

WHERE CTE, DIET, and NEURODEGENERATION MEET.

READERS SUMMARY:

1. HOW DOES CONCUSSION, MSG, AND NEURODEGENERATIVE DISEASE ALL FIT TOGETHER?
2. WHO IS AT RISK? DOES AGE MATTER? DO I KNOW ANYONE WHO HAS HAD THIS?
3. IS ANCEL KEYS A PLAYER IN THE MSG NIGHTMARE TOO?
4. HOW IS ALS TIED TO CONCUSSIONS AND TO EXOGENOUS and ENDOGENOUS EXCITOTOXINS?
5. ARE CONCUSSIONS, AD, ALS and MSG BASICALLY THE SAME DISEASE?

In the first two blogs (1) (2) in this series we looked at the fundamental neurobiology of how excitatory neurotransmitters and exogenous food additives can cause human disease. We discussed that the mechanism of disease progression is affected by age, species, and the energy status of the neuron at the time of exposure or injury. Today we are going to explore how acute neurologic aspects of cranial trauma relates to progression to long term neurodegenerative disease. We also must remember that these athletes, soldiers, and high school students are simultaneously ingesting huge amounts of MSG and aspartate in a standard American diet. I would hope that every person reading this would avoid exogenous sources of excitotoxins going forward. This is especially true if you have sustained a traumatic brain injury or a concussion in your lifetime. Realize that even one concussion can cause this affect to steam roll if you either continue to add insult to the injury exogenously (MSG or Aspartame) or endogenously (injury or disease). Traumatic brain injury accounts for more than 1 million emergency room visits each year. According to the Centers for Disease Control and Prevention, an estimated 3.8 million sports and recreation-related concussions occur in

the U.S. each year. So most of these injuries never come for any treatment at all. Moreover, MSG and aspartame sensitize injured human nerves to the effects of acute concussion when they occur. The more processed food you eat as an athlete, the more likely you will suffer long term damage from your concussion. The age the injury occurs also is a cause for concern. The younger this occurs, the worse the outcome will be long term. The more occurrences of the insult will increase the severity and depth of the disease you get. I will share with you many examples of where this has already happened to many people you have an ambient awareness of. The people who usually sustain "minor" traumatic brain injuries are athletes, soldiers, and people in driving accidents. Falls, blast injuries and projectile injuries are also some common causes of concussion and chronic traumatic encephalopathy (CTE).

Short Historical Overview of the Concussion debate:

With the autumn now upon us, it is football season in all age groups and in the professional ranks in America. In the last decade, acute neurologic trauma in the form of concussions has made huge national news because of high profile injured athletes whose careers were cut short and in some cases their life ended. For decades the issues of concussions in the NFL was accepted as collateral damage to the dangerous sport. We had leading physicians working for the NFL (Elliot Pellman MD) telling us that there was absolutely no connection between trauma and early onset neurologic disease and early death. Dr. Pellman's medical position was an insult to every neurosurgeon's intelligence back then. When he retired from the committee in 2007 I thought the NFL was making a prudent medical legal decision. When I heard from some of my former patients who were NFL players that he was still working for the NFL in an advisory role of return to play decisions I was floored. It was clear he was acting as "a friend" to an 8 billion dollar business. He was the commissioner's doctor beginning in 1997, and many of the medical doctors in NFL

circles knew this. He was a politician and he used his influence with NY Jet owner Leon Hess and then NFL commissioner Paul Tagliabue to sit as committee chairman on the NFL mild TBI committee. In 2007, the data became so overwhelming that changes were finally made. Pellman resigned, but what he did to several Jet players in my mind was unconscionable. What caused these changes was data collected on high school and college athletes. A concussion is a form of traumatic injury. When a concussion occurs there is a temporary loss of neurologic function due to uncoupling of energy metabolism from cerebral blood flow. The acute injury causes a massive release of endogenous excitatory neurotransmitters into the damaged area and causes a disruption of the blood brain barrier (BBB). The mechanism of the injury decreases local energy supply in those damaged nerves, while increasing released excitotoxins locally from damaged neurons. The trauma simultaneously, allows for free passage of toxins across the blood brain barrier and the intestinal brush border. We saw in the last two blogs this is precisely what sensitizes the brain to chronic neuronal degeneration in Alzheimer's, Parkinson's, Huntington's, and in ALS. Electron microscope studies of the astrocytes that form the BBB have shown that concussion trauma allows for "leakiness" to occur at this protective brain layer. Several proteins have been found to be present in the CSF after acute injury and can be used as a biomarker. This protein is called TDP-43. There are many others being looked at as well. We will talk about this protein later.

Remember from the last blog, we now know that dietary excitotoxins concentrate in the brain where glutamate receptors are located. We also reviewed data that shows humans absorb these compounds far more than any other species. Younger patients absorb them faster and concentrate them faster in the brain. While there are philosophical questions concerning head injury regulations for professional athletes, it is clear that the athletes whose interests are least

protected and who are most at risk for injury are the young male and female athletes who, by virtue of their less developed physique and developing brains, and concentrated diets filled with excitotoxins, are more prone to concussions and potentially to CTE. Adding to the concern are data that their guts and blood brain barrier are more permeable to excitotoxins once the injury occurs. Most glutamate receptors are found in the frontal and temporal lobes where most concussions tend to occur. While many parents and athletes think that concussions rarely occur in sports such as lacrosse, soccer, softball, and baseball, recent data suggests that concussions occur more frequently than previously thought in these sports. Kevin Guskiewicz, PhD, ATC, who is a professor and Director of the Sports Medicine Research Laboratory at the University of North Carolina at Chapel Hill reported dramatic data on the increased incidence of concussions in a study done in 2007. It was thought that repetitive concussions led to the development of CTE in the mid 2000's. This changed abruptly in 2009, by way of research, and the case of a suicide of a 21 year old college football player.

CTE at first, was considered a disease of older athletes, but recent studies also have identified it in younger athletes. In 2009 a study commissioned by the NFL and conducted by the University of Michigan Institute for Social Research on 1,063 retired NFL athletes found that 6.1 percent of athletes 50 and older reported that they had received a dementia-related diagnosis; this rate is five times higher than the national average of 1.2 percent. Importantly, those age 30 through 49 showed a rate of 1.9 percent, or 19 times that of the national average (0.1 percent).

Simultaneously, some high profile NFL concussion cases began to show up on the national radar. The deaths of NFL players Mike Webster, Andre Waters, Terry Long, Tom McHale, and Justin Strzelczyk were the first wave of evidence that concussions and CTE were linked. There were many other cases that where

yet to be explored. Drs. Ben Omalu (neuropathologist) and Julian Bailes (neurosurgeon) have played a pivotal role in CTE research, having reported on the first three cases of CTE in professional American football players. They formed the Sports Legacy Institute to study concussions and CTE and the future development of addiction, depression and eventually neurodegenerative diseases. As soon as they began to study these issues, the case of Chris Benoit hit the presses. He was a WWE wrestler who killed his wife and son before committing suicide at age 40. Dr. Omalu examined his brain and confirmed that he suffered from the classic pathologic findings of CTE. This was followed by the unexpected death of WR Chris Henry from the Cincinnati Bengals when he fell out of the back of his pick up truck. His brain was examined and found to have CTE at age 26. His college and NFL career was marred by behavioral problems that were well documented. Dave Duerson, a retired NFL player who played for the Bears in their heyday, then committed suicide at age 50. He was the 1987 NFL "Man of the Year" and sat on the board of Notre Dame University. He was well educated and well respected. Prior to committing suicide he texted his friends and family and asked them to donate his brain to the Boston University School of Medicine which studies CTE. He knew this information ironically, because he worked for the NFLPA's union and reviewed retired players medical benefit cases. He knew something was wrong with himself. His behavior and emotional state dramatically drifted. He had enough cognitive functioning remaining to plan his suicide by shooting himself in the chest to allow his brain to be studied. This case made the NFL really take note of the causal relationship of concussion to CTE. Boston University has examined the brains of 14 former NFL players and found that every one of them have some form of CTE.

In 2010, 21 year old University of Pennsylvania lineman Owen Thomas suffered from post concussion syndrome of severe memory loss , depression, and headache. He committed suicide and his brain also revealed profound CTE present. What made his case

dramatic was his age and quick onset of symptoms with limited recorded trauma. His case has been closely scrutinized because of his amateur status, his age, and his college dorm diet. Thomas was the second amateur football player diagnosed with CTE, after Mike Borich, who died at 42. Pathological evidence of CTE also has been found in an 18-year-old high school football athlete who had sustained multiple concussions. With more than a million teenagers competing in football every year, the risk of CTE looms as a potential public health disaster. Neuropathologists at Boston University also diagnosed Reg Fleming as the first hockey player known to have the disease. This discovery was announced in December 2009, six months after Fleming's death.

On December 21, 2009, the National Football League Players Association announced that it would collaborate with the CSTE at the Boston University School of Medicine (BUSM) to support the Center's study of repetitive brain trauma in athletes. Additionally, in 2010 the National Football League gave the Center for the Study of Traumatic Encephalopathy (CSTE) a \$1 million grant with no strings attached. In 2008, twelve living athletes (active and retired), including hockey players Pat LaFontaine and Noah Welch as well as former NFL star Ted Johnson, committed to donate their brains to CSTE after their deaths. In 2009, NFL Pro Bowlers Matt Birk, Lofa Tatupu, and Sean Morey pledged to donate their brains to the CSTE. In 2010, 20 more NFL players pledged to join the CSTE Brain Donation Registry, including Chicago Bears linebacker Hunter Hillenmeyer, Hall of Famer Mike Haynes, Pro Bowlers Zach Thomas, Kyle Turley, and Conrad Dobler, and Super Bowl Champion Don Hasselbeck. Casey Fitzsimmons a TE for the Lions was forced out by the Detroit Lions neurologic consultants because of his history in 2010. He has also agreed to have his brain studied at his death. In 2010, professional wrestlers Mick Foley and Matt Morgan also agreed to donate their brains upon their deaths. Andrew Martin, a former professional wrestler, who also died of complications related to TBI was

also found to have CTE at his autopsy. As of 2011, the CSTE Brain Donation Registry consists of over 300 current and former athletes.

In July 2010, NHL enforcer Bob Probert died of heart failure induced by trauma. Before his death, he asked his wife to donate his brain to CTE research because he noticed that he experienced a mental decline in his early 40s. In March 2011, researchers at Boston University concluded that Probert had CTE upon analysis of the brain tissue he donated. He is the second NHL player from the program at the Center for the Study of Traumatic Encephalopathy to be diagnosed with CTE postmortem.

In July, 2011, Hall of Fame Baltimore Colt tight end John Mackey died after several years of deepening symptoms of frontotemporal dementia (FTD). FTD is another lesser known neurodegenerative disease cut from the same neuropathologic cloth as AD, PD, ALS, HD, and hypothalamic damage associated with excessive amounts of glutamate and aspartate. BUSM was reported to be planning to examine his brain for signs of CTE. In the summer of 2011, the deaths of three hockey “enforcers” – Derek Boogaard from a combination of too many painkillers and alcohol, Rick Rypien, an apparent suicide, and Wade Belak. All three, as Rypien, had reportedly suffered from depression; and all with a record of fighting, blows to the head and concussions. This led to more concerns about CTE in professional hockey. Boogaard’s brain was recently examined by BUSM but no public results have yet been released. One National Hockey League player known in part for leading “enforcer role”, John Thornton of the Boston Bruins, mulled the “tragic coincidence” of the three recent league deaths and said their concurrence was just that, while defending the role of fighting on the rink. This incongruence can’t and won’t stand under the scientific evidence that is mounting. Stu Grimson, a recently retired NHL enforcer, also was forced to quit the NHL due to post concussive syndrome. He is now a

lawyer in his post career.

Suspected but not proven cases of CTE include Muhammad Ali and his Parkinson's disease diagnosis, Jimmy Ellis, Floyd Patterson, Bobby Chacon, Wilfred Benitez, Emile Griffith, Freddie Roach and Sugar Ray Robinson. CTE also has been documented in nonathletes with repetitive head trauma including those who have suffered physical abuse, autism with head-banging behavior, or epileptic seizures, and those engaged in dangerous occupations such as a man who made his living as a clown shot from a cannon.

IS ALS TIED TO THIS TOO?

Boston University has also found indications of links between ALS and CTE in athletes who've participated in contact sports. A study by Dr. Ann McKee (neurologist) and her colleagues of Boston University CSTE suggests that tau protein deposition may provide a link between CTE and some cases of sporadic amyotrophic lateral sclerosis (ALS), which has been associated with previous head injuries. Three athletes with CTE and motor neuron disease characterized by weakness, atrophy, spasticity and fasciculations were found to have tau protein deposits, TDP-43, in the brain and spinal cord with axonal loss in the corticospinal tracts and medullary pyramids as well as loss of anterior horn cells. While the exact function of TDP-43 is unknown, it is widely expressed and likely is involved in multiple biological processes by binding with DNA, RNA and other proteins. TDP-43 overexpression has been demonstrated to cause neurodegeneration and cell death, both in vitro and in vivo. TDP-43 is the protein that is found in the CSF of the brain and spinal canal after concussion mentioned earlier. There are other biomarkers being studied by the US military. One hypothesis suggests that mild traumatic brain injury causes an axonal shear injury and cytoskeletal disruption, that releases excitatory neurotransmitters into the surrounding area. The shear injury leads to reorganization of neurofilament proteins. This shear allows for TDP-43 to appear

from the repair process and it is highly expressed in the CSF post injury. TDP-43 is upregulated and binds to neurofilament mRNA in order to stabilize the transcript and mediate the injury response. This upregulation of tau causes protein aggregation, misfolding of proteins and then inclusion body formation, neurofibrillary tangles and, ultimately, neuronal death. When the areas around the neurofibrillary tangle are studied by neurochemical analysis there is a startling amount of glutamate found in the surrounding neurons. To me this research finding is critical in understanding how ALS occurs in cases without cranial trauma. It firmly is making scientists review cumulative damage of dietary additives in the etiology of this disease. If trauma increases endogenous release of glutamate and aspartate and can cause ALS and CTE like diseases, it raises even more questions about the exogenous supply of the same chemicals in the Standard American diet our government allows industry to use. Most processed foods use some form of MSG and most "low fat or low carb" foods use aspartate in the form of an artificial sweetener. This is especially true in fast foods and the foods used in infant formulas and baby food. It is also used in many low fat foods that are marketed as healthy to young athletes. Tissues for this study was donated by twelve athletes and their families to the CSTE Brain Bank at the Bedford, Massachusetts VA Medical Center for future ALS studies.

The sports injury data have even made the US government consider the military theater and soldiers risks. The U.S. military is now considering studying this issue as well because of the sheer number of blast injuries that occur in active duty and looking at their use of food additives. These additives were added to K-rations in WW2 after it was found that Japanese POW's food tasted a lot better than US military rations. The reason was that the Japanese added MSG to their militaries foods. The person who altered K-rations was none other than Ancel Keys. The K in K-ration comes from his last name. The Paleo community knows of his scientific

deficiencies. Ancel Keys doctored the Seven Countries Study by self selecting data to prove his belief and sold it to the federal government in the 60s. This study was used to foster the still current belief that serum cholesterol levels cause heart disease. I find it remarkable he was also responsible for adding MSG to K-Rations for our soldiers which has sensitize them to cranial injury and neurodegenerative diseases as they aged. What an amazing legacy for America's best known nutritionist huh?

The Neuropathology Connection:

The fundamental neuropathologic feature of CTE is the topographic distribution of sparse, moderate, and frequent band-shaped, flame-shaped, small and large globose neurofibrillary tangles and neuritic threads in the cerebral cortex, subcortical nuclei/basal ganglia, hippocampus, and brainstem nuclei. Sparse to frequent diffuse amyloid plaques may accompany tauopathy and was seen in only 2 CTE cases. All 7 CTE-positive professional athletes with known apolipoprotein E genotypes had at least 1 E3 allele comprising 5 E3/E3 (71%) and 2 E3/E4 (29%). Alcohol- and drug-related deaths, suicides, and accidental deaths were overrepresented in CTE cohort of brains studied. The slides look identical to those seen in AD or in PD.

The connection is clear. The neuropathology of CTE, Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Fronto-Temporal dementia, olivopontocerebellar atrophy, ALS, and hypothalamic damage from MSG are exactly the same under the microscope of the neuropathologist. There are some subtle anatomical differences due to the time lapse and severity of the trauma and the exposure of the brain to excitotoxic damage. We must continue to follow people, athletes, and soldiers who are suffering from traumatic brain injuries to see how what diseases they develop as they age. Their dietary intake of aspartame, MSG and its derivatives, and L-cysteine must also be followed. It is a critical point

to know that the trauma damages the blood brain barrier to allow these substances to continue to collect in areas where the previous injuries occurred. This is why so many people develop different neurologic syndromes. It helps explain why Muhammad Ali has Parkinson's, why Chris Benoit emotionally charged death was due to severe frontal lobe damage, and why Andre Waters had rapidly progressive Alzheimer's disease with crippling depression. The place of injury dictates where the excitotoxins collect and where the neurologic damage will progress from. Once the injury occurs and the athlete clinically improves the diet needs to be screened for these substances because they will concentrate there and cause severe free radical damage. This damage will "use up" all the neural protectants (antioxidants) like glutathione, progesterone, and the sex steroid hormones in the brain and allow disease to progress. If the person has continued assault by exogenous excitotoxins, a leaky gut barrier, or by a leaky brain blood barrier the incidence of neurodegenerative disease can be easily estimated. The younger this patient is the worse we can expect the disease to be. This poses huge issues for athletes with T2D, IBD, Crohn's, Autoimmune disease, brain tumors, AVM's, seizures, celiac disease, or infectious disease that decreases their immunity. Based upon this data we should be looking at unprecedented neurodegenerative diseases going forward. This is precisely what we are seeing in medicine today. The pathways to this process are diverse but all share a common disease pathway eventually.

Concussions, MSG and Alzheimer's are basically the same disease at different points on the continuum of neuropathology. This explains why so many former NFL players suffer from addiction, depression, neurodegeneration, cognitive decline, obesity, and decreased longevity. Their should be recommendations made to offset the damage based upon what we know. In my opinion not enough is being done. I treat post concussive syndrome much more aggressively and quite differently than most of the published guidelines because I

feel I understand the neurobiology and the connections to other diseases we mentioned in this blog. I don't believe many others do. And those who do won't act because there is an expensive price tag tied to what should be done. The more they muddy the water the longer the status quo can exist. Studying this particular problem really allows us to tie many concepts together that previously were thought to be unrelated independent medical conditions. It is clear they are not. Many other diseases are also propagated this way and that is why the QUILT is so vital to understanding truly how interconnected things really are.

Next up will be what we should do to prevent this injury and treat it after it occurs.

CITES

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