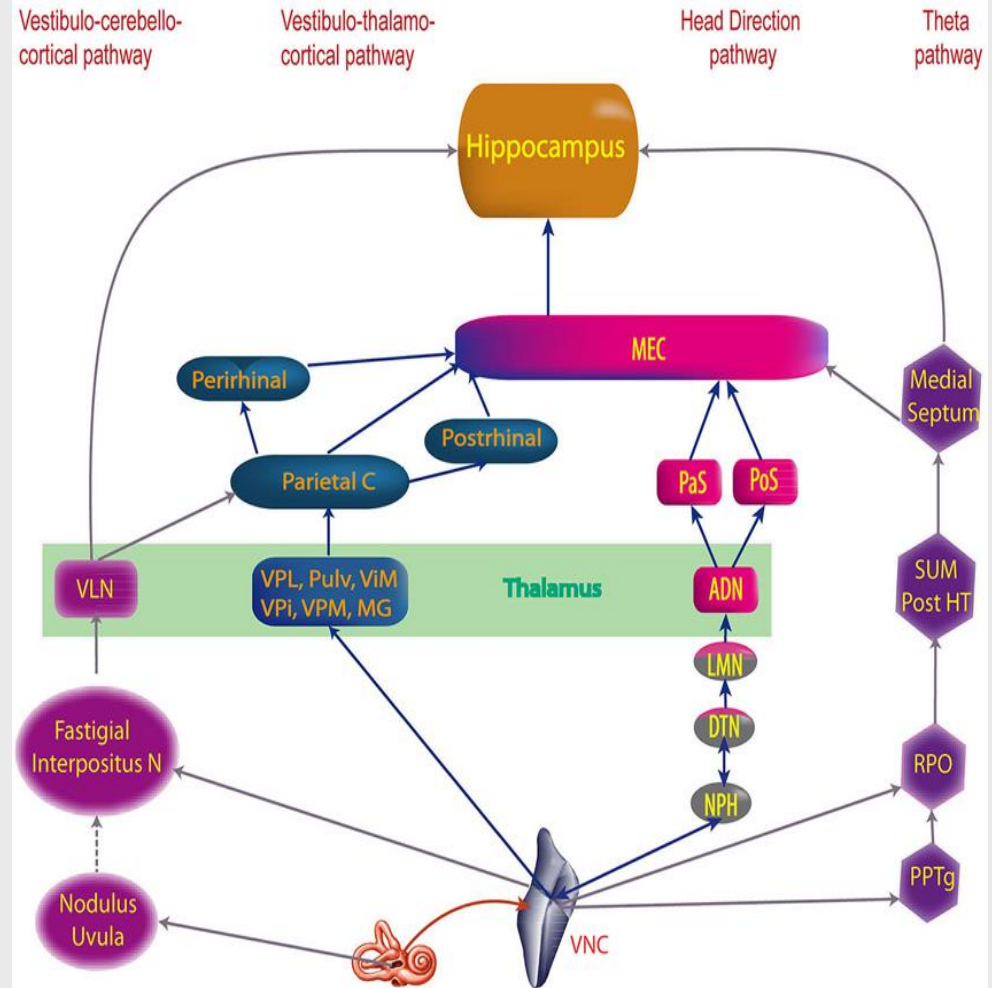
Caloric Vestibular Stimulation Modulates Affective Control and Mood. *Brain Stimulation*. 2014.

- Clinical evidence suggests comorbidity between vestibular dysfunctions and psychiatric disorders such as panic disorder.
- Widespread vestibular-cortical projections may explain the influence of vestibular signals on cognitive and affective processes.
- We conclude that vestibular and emotional processes share some common neural correlates and by activating left hemispheric vestibular areas by means of right ear CVS may interact with the prefrontal emotional network and therefore improve affective control, specifically for emotionally positive stimuli.
- Vestibular stimulation increases activation in regions associated with vestibular sensorimotor processing, interoceptive regions of the insula (parieto-posterior insular vestibular cortex and anterior insula) and regions involved in cognitive processes such as the posterior and anterior cingulate gyri, orbitofrontal cortex and several prefrontal fields.
- It is noteworthy that CVS can alleviate chronic pain symptoms such as phantom limb pain, spinal cord injury pain, complex regional pain syndrome and central post-stroke pain. The underlying mechanism has been attributed to a dynamic inhibitory influence of the insula on the ACC, thus leading to a suppression of pain perception.



Vestibular Pathways Involved in Cognition. *Frontiers in Integrative Neuroscience*. 2014.

- Recent discoveries have emphasized the role of the vestibular system in cognitive processes such as memory, spatial navigation and bodily self-consciousness.
- Four major pathways have been hypothesized to transmit vestibular information to the vestibular cortex:
 - (1) the vestibulo-thalamo-cortical pathway, which probably transmits spatial information about the environment via the parietal, entorhinal and perirhinal cortices to the hippocampus and is associated with spatial representation and self-versus object motion distinctions;
 - (2) the pathway from the dorsal tegmental nucleus via the lateral mammillary nucleus, the anterodorsal nucleus of the thalamus to the entorhinal cortex, which transmits information for estimations of head direction;
 - (3) the pathway via the nucleus reticularis pontis oralis, the supramammillary nucleus and the medial septum to the hippocampus, which transmits information supporting hippocampal theta rhythm and memory;
 - (4) a possible pathway via the cerebellum, and the ventral lateral nucleus of the thalamus (perhaps to the parietal cortex), which transmits information for spatial learning.
- Finally a new pathway is hypothesized via the basal ganglia, potentially involved in spatial learning and spatial memory.



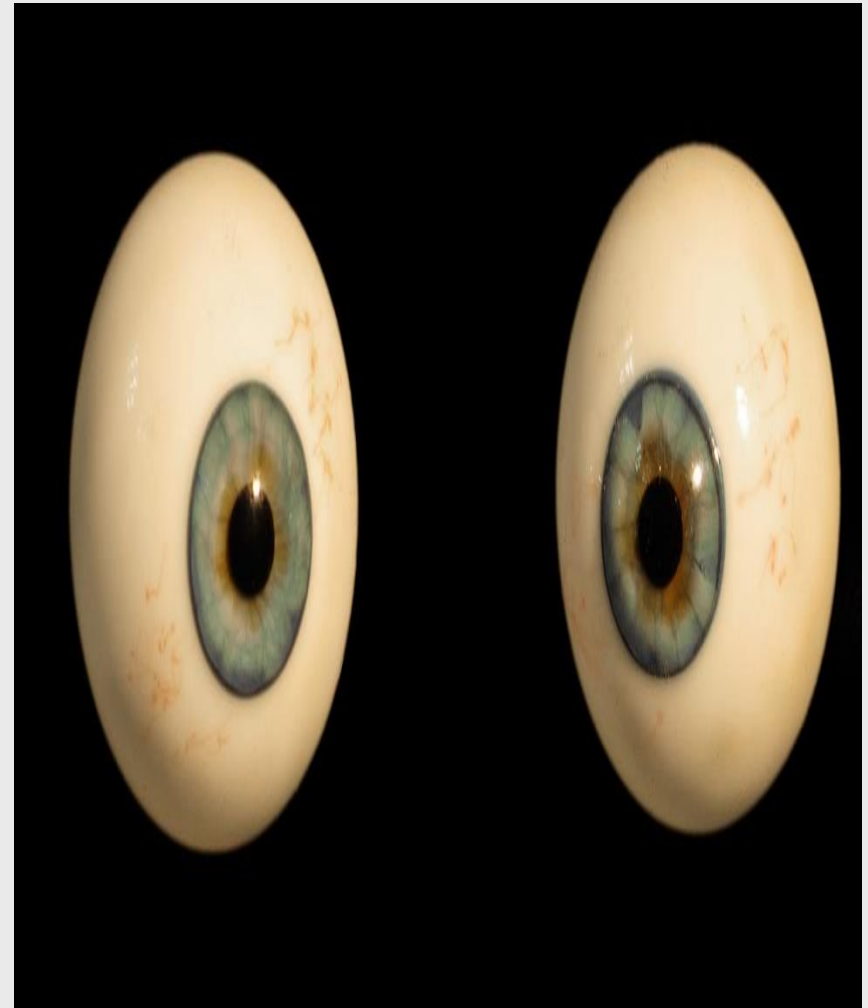
Vision Therapy for Oculomotor Dysfunctions in Acquired Brain Injury: A retrospective Analysis. *Optometry*. 2008.

- The current findings showed a wide range of vergence, versional, and accommodative problems that could be remediated successfully, at a level of 90% or better, incorporating conventional optometric vision therapy in the affected oculomotor areas.
- Both symptoms and signs, with most being related to near vision activities, were either markedly reduced or totally eliminated.
- These findings suggest the presence of considerable visual system plasticity in response to the targeted vision rehabilitation in this brain-injured sample.
- Thus, despite the presence of brain damage in this predominantly adult population, considerable improvement in oculomotor skills was evident.



Effect of Oculomotor Rehabilitation on Vergence Responsivity in Mild Traumatic Brain Injury. *Journal of Rehabilitation Research & Development*. 2013.

- Based on the severity and location of the injury, TBI results in a spectrum of dysfunctions involving sensory, motor, perceptual, physical, behavioral, cognitive, linguistic, and emotional aspects.
- Approximately 90 percent of individuals with mTBI having vision-related symptoms examined in an optometric clinic setting were diagnosed with one or more oculomotor dysfunctions following their acute care phase and natural recovery period. Identifying these abnormalities and rehabilitating them are essential in improving reading ability and overall quality of life.
- There are several separate subsystems believed to be involved in the neural control of vergence. While the midbrain comprises the majority of neurons, evidence for the existence of neurons that also discharge during vergence have been located in the pons, cerebellum, and some areas of the cerebral cortex, such as the frontal eye field, parietal lobe, middle temporal and medial superior temporal visual areas, and primary visual cortex. Since the vergence neural pathway is extensive, any injury to the multitude of related brain and contiguous structures may adversely affect the vergence system.
- Under normal circumstances, repeated synaptic stimulation, along with its coincident activation, results in an increased synaptic strength and memory storage. This experience-dependent neuroplasticity is composed of biochemical-, cellular-, physiological-, and structural level changes. Recovery following an insult to the brain has been categorized as “spontaneous reorganization” (or natural recovery) and “training-induced recovery”. Significant oculomotor improvements can occur even 5 to 10 years after the first injury. Remapping and reconfiguration of neural circuits both within and across relevant regions play a significant role in the recovery process.
- Functional magnetic resonance imaging technique in two individuals with mTBI before and after intensive vergence-based Oculomotor training was performed. Their results showed increased amount of voxels and correlation within specific regions of interest (brain stem, cerebellum, frontal eye fields, and supplementary eye fields) following a total of 18 h of clinically based and laboratory-based vergence.
- Vergence-based OR was effective in individuals with mTBI who reported nearwork-related symptoms. Overall improvement in nearly all of the critical, abnormal measures of vergence was observed both objectively and clinically. Improved vergence motor control was attributed to residual neural visual system plasticity and oculomotor learning effects in these individuals. Concurrently, nearwork-related symptoms reduced, and visual attention improved.



Effect of Oculomotor Rehabilitation on Vergence Responsivity in Mild Traumatic Brain Injury. *Journal of Rehabilitation Research & Development*. 2013.

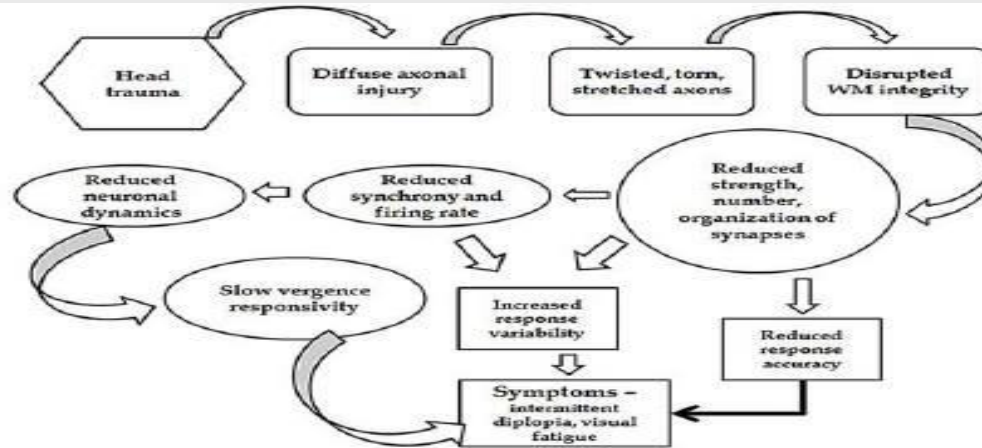


Figure 5. Proposed neural mechanisms of traumatic brain injury causing vergence dysfunction. WM = white matter.

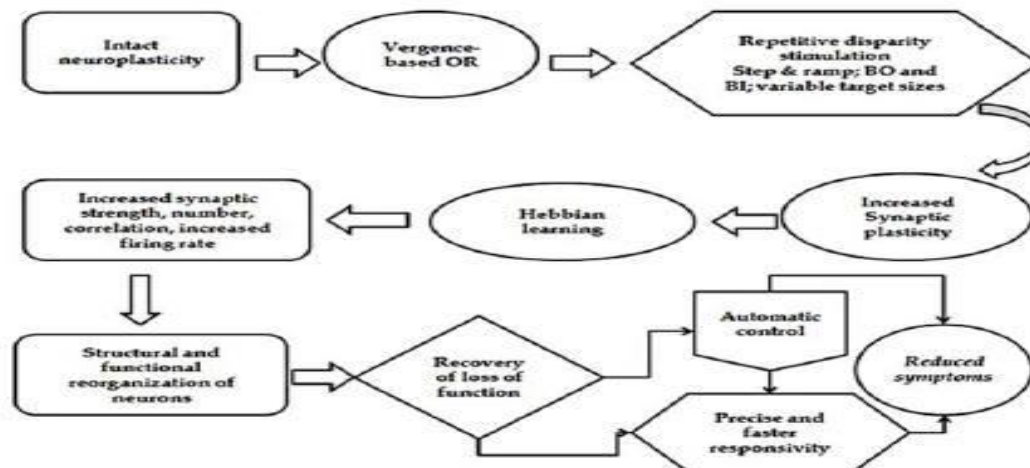
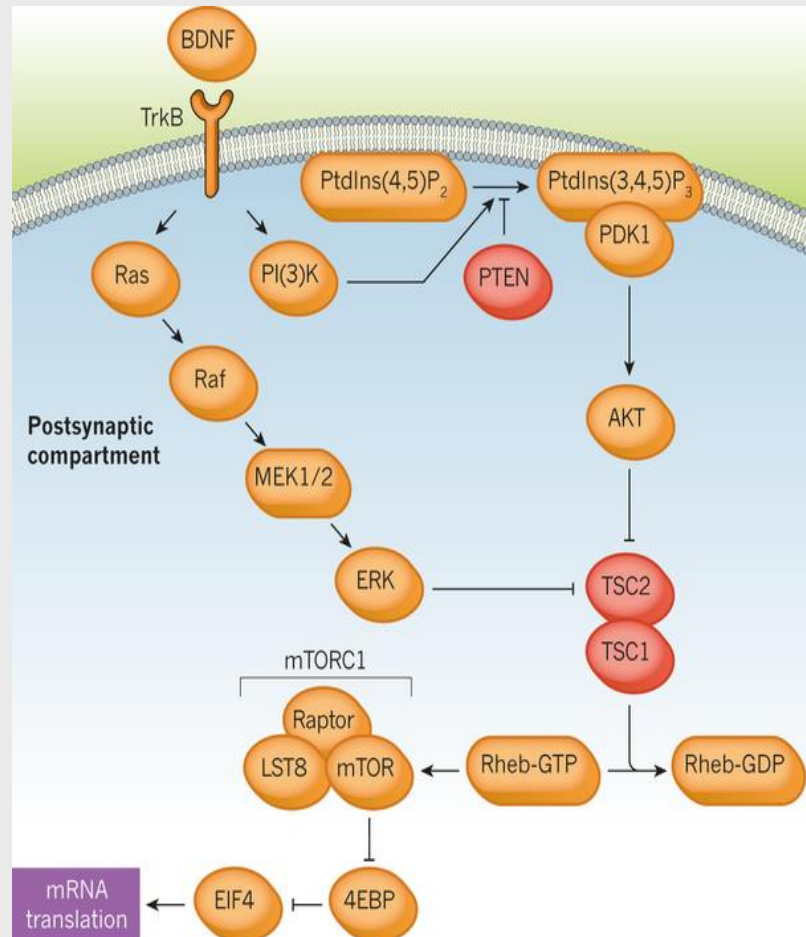


Figure 6. Proposed underlying mechanisms of vergence-based oculomotor rehabilitation (OR). BI = base-in, BO = base-out.

Activation and function of immediate-early genes in the nervous system. *Biochemistry and Cell Biology*. 2011.

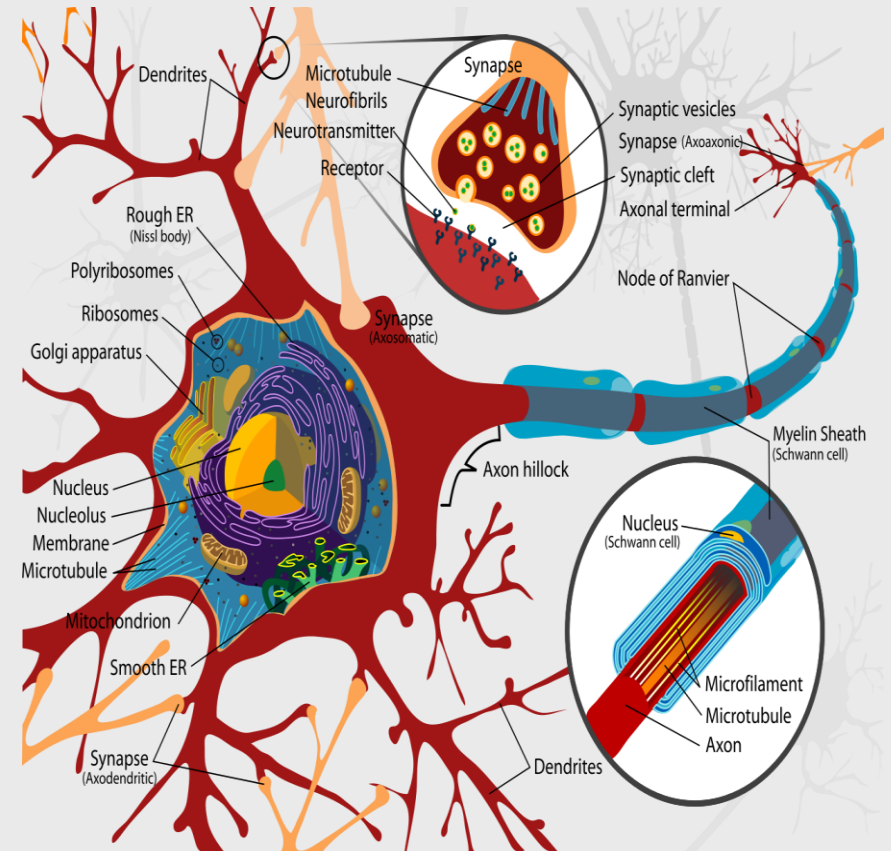
- Plasticity refers to the neuron's capability of showing short or long lasting phenotypic changes in response to different stimuli and cellular scenarios.
- Neuronal responses to stimuli can be classified as early and late responses.
- The early response occurs rapidly after stimulation and lasts from milliseconds to minutes. During this process, a first messenger interacts with cell surface receptors and activates the second messenger system composed of protein kinases that phosphorylate certain neuronal proteins to execute the appropriate neuronal response.
- The late responses last from hours to days and can even result in permanent changes under certain circumstances within the neuron.
- Over 500 rapid response genes have been reported in the neural system, and encoded proteins act as mediators, linking nerve cell membrane events to the neuronal genome.



The function of activity-regulated genes in the nervous system.

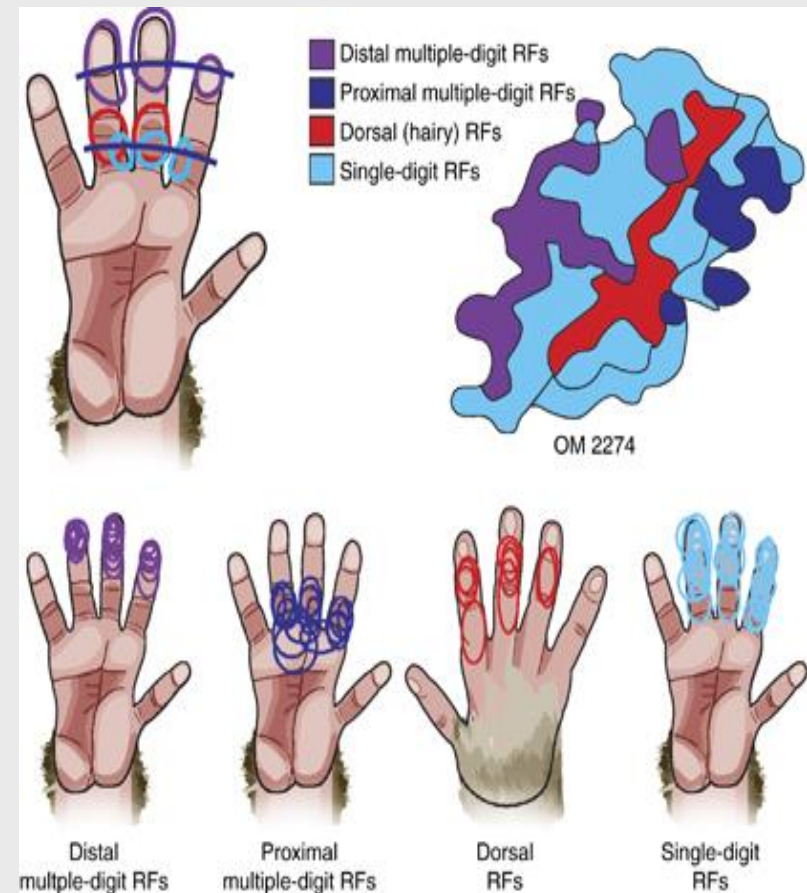
Physiological Reviews. 2009.

- Groundbreaking work in the 1960s and 1970s demonstrated that brain plasticity is shaped by sensory input during critical periods of development.
- Later studies demonstrated that brain plasticity is not limited to development but persists in adulthood and seems to be an inherent feature of everyday brain function, critical for learning and memory, and the adaptability of primary sensory maps.
- In work for which they received the Nobel prize, Bishop and Varmus showed the first molecules to translate extracellular signals to transcriptional programs that alter cell properties.
- Studies of protooncogene IEGs such as c-fos introduced the general concept that gene transcription in the nucleus is part of the cellular response program to alterations in signaling from outside the cell. Neuronal plasticity is a consequence of potentially overlapping and interacting actions of a wide number of genes.
- The large number of genes induced by neuronal activity are the backbone of the synaptic and cellular machinery and their regulated expression is a means to dynamically tune everyday neuronal function.
- Endogenous immediate early gene expression in the brain is a result of normal synaptic activity and could therefore be influenced by neuronal stimulation or activity blockade in a pathway and stimulus specific manner. IEG activation is a part of a neuronal response program to natural stimuli, their expression could be used as a metabolic marker for mapping functional pathways at a cellular level.



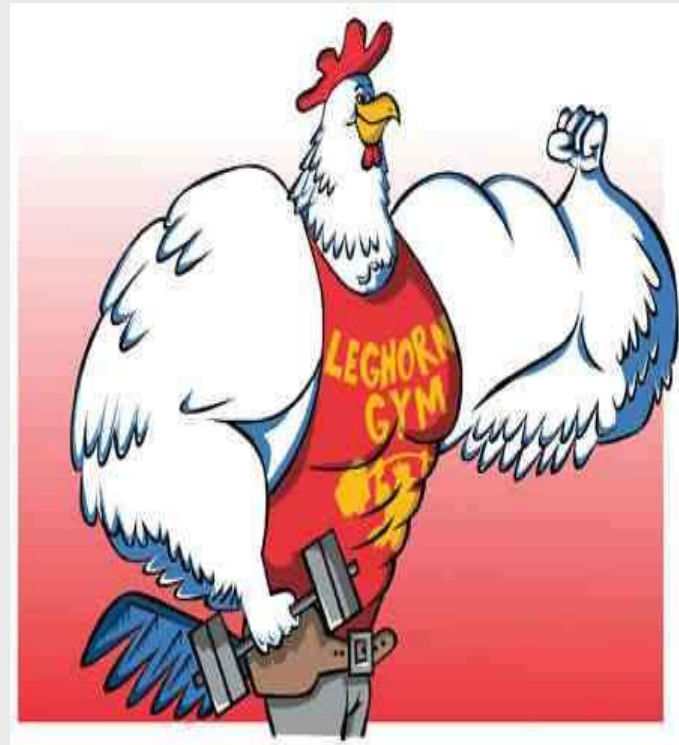
Activity-dependent structural plasticity. *Brain Research Reviews*. 2009.

- Neuronal activity is crucial for governing structural plasticity and maintaining neuronal homeostasis.
- Structural plasticity comprises changes in synapse numbers, axonal fiber densities, axonal and dendritic branching patterns, synaptic connectivity patterns, and even neuronal cell numbers. Changes in the synaptic wiring scheme of a neuronal network arise from deleting and/or forming new synapses.
- Sensory deprivation during development causes severe miss-wiring of the visual as well as the somato-sensory cortex. Visual deprivation during development causes suppression in axonal outgrowth and branching of thalamic and primary visual cortical neurons.
- Peripheral lesions are able to induce reactive plasticity in the primary somato-sensory cortex. Cutting the medianus nerve in monkeys innervating the medial half of the hand and the first two and a half fingers is compensated by the nervus ulnaris taking over the lost innervation. Sensory deafferentation of cortical tissue can lead to substantial remapping of somato-sensory representations.
- Reactive structural plasticity was not restricted to the primary motor cortex of the contra-lateral hemisphere but included the corresponding cortex area ipsi-lateral to the lesion. Bilateral rewiring may be caused by interhemispheric disinhibition.



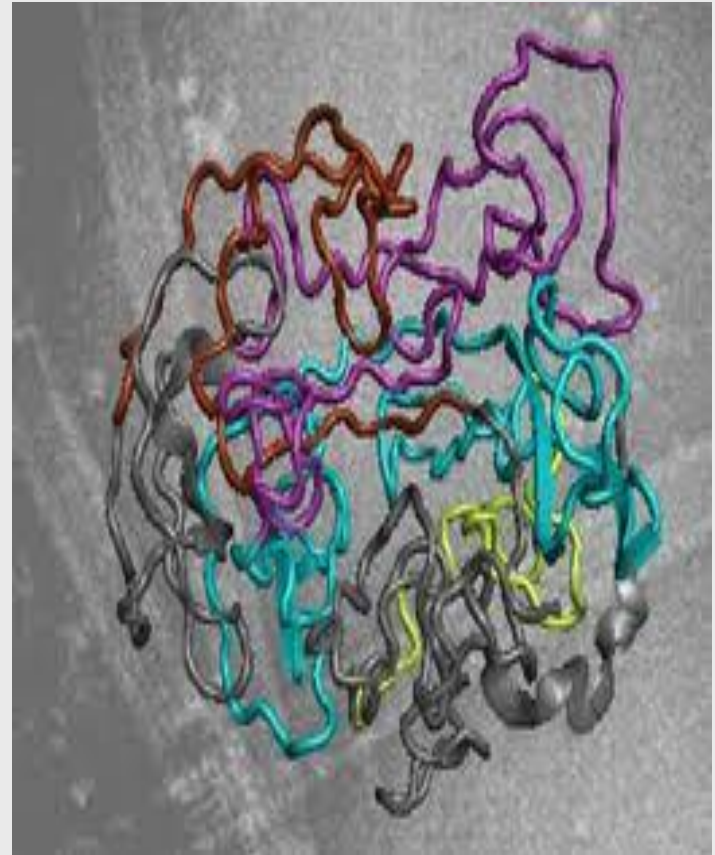
Identification of the location, extent, and pathway of sensory neurologic feedback after mechanical stimulation of a lateral ligament in chickens. *Spine*. 1997.

- **OBJECTIVE:** Trace the location, extent, and pathway of sensory feedback after the mechanical stretching of a lateral spinal ligament in young chickens.
- **CONCLUSION:** FOS protein was identified in nerve cell bodies in the dorsal root ganglia, intermediate gray matter of the spinal cord sympathetic ganglia, nucleus cuneatus and gracilis, vestibular nuclei, and the thalamus. These sites of FOS production suggest involvement of both dorsal columns and spinocerebellar tracts.



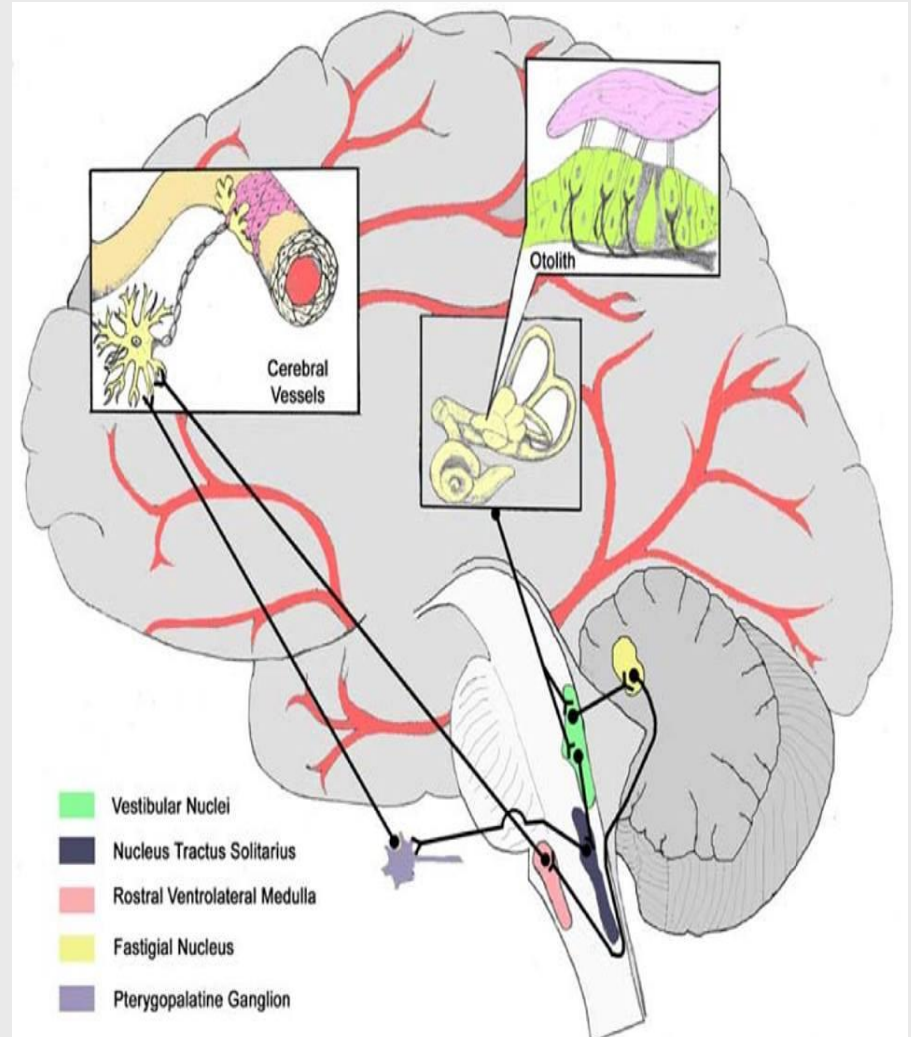
Physiological release of endogenous tau is stimulated by neuronal activity. *European Molecular Biology Organization Reports*. 2013.

- **OBJECTIVE:** Investigate mechanism of physiological release of endogenous tau.
- **CONCLUSION:** Stimulation of neuronal activity, or AMPA receptor activation, induces tau release from healthy, mature cortical neurons. Tau secretion is therefore a regulatable process, dysregulation of which could lead to the spread of tau pathology in disease.



Vestibular effects on cerebral blood flow. *BMC Neuroscience*. 2009.

- Humans demonstrate a number of unique adaptations that allow for the maintenance of blood pressure and brain blood flow when upright.
- Anatomical evidence in animals demonstrates that neural connections are present between the vestibular nuclei and cerebral vessels through two possible pathways.
- Connections have been found between the Vestibular Nuclei and the Fastigial Nucleus, then to the Rostral Ventrolateral Medulla, followed by vasodilatory connections to the cerebral vessels.
- Similarly, neurons travel from the Vestibular Nuclei to the Nucleus Tractus Solitarius and then to the Pterygopalatine Ganglion, resulting in cerebral vasodilation.
- The experimental results support our hypothesis and provide evidence that activation of the vestibular apparatus, specifically the otolith organs, directly affects cerebral blood flow regulation, independent of blood pressure and end tidal CO₂ changes.



Saccades Improve Postural Control: A Developmental Study in Normal Children. *Plos One*. 2013.

- Our results showed that performing saccades improves postural stability with respect to a simple task (fixation) regardless of age.
- This study shows an interaction between the oculomotor and the postural system, according to the fact that the same structures of the central nervous system play an important role in postural control as well as in programming and executing saccadic eye movements.



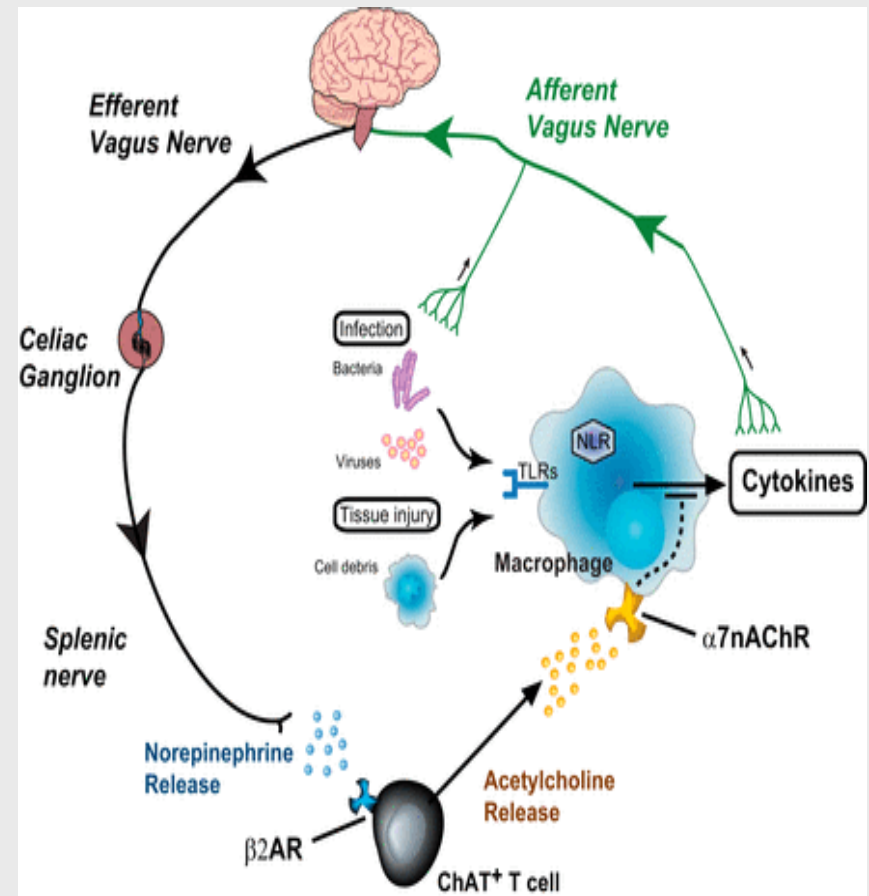
Medical Therapies for Concussion. *Clinical Sports Medicine*. 2011.

- Previous literature has grouped the symptoms after a sport-related concussion into 4 general categories.
- Sleep Disturbance
 - The management of sleep disturbance should include, and perhaps start with, a discussion of sleep hygiene. Eliminating these distractions from the bedroom, and lying down to rest in a quiet, dark room, helps the athlete to fall asleep.
 - Melatonin, an endogenous hormone produced primarily by the pineal gland from serotonin, and Trazodone, a serotonin reuptake inhibitor, are commonly used agents to treat sleep disturbance after traumatic brain injury.
- Somatic
 - Headache is the most common symptom reported after concussion. Ibuprofen may be beneficial in the short term, but the rebound headaches complicate treatment and recovery and are discouraged. Antidepressants, Amitriptyline, Beta-blockers, calcium channel blockers, valproic acid, topiramate, triptans, dihydroergotamine, and gabapentin are all prescribed for headaches.
 - Biofeedback, physical therapy, trigger point injections, and psychotherapy may all either be primary or adjunctive treatments for posttraumatic headaches.
- Emotional
 - Tricyclic antidepressants and serotonin reuptake inhibitors are recommended as options in the treatment of traumatic brain injury-related depression.
- Cognitive
 - Cognitive symptoms, such as difficulties with memory, difficulties with concentration, and slowed processing speed, are common complaints after concussive brain injury.
 - Methylphenidate, a dopamine reuptake inhibitor, Amantadine, a dopaminergic agent with possible NMDA effects, have shown some improvements in cognition after a mTBI.



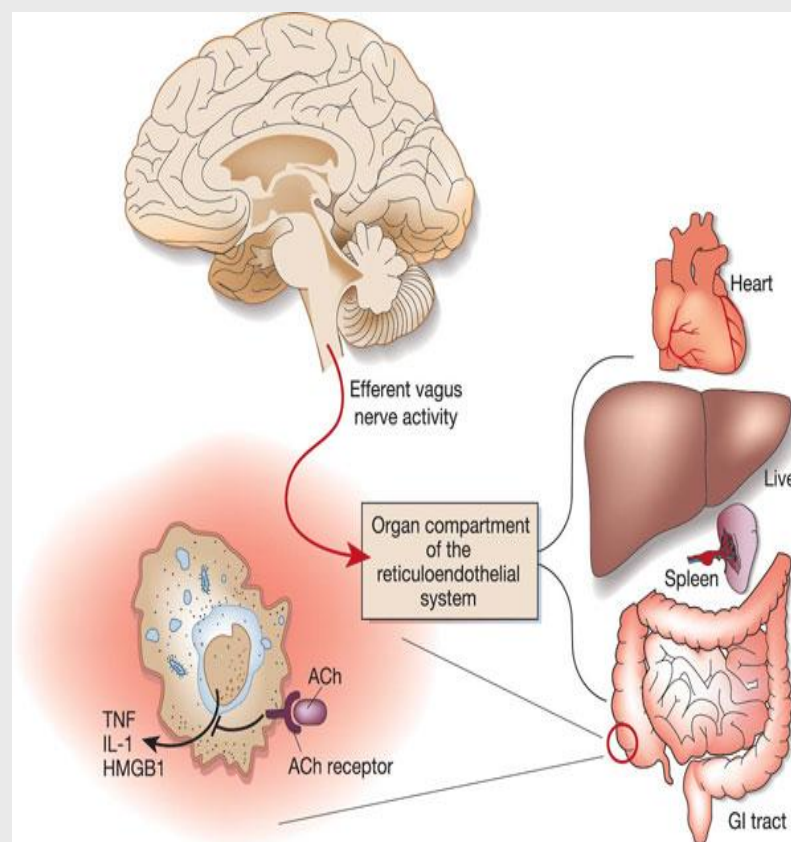
Neural control of the immune system. *Advances in Physiology Education*. 2014.

- Recent advances in neuroscience and immunology have revealed that neural reflexes also regulate the immune system. Activation of the vagus nerve modulates leukocyte cytokine production and alleviates experimental shock and autoimmune disease, and recent data have suggested that vagus nerve stimulation can improve symptoms in human rheumatoid arthritis.
- Neural reflex circuits regulate and optimize organ function, including immune responses, in evolutionarily ancient animals and mammals. Developments in the field of neural immune control have spawned clinical trials focused on novel therapies for inflammatory disease, for example, drugs that modulate α_7 nAChR signaling and implantable nerve stimulators. The emerging field of bioelectronic medicine holds promise, and it is possible that nerve stimulators will be part of the standard treatment for select inflammatory diseases in a not very distant future.



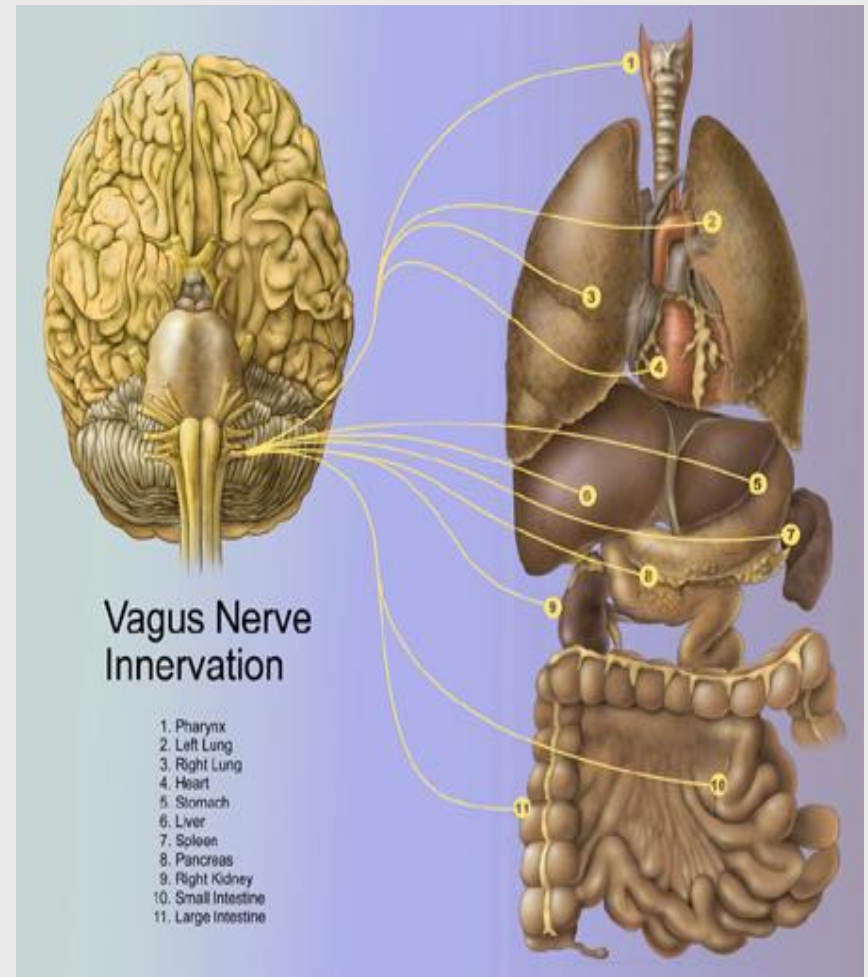
Efferent Vagal Nerve Stimulation Attenuates Gut Barrier Injury After Burn: Modulation of Intestinal Occludin Expression. *The Journal of Trauma*. 2010.

- **OBJECTIVE:** Severe injury can cause intestinal permeability through decreased expression of tight junction proteins, resulting in systemic inflammation. Activation of the parasympathetic nervous system after shock through vagal nerve stimulation is known to have potent anti-inflammatory effects; however, its effects on modulating intestinal barrier function are not fully understood. We postulated that vagal nerve stimulation improves intestinal barrier integrity after severe burn through an efferent signaling pathway, and is associated with improved expression and localization of the intestinal tight junction protein occludin.
- **CONCLUSION:** Vagal nerve stimulation performed before injury improves intestinal barrier integrity after severe burn through an efferent signaling pathway and is associated with improved tight junction protein expression.
- **COMMENTS:**
 - Cervical vagal nerve stimulation decreased burn-induced intestinal permeability to FITC-dextran, returning intestinal permeability to sham levels. Vagal nerve stimulation before burn also improved gut histology and prevented burn-induced changes in occludin protein expression and localization. Abdominal vagotomy abrogated the protective effects of cervical vagal nerve stimulation before burn, resulting in gut permeability, histology, and occludin protein expression similar to burn alone.



Stimulating the Central Nervous System to Prevent Intestinal Dysfunction After Traumatic Brain Injury. *The Journal of Trauma*. 2010.

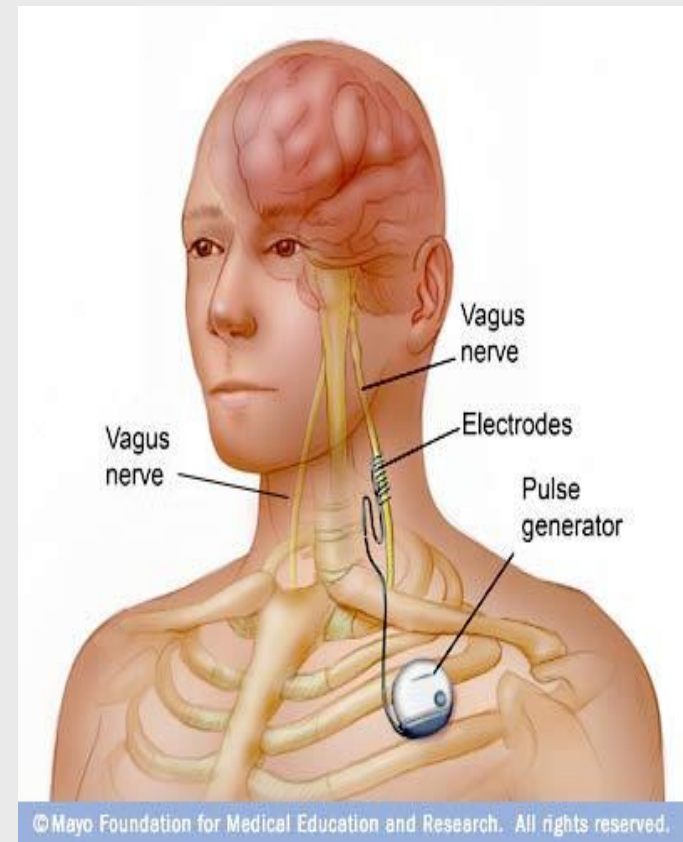
- Intestinal dysfunction, specifically blunting and necrosis of intestinal villi and increased intestinal permeability, can occur as early as 6 hours after TBI.
- The mechanism causing post-TBI related intestinal dysfunction is likely multifactorial and probably include an unchecked inflammatory cytokine milieu, altered intestinal cellular architecture, epithelial cell apoptosis, and changes in tight junction integrity.
- Vagal stimulation before TBI prevented an increase in intestinal permeability, preserved intestinal architecture and decreased intestinal TNF-alpha after TBI.
- Vagal stimulation increases levels of synaptic acetylcholine specifically at the α_7 muscarinic receptor of immune cells (i.e. macrophages), which consequently decreases the release of TNF-alpha.
- A decrease in neuron proliferation of the dorsal motor nucleus of the vagus (DMNV) from adult rats with chemically induced colitis compared with normal adult rat intestine, suggesting that intestinal inflammation adversely affects neuronal survival and function in the DMNV. If the brain, and specifically the DMNV, is responsible for maintaining intestinal homeostasis, TBI-induced intestinal dysfunction may be a result of dysregulation of the neuroenteric axis.
- In a mouse model of TBI, our preliminary results show vagal nerve stimulation prevented TBI-induced intestinal permeability, prevented intestinal injury, and significantly reduced intestinal TNF-. Vagal nerve stimulation also increased enteric glial activity as measured by an increase of enteric GFAP and may represent a pathway for central nervous system regulation of intestinal barrier dysfunction.



Vagal Nerve Stimulation Decreases Blood-Brain Barrier Disruption After Traumatic Brain Injury.

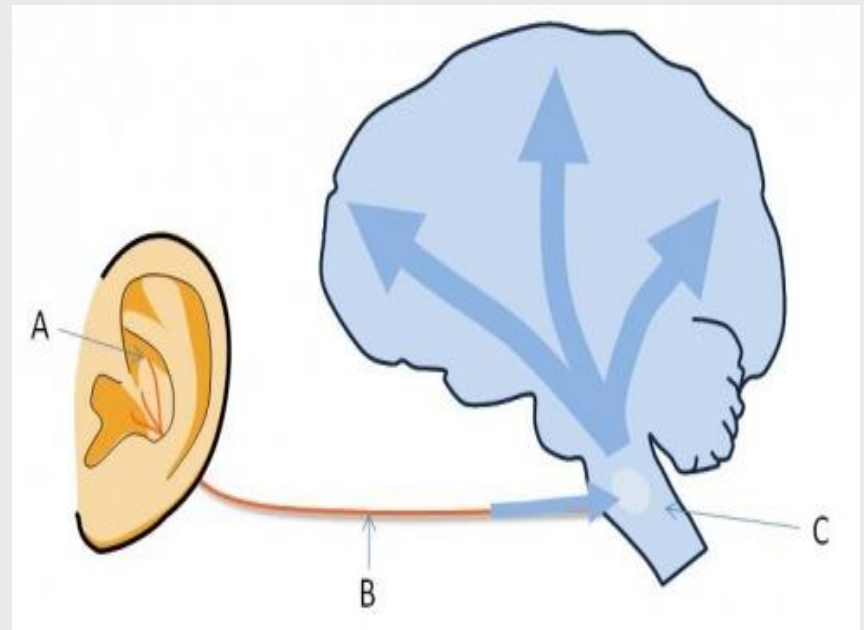
Journal of Trauma and Acute Care Surgery. 2012.

- **OBJECTIVE:** Traumatic brain injury (TBI) may alter sympathetic tone causing autonomic abnormalities and organ dysfunction. Vagal nerve stimulation (VNS) has been shown to decrease inflammation and distant organ injury after TBI. It is unknown whether VNS may reduce blood-brain barrier (BBB) dysfunction after TBI. We hypothesize that VNS prevents TBI-induced breakdown of the BBB, subsequent brain edema, and neuronal injury.
- **CONCLUSION:** Six hours after TBI, cerebral vascular permeability was increased fourfold compared with sham. VNS prevented the increase in permeability when compared with TBI alone. Vagal nerve stimulation attenuates cerebral vascular permeability and decreases the up-regulation of AQP-4 after TBI. Future studies are needed to assess the mechanisms by which VNS maintains the BBB.
- **COMMENTS:**
 - Perivascular expression of AQP-4 was increased twofold in TBI animals compared with sham.
 - VNS decreased post-TBI expression of AQP-4 to levels similar to sham.



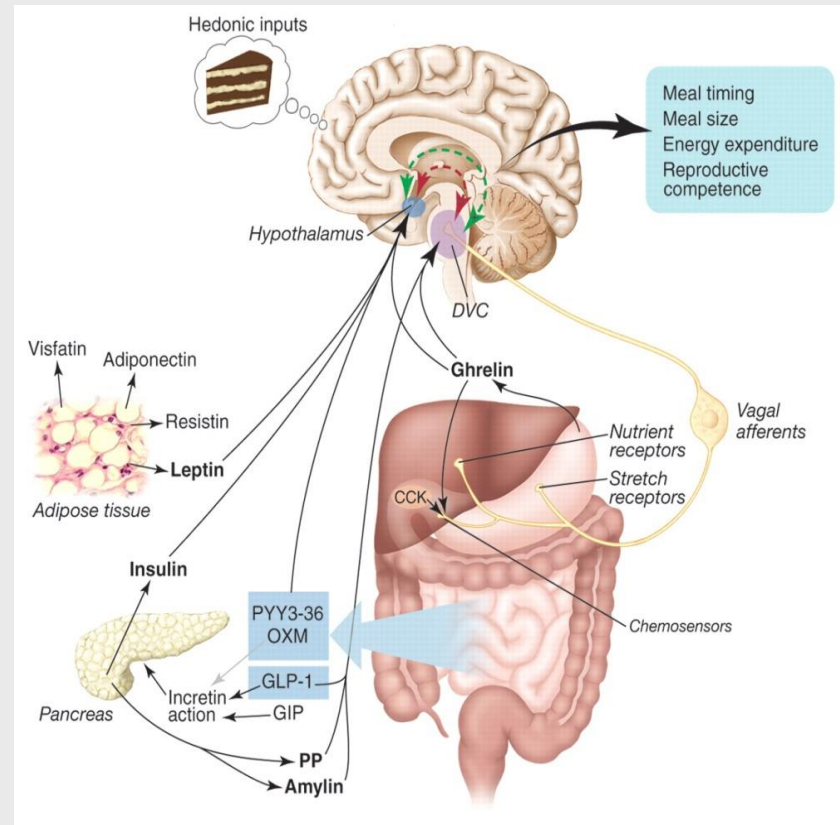
The auriculo-vagal afferent pathway and its role in seizure suppression in rats. *BMC Neuroscience*. 2013.

- **OBJECTIVE:** The afferent projections from the auricular branch of the vagus nerve (ABVN) to the nucleus tractus solitaries (NTS) have been proposed as the anatomical basis for the increased parasympathetic tone seen in auriculo-vagal reflexes. As the afferent center of the vagus nerve, the NTS has been considered to play roles in the anticonvulsant effect of cervical vagus nerve stimulation (VNS). Here we proposed an “auriculo-vagal afferent pathway” (AVAP), by which transcutaneous auricular vagus nerve stimulation (ta-VNS) suppresses pentylenetetrazol (PTZ)-induced epileptic seizures by activating the NTS neurons in rats.
- **CONCLUSION:** : There existed an anatomical relationship between the ABVN and the NTS, which strongly supports the concept that ta-VNS has the potential for suppressing epileptiform activity via the AVAP in rats. ta-VNS will provide alternative treatments for neurological disorders, which can avoid the disadvantage of VNS.



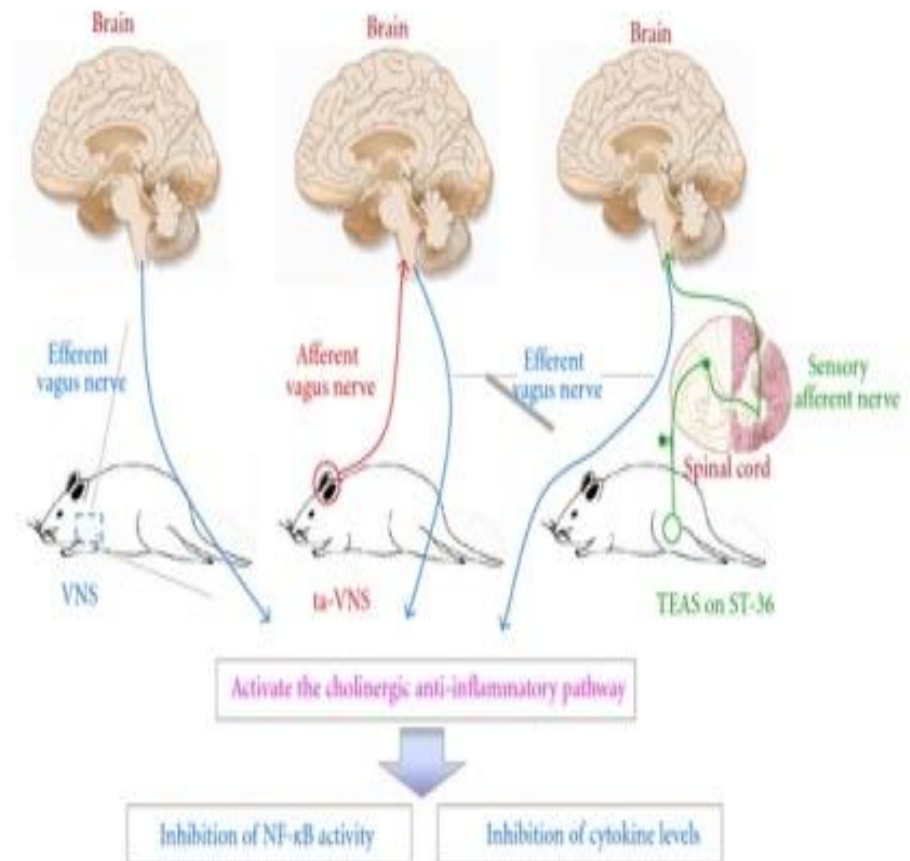
Effect of transcutaneous auricular vagus nerve stimulation on impaired glucose tolerance: a pilot randomized study. *BMC Complementary Alternative Medicine*. 2014.

- **OBJECTIVE:** Impaired glucose tolerance (IGT) is a pre-diabetic state of hyperglycemia that is associated with insulin resistance, increased risk of type II diabetes, and cardiovascular pathology. Recently, investigators hypothesized that decreased vagus nerve activity may be the underlying mechanism of metabolic syndrome including obesity, elevated glucose levels, and high blood pressure.
- **CONCLUSION:** Our study suggests that taVNS is a promising, simple, and cost-effective treatment for IGT/pre-diabetes with only slight risk of mild side-effects.



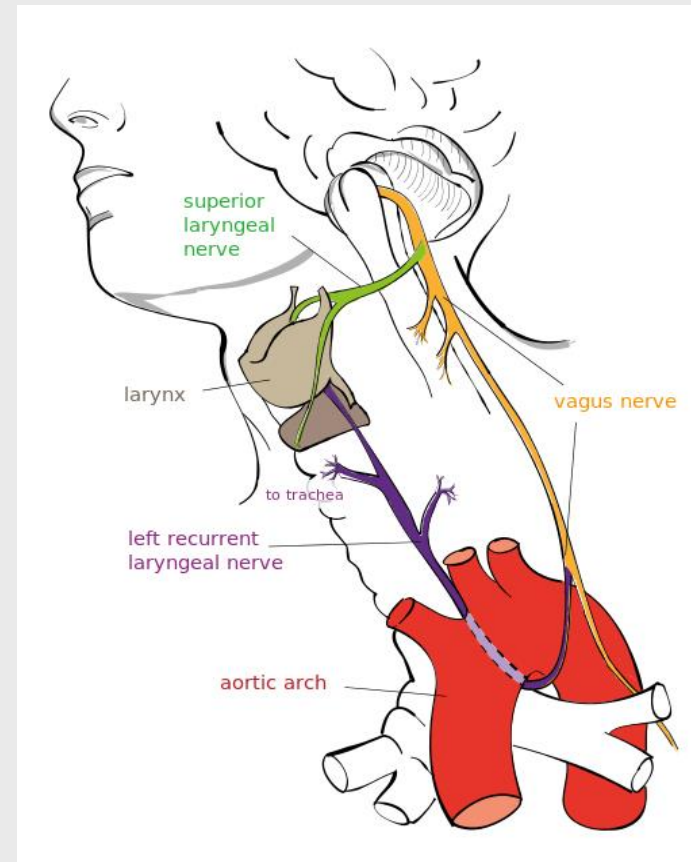
Transcutaneous auricular vagus nerve stimulation protects endotoxemic rat from lipopolysaccharide-induced inflammation. *Evidence Based Complementary Alternative Medicine*. 2012.

- **OBJECTIVE:** Transcutaneous auricular vagus nerve stimulation (ta-VNS) could evoke parasympathetic activities via activating the brainstem autonomic nuclei, similar to the effects that are produced after vagus nerve stimulation (VNS). VNS modulates immune function through activating the cholinergic anti-inflammatory pathway.
- **CONCLUSION:** Transcutaneous auricular vagus nerve stimulation plays an important role in immunoregulation, through the activation of the cholinergic anti-inflammatory pathway and the down-regulation of proinflammatory cytokine expressions and NF- κ B activities. VNS and TEAS on ST36 might suppress the inflammatory responses via different mechanisms.



Non-invasive vagus nerve stimulation in healthy humans reduces sympathetic nerve activity. *Brain Stimulation*. 2014.

- **OBJECTIVE:** Investigate a non-invasive method of VNS through electrical stimulation of the auricular branch of the vagus nerve distributed to the skin of the ear – transcutaneous VNS (tVNS) and measured the autonomic effects.
- **CONCLUSION:** Transcutaneous vagal nerve stimulation (tVNS) increases heart rate variability and alters cardiovascular autonomic control towards parasympathetic predominance. tVNS causes a decrease in vasoconstrictor sympathetic nerve activity recorded using microneurography. As sympathoexcitation is a hallmark of many conditions, including heart failure, tVNS may be a simple and inexpensive therapy for such conditions.



Carrick Brain Centers Concussion Rehabilitation

