Alzheimer's Talks Transcript

Do Sports Concussions Increase the Risk of Alzheimer's?
with Dr. Mark Burns, Assistant Professor of Neuroscience and Director, Laboratory for Brain Injury and Dementia at Georgetown University
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George Vradenburg: Good afternoon. This is George Vradenburg. I'm the Chairman and Co-founder of USAgainstAlzheimer's. Welcome today to Alzheimer's Talks. I thank all of you for joining us this afternoon, at least the afternoon on the East Coast, for what promises to be a very interesting discussion around concussions and Alzheimer's.

USAgainstAlzheimer's, as most of you know who have participated in these talks, is a national effort - and actually now global effort - to mobilize people to enforce the political commitments and the industry commitments that we need in order to get to a means of prevention and treatment of Alzheimer's within the next decade. We are moving forward a great deal, a great deal of more activity, a great deal of political support emerging, a great deal of international political support growing and a good deal of innovation on the basic scientific community. We're still lagging because we still haven't been able to get a successful drug candidate through the pipeline. But a lot is happening, a lot of bets are being made, major announcements yesterday by the NIH of roughly $45 million in additional investment in Alzheimer's research both in a prevention trial and some advanced investments in molecular pathways and new targets for potential drugs in the future. So it is a time of great ferment, great activity, and we are hopeful that we can in the next few years drive huge dividends from the investments being made today.

Concussions have been very much in the news as football season begins. The NFL's recent settlement with former players who have sued the NFL for damages to their brains as a result of football, and of course children are going back to school and starting falls sports. So mothers who are concerned about their sons in football, mothers concerned about their daughters in soccer, and of course fathers too.

Today we are fortunate to have as our guest, someone who is focused on traumatic brain injury and the connection to Alzheimer's. Dr. Mark Burns, is an Assistant Professor in Neuroscience and he directs the laboratory for Brain Injury and Dementia at Georgetown University. He will talk with us today about the impact of concussions and traumatic brain injury on the brain and will explain some of his exciting research on how brain trauma can lead to the development of Alzheimer's disease or other dementias.

Just a reminder for everyone on the phone, if you have a question during the call please press *3 on your phone. By pressing *3 you'll be placed into a question queue and you'll speak to someone about the question it is that you wish to put forward. Please have your question ready to share briefly with a member of our staff and then they will get you live on the air as soon as possible, when we open it up for questions in about 30 minutes.

With that introduction, I'd like to turn it over to Dr. Mark Burns of Georgetown University. Mark, thank you for joining us today.

Dr. Mark Burns: Thank you, George and I'd like to start by just saying thank you for the great work that USAgainstAlzheimer's does to educate the population about Alzheimer's disease and your continuing support of AD research, it really does make a big difference. I'd also like to thank Shawn Taylor who's sponsoring this call and who has been a friend to my lab for many, many years and it's great to have her support.

My lab focuses on the links between traumatic brain injury and dementia. We primarily focus on biochemical pathways and finding drug targets for future treatments. I should probably stress that I'm not a medical doctor. I do work a lot with cell cultures, with animal models of traumatic brain injury and Alzheimer's disease and also with human tissue from postmortem tissue.

So what I'm going to do today is, first, I'm going to start by describing the different types of traumatic brain injury. I think there remains quite a large amount of confusion about exactly what a brain injury is. And traumatic brain injury is such an all encompassing term from everything from a gentle bump on your head to getting a spear through your brain, but we're just going to spend 5 or 10 minutes talking about the different types of brain injury and how we classify those different types of brain injuries. And that's going to be very important for the later parts of our discussion to tell the difference between a mild, a moderate, and a severe TBI and where concussion fits onto that spectrum. So we're going to spend the first 15 minutes talking about the effects of a single moderate to severe traumatic brain injury and how that affects your risk of developing Alzheimer's disease in later life. We're going to spend the final 10 minutes discussing concussion and the risk of developing Alzheimer's disease and similar dementias. And at the end of each of these segments I'm going to just quickly stop and discuss how we can use what we've learned in the lab and from our human studies for future treatments and prevention.

I've also received a list of many of the questions that you submitted prior to this call and what I've trying to do is incorporate my answers to those questions within the talk. So hopefully you can get the information that you were looking for. And if I don't address your questions in enough detail, I'd be very happy to take those questions after the talk.

So traumatic brain injury is commonly called TBI, the acronym for Traumatic Brain Injury, and that's what I'm going to be calling it throughout the talk, so TBI stands for traumatic brain injury. We also need to understand a few certain terms that I'll be using in this talk. The first is a risk factor, you'll often hear about risk factors for developing Alzheimer's disease. And so a risk factor is a variable that is associated with the increased risk of getting the disease. It's important to stress that if you have a risk factor it does not necessarily mean that you will get the disease. We're also going to be talking a lot about pathology that happens. Pathology is something that's occurring within the brain of patients. So in Alzheimer's Disease patients they build up two signature proteins, first is called amyloid, beta amyloid or Abeta and this is something that's made inside the cell. But it's made in such large levels in the Alzheimer's disease brain that it kind of gums up the brain, it begins to accumulate outside the brain as an amyloid plaque. Within the neurons we also get a build up of a different protein called tau, we get these tau tangles accumulating inside the neurons. And tau is an interesting protein because it's not just accumulating in Alzheimer's disease, there's a whole bunch of different diseases where a tau accumulates, it's called the tauopathy. And so some of them that you might know, might be frontotemporal dementia and corticobasal degeneration that are similar but different to Alzheimer's disease. They have a build up of tau within their brains as well.

So what is a traumatic brain injury? Well, traumatic brain injury is that all encompassing term. And a Traumatic Brain Injury can occur with or without the loss of consciousness. So many people don't realize that you don't have to lose consciousness to have a TBI. It can occur with or without a fracture of the skull, it can occur with or without bleeding in the brain, it can occur with or without something penetrating into your brain. It can occur as the result of a blow to the head, so that's what we commonly think of when we think of TBI; so you know if we bang our heads in car crashes, if we fall and hit our heads, if we are assaulted and get hit on the head. These are common methods about having a traumatic brain injury. And those kind of TBI's are known as focal injuries, where we have a point of impact that we can identify, we can usually see on scans that we've had some brain damage in that point and so that's a focal injury.

It can also occur without any impact happening at all, so the best way to describe that is to think about whiplash injury. So if you get into a car accident even though you sometimes don't hit your head, when the car suddenly stops your head is going to accelerate forward very, very quickly and because your brain is sitting inside your head is floating in cerebral spinal fluid, it has a slower reaction time. So as your head moves forward, the brain will impact against the back of the skull. And then as you come to a complete stop and your heads whips back again and starts to look up towards the sky, now what's going to happen is that the skull is moving faster than the brain and the brain is going to hit into the front of the skull. So we can get multiple types of damage in the brain from the brain moving around inside the skull.

We can also get breakage of the axons within the brain. I think you shall all know neurons are a very important component of your brain. And the way they work is that there is a cell body and that neuron needs to communicate with another neuron to keep communication going on within your brain and so the communication goes along, a long thin piece of the neuron called an axon. And these axons are very susceptible to breaking and if they break you'll lose a lot function without ever seeing anything on a CAT Scan. So people can be in a coma and their CAT Scans can be quite clear but it's obvious that they've had some kind of injury to the brain, and that's called diffuse axonal injury.

So all of these things come under the umbrella term of traumatic brain injury. So if you end up in the ER with a traumatic brain injury and you'll get graded on something called the Glasgow Coma Scale. So they'll look at different responses, how well you open your eyes in response to different commands, whether you can move limbs to different commands or in response to pain, whether you're confused or you're giving confused conversation or you're not able to talk at all. So we grade it all in different scales and as you can image if you turn up with a concussion sometimes you can be disoriented to what day it is, what's happening. I know when I got a concussion I couldn't remember what state I was in, that the day before was Christmas day, and these are pretty big events that I was very confused about. So you lose points on the Glasgow Coma Scale and they grade you into a mild, a moderate, or a severe TBI. For moderate and severe TBI you're usually in some level of consciousness or coma, but for a mild TBI you can be quite normal and just a bit confused. So this isn't very informative to those with a mild TBI or concussion, but it works quite well for those with moderate to severe TBIs.

So if we move on to the data that is available for looking at the risk of developing Alzheimer's disease after brain injury, probably the best study that's been out there is a study that was published in the year 2000. And this was a study where the authors followed up with World War II Veterans. These were people that had a traumatic brain injury back in 1944 and 1945. So they followed them up 50 years later in 1996 and 1997. The patients where found through their military records, so they went to the hospital military records found the data, they found 550 people who had a traumatic brain injury and they found over 1,200 controls. These were people that were in the hospital for other things, other than a traumatic brain injury. The classifications that they used for these patients were to call it a mild TBI, these patients had to have a loss of consciousness or amnesia for less than 30 minutes. So this was on the severe end of the mild spectrum, so this was a concussion where they were knocked out for up to 30 minutes or have amnesia for up to 30 minutes. A moderate injury was a patient that had a loss of consciousness or amnesia for more than 30 minutes but for less than 1 day. And a severe injury for them was somebody who had a loss of consciousness or amnesia for greater than 1 day. So they had a quite a wide spectrum there. And what the study found is that those who had a mild TBI, so these are people who were knocked unconscious and had difficulty remembering and were unconscious for up to 30 minutes. They did not have any increased risk of developing Alzheimer's disease at all. But as you got into the more moderate ones, so people that were unconscious for up to 1 day post injury, they did increase their risk of developing Alzheimer's disease by just over a two-fold increase of risk and the severe increase the risk of developing Alzheimer's disease by over four-fold. So we do seem to be seeing that traumatic brain injury can increase your risk of developing Alzheimer's disease later in life, 50 years after the injury, but it's important to stress that it was very dependent on how severe that injury was. That even you were knocked unconscious and you had difficulty it didn't mean that you were going to increase your risk of Alzheimer's. This study also looked at the rates of other dementias not just Alzheimer's disease and they found that many of the other types of dementias also had similarly increased rates which were in the same 2 to 4 fold increased risk as you got into the moderate and severe TBI. So what this is really saying is that it's not just Alzheimer's disease but something is happening in a brain that's had traumatic brain injury that's leading to dementia in later life.

One of the questions I was asked prior to the talk, are using brain games important for delaying the onset of Alzheimer's disease after a traumatic brain injury. And the idea of doing brain games and keeping your mind active is one that is very, very popular in Alzheimer's disease and it's based on the concept that the more active you keep your brain, the stronger the connections between your neurons will be, the synapses will be, and the more synapses you have, the harder the disease will have to work to cause disruption within your brain. This is something we call cognitive reserve. And it's based on the fact that the better educated you are, the less chance you have of having Alzheimer's disease, so those who go through a college and graduate school education have lower rates of Alzheimer's disease compared to those who didn't finish high school.

So one of the great things about having a large military population is that there are very nice records out there that the military do on their soldiers before they are deployed. And so there's been a nice study of Vietnam veterans with the history of penetrating brain injury that was suffered in Vietnam more than 30 years previously. And what the authors found was that these Vietnam veterans who'd had a penetrating traumatic brain injury, so something had gone into their brain, was associated with long-term cognitive decline, so they had memory issues about 30 years later. All of these soldiers had baseline intelligence testing from before their injury and they found that those that had higher scores on their intelligence testing before they were deployed were more protected after injury. So they had better outcome long term after injury than those who had lower intelligence scores prior to injury. So I think the question about you know improving your cognitive reserve by doing games and keeping your brain active no matter what the disease I think is a very, very good idea to help build up your cognitive reserve.

So to understand why traumatic brain injury patients might be developing Alzheimer's disease, we need to look up what's happening in the brain for TBI patients in their fatality. So one of the best brain banks in the world that collects traumatic brain injury victims, it's based outside of Glasgow, Scotland. And they've actually been collecting the brains of TBI victims and long-term survivors for decades. So they've got people in their brain bank that have died up to as little as 1 hour after a traumatic brain injury and those who've survived up to 40, 50 years after a single traumatic brain injury. They've also got a lot of repeat concussion brains and they really do an excellent job in maintaining their bank. So this group in a landmark study done, it's more than 20 years old now, they look at these patients that had died, these are brains from TBI patients that had died about 2 weeks after a traumatic brain injury. And they decided to look for amyloid beta, that's the same protein that's found in Alzheimer's disease brains. And what they found was quite striking in that one in three of those TBI brains, the brains looked like Alzheimer's disease patients. They had a lot of amyloid plaque built up in the brain. What was most surprising was the age of some of the victims. So in normal brains we do begin to accumulate amyloid probably starting at the age of late 50's or early 60's, as part of the normal aging process we will begin to accumulate amyloid in our brain. But before the age of 60 you shouldn't really see it. And what these researchers found was that even in the brains of 10-year-old boys, they found a lot of amyloid built up in that it looked like an Alzheimer's disease brain. So this is very, very unusual and this is one of the first clues that we had that that kind of linked traumatic brain injury to Alzheimer's disease. So these researchers also went through and divided the cases up into different age groups, so they had one group that was under the age of 40, and then 40 to 50, 50 to 60, and then over the age of 60. And in their control cases you don't see amyloid plaque under the age of 60, so they had no plaque at all. And what they found was that in TBI cases under the age of 40, 20% of them had amyloid plaque. In the 40 to 50 year old age group all of a sudden it was 30% of cases. In the 50 to 60 age group, this is 60% of all cases had amyloid plaque. So you can see there was definitely an affect of age in that the older the patient was when they died, when they had their traumatic brain injury, the more amyloid was found in their brain after that TBI. This also happened in the control brains over the age 60, they found 50% of their controls already had amyloid, but after traumatic brain injury this rose to 70-80% of their cases had amyloid.

I've met quite a lot of people over the past few years that have said to me about their parents that have had a fall and all of a sudden in the next 6 months to a year seem to rapidly progress onto Alzheimer's disease that wasn't there prior to the fall. And I think some of this data helps to explain that those patients might have already begun the process of accumulating amyloid that would cause Alzheimer's disease. And after a traumatic brain injury all of the sudden we're almost pumping more amyloid into the system and we're pushing those patients over the threshold for the amount of amyloid that they can cope with and it's causing full blown Alzheimer's Disease.

So what my lab has been focusing on is to understand why the brain makes large amounts of amyloid after traumatic brain injury. As I said to you earlier, it really helps to visualize the neuron and understand the structure, the axon, that long axon, that goes from the main body of the neuron down to the synapse so it can communicate. To keep that neuron alive they need to make a lot of proteins up in the cell body and they need to transport them up and down the axon very, very quickly. Essentially it's like a train track, if you think of a cargo train pulling these very important proteins up and down, up and down the long axon. And after we get a traumatic brain injury we break the axon, we essentially cause a break in the railroad tracks and just like a train derailing, when you think of a train derailing, if you've got a hundred carts coming along and they just keep going and keep pushing off, they just keep piling up at that one break and that's what happens in our axons as well. We have all the proteins that are needed to make Abeta, for you to make amyloid, are derailing off the axon and they've been made in a very, very unusual spot. This is not a place we usually make these proteins at all. So it's quite unusual and very different to normal aging and normal Alzheimer's disease.

So what does all this mean for us? Right now what we have learned is that we're beginning to understand why a moderate to severe traumatic brain injury might be increasing your risk of developing Alzheimer's disease. Because it's not just amyloid this is happening with, this is also happening with tau. Tau is used to stabilize those axons, and when we break them the Tau comes off and begins to turn into the abnormal form and build up within the neuron. And that's why we're seeing this Alzheimer's disease pathology very quickly after a traumatic brain injury.

I think that as George said at the beginning of the talk, we've had a lot of drugs goes through the pipeline to try and treat Alzheimer's disease over the past 5 to 10 years. And these are all drugs that are called disease-modifying drugs. These are drugs that target amyloid and tau. And these are the things that we think cause the disease and none of them are actually available on the market yet. Because they've been failing when we give them to late-stage Alzheimer's disease patients. But I do believe that as these drugs become available, they'll be used after traumatic brain injury to try and reduce the amount of AD pathology that we're seeing in the brains after injury. And research from my lab has already shown that if we use these drugs in mice that we cannot only stop the build up of this Alzheimer's disease pathology but we also reduce the amount of neuronal cell death and brain damage that we're getting in the brain after injury. So to me, a large benefit that we can see using these drugs after TBI. And I think that's something that got a lot of potential for the future. So that's all I'm going to talk about in terms of moderate to severe traumatic brain injury.

And now I'm going to switch my focus to talking about concussion and repeat concussions. And as George said this is getting a lot of press at the moment and I think it's driven a lot of interest and a lot of fear in people because so many of us are exposed to concussions on a daily basis and most of us have had concussions and we certainly worry about our children going to play sports and being exposed to these concussions.

So what is a concussion? I've already spoke to you about mild traumatic brain injury and the fact that on the Glasgow Coma Scale, not much has to be wrong with you, you look pretty normal even after a mild TBI. But it does result in a temporary loss of brain function and this can manifest itself into a variety of emotional, physical and cognitive impairments. So the trouble is, it looks so different in different people, so if some people have difficulty thinking clearly and difficulty concentrating, difficulty reading, you can have physical symptoms like headache, nausea and vomiting, balance problems and fuzzy vision. You can have emotional problems such as anxiety, depression and irritability and also very common are sleep disturbances. One patient might sleep a lot more than usual, somebody else will sleep a lot less than usual. So the symptoms are very diverse and that makes seeing this disorder quite complicated. Because if we could just say okay if somebody lost consciousness, then they're going to go on and have problems, it would be much easier for us to identify the population of people that will go on to have problems but that doesn't seem to be the case.

So when, I work on concussions, I find it very helpful to know the actual definition of concussions. So the first international conference on concussion in sport came out with a definition, only in 2001, that is very, very helpful. And this is what it is: "concussion typically results in a rapid on set of short-lived impairments of neurological function that resolves spontaneously." So you have these impairments of functions that happen immediately after the impact, but they resolve spontaneously. So they supposed to fix themselves and it's good that they should fix themselves because currently we've got absolutely nothing we can do, there are no pharmacological treatments or medical interventions and that's true for not only concussion but also for the more severe TBI as well. So what happens when, when you have a concussion and you end up at the doctors - they prescribe rest. They just want you to not use your brain at all. And what quite often what happens is you're told to sit in a dark room, no reading, no watching T.V., no thinking just doing nothing, your brain needs time to repair itself. And so this can be quite frustrating to deal with, especially when you're dealing with kids who don't understand, and people I've spoken to in the past have been concerned especially because their children have important exams coming up and you know it can be a worrying time. I must say that I think it's the single most important thing you can do. The evidence we're seeing from our animal studies show that even a very, very, very mild traumatic brain injury, that we have no cell death, the brain isn't inflamed, but we lose a lot of the connections, those synapses between neurons immediately after the brain trauma. And what we find is that if we leave the mice to recover, they recover just fine, everything goes back to normal again. And so this is very, very encouraging.

So if this is spontaneously repairable, why are we interfering, why are we still studying this? Well, it turns out that 25% of concussion patients still have symptoms at 3 months post-injury. And up to 10% might still have symptoms 1-year post injury. This is something called post-concussion syndrome. And this is very, very worrying because obviously you can't just sit in a dark room doing nothing for a year after your injury. So we're still trying to understand which of those patients are going to be more susceptible to long-term problems after their concussion.

We're also very worried about something called second impact syndrome, so this is something that's quite rare and isn't really the focused of what we're here to talk about today. But the second impact syndrome occurs primarily in teenagers. And it occurs when, usually in a sports game, somebody suffers from a concussion is then not removed from the field of play and they have a second concussion and they drop dead. It's quite rare, in fact Ireland where I'm from, has just had its first case recorded in the last couple of weeks. And we know that this is a true phenomenon and this is something we can indeed repeat in our animal models that if we take a very mild traumatic brain injury, the mice show some effects, we leave them to recover for up to a week, we hit them a second time and they're okay. It's looks exactly like the first injury, so the two concussions look very similar. However, if we move that second concussion up, if we hit the mouse once, we wait a day and give that same concussion, all of a sudden you can cause a tremendous amount of damage in that mouse brain. And so the brain hasn't had time to recover itself, you get much more injury than you would have had even if you had that second impact a week later and it seems to be quite damaging, especially in teenagers. So that's called second impact syndrome.

But what we're going to talk about today is the risk of developing Alzheimer's disease after a repeat concussion and obviously that's something that’s come up before, there's a lot being discussed right now with the NFL. These are professional athletes who suffer from repeat concussions and this dementia that they are getting looks very similar to Alzheimer's disease. So the first big study that looked at NFL players only got published in 2005 and they followed up more than two and half thousand retired NFL players, and these are people who had an average professional career of about 5 and a half years in the NFL. What they ask these players to do is report how many concussions they had over their career and 60% of them said they had one concussion and 24% of them said they had three or more concussions. And what they also found was that the players that had three or more concussions were 5 times more likely to be diagnosed with mild cognitive impairment, so that's the precursor to Alzheimer's disease. And they were more likely to develop Alzheimer's disease at an earlier age than the general population. So while the rates of Alzheimer's seemed to be similar, it seemed to start earlier in retired NFL players. And this is a really, really excellent study. I mean this is the first study that began to get all this concussion work back into the public eye. I do have a problem with it because when this gets reported in the press the fact that it only appears to take three concussions to cause Alzheimer's disease causes a lot of worry with people and it caused a lot of worry with me as well and one of the things I had difficulty with is, you know, what exactly is a concussion? What are these guys talking about when they talk about concussion? I think first off is that most people think that you have to lose consciousness to have a concussion and that was certainly true with the NFL football players as well, they're self-reporting the amount of times that they were unconscious in their football career. But this is untrue, you do not have to be unconscious to have a concussion. And it's only in the last couple of years that I've realized myself that the symptoms of a concussion are things like seeing stars and having a slow reaction time and dizziness when you get hit in the head. And that was quite concerning to me at the beginning because I grew up in a house with five boys and we were extremely rowdy and I can tell you I've had way more than three concussions and I really suspect that almost all pro-football players have had more than three concussions as well.

So there's a disconnect between what's being reported and on what are people are calling a concussion and what might be calling Alzheimer's disease. And I also think a big difference when we think about what people in the general population and people who play sports for fun, is that pro-sports athletes have had literally thousands of sub-concussive blows in their careers. These are hits to their head that have not caused overt symptoms, so they haven't caused concussion-like symptoms but can definitely add up over time. And a very surprising statistic I heard just last year was from a researcher that was monitoring a high school football program and he said they had one kid there who received over 700 hits to his head in nine high school games over the season. And we'd look to the G's of that, it was quite surprising that one of the hits went up to high as 300 G's of force, which is an incredible amount of force to the head. But that kid had never had a concussion all year in fact none of the people that were being monitored had a concussion in that year. So I think the role of sub-concussive blows as well is very, very important and the fact that these blows are happening over a career through Pee Wee Football, high-school football, college football and pro football are definitely adding up over time.

So the disease that these football players are getting is actually not Alzheimer's disease it's called Chronic Traumatic Encephalopathy or CTE. And so CTE is form of brain damage that we've known about for quite a long time. The symptoms of it were first recorded in boxers back in 1928. So we've known about this disease for almost 90 years and it's one of the reasons why doctors for many, many years called for the banning of boxing because it just seemed like such an easy way to prevent this disease. But now it seems that it's occurring in multiple types of sports including football, ice hockey, rugby, soccer, or any sport associated with an impact to the head.

One of the questions I had was “can this occur after a non-sports injury condition?” There have been reports in the literature, we don't have that many brains, but there have been reports of an elderly women who was a long-term domestic abuse victim and there was another one of a fairly young woman who had psychological issues where she repeatedly used to bang her head against the wall and do self damage. So there are cases outside of sports but they really have to be associated with many, many blows to the head as well.

We know that this is a progressive neurodegenerative disease just like Alzheimer's, it's quite aggressive. In boxers we know that the average time of onset is about 14 years after the start of a career in boxing. So if you think about boxers turning pro at the age of 18 this means they're getting symptoms in their mid 30's. I think one of the things that happened with all the press coverage recently is there's a bit of a misconception that almost all football players are getting this, there have been some very high profile cases. The boxing literature has been studied a lot more extensively and what we know is that about 17% of professional boxers get this condition. So 17% is extremely high, I think that's still unacceptably high, but it's certainly not 100%. Again we are talking about risk factors, it does not mean that all of these people are going to get this disease. And the most common symptoms of CTE are aggression, depression, cognitive impairment, dementia and Parkinsonism and that's one of the most complicated things about it, is that it can look like Parkinson's Disease, it can look like Alzheimer's disease, or it can look like, as somebody astutely mentioned in their questions, the cases of TBI causing Alzheimer's all look more like frontotemporal dementia. And that's exactly what happens, is that they have a lot of problems early on that look more like frontotemporal dementia. When we look in the brains of these patients they look very similar to Alzheimer's disease but it's mainly tau that we see in their brains. So even though we can see amyloid, it appears to play less of a role and be less important than the tau. And it's also a progressive disease and so it can be tracked and we can see where it occurs first and it seems to occur first around blood vessels in the brain and, and for those who've seen a brain you know that the brain surface has all these folds in them. And it also happens down deep in the folds of the brain. And these would be two areas that would be very susceptible to the movement of the brain. You know, if it wasn't causing overt brain damage, the movement of the brain, these are areas that could be stressed out quite easily. So if you have a repeat low-level trauma that keeps causing stress on these points, I think that would help explain why we're seeing these things in those places.

And the stages of those diseases, it's quite progressive as well. So it starts off with a headache, a loss of attention and concentration. It progresses on to include depression, aggression and temporal problems and short-term memory issues. And then it goes on to the executive function in cognitive impairments that are more likely when you have problems with the front of your brain and then it finally, it develops into full-blown dementia and also Parkinsonism as well.

So what can we do to address this if we know that this is an issue and we worry about protecting especially our children who are going to be off in sports? What is it we can we can do to address this? I think the first thing is to work on protection, there were a number of questions about helmet design and how that might be able to prevent brain trauma. And a helmet is actually designed to protect the head. So it's been very, very effective at stopping broken skulls and skull fractures and death through that kind of mechanism. But they've never really been design to prevent a loss of consciousness, so now there are some moves afoot and you'll often see players wearing neck braces and that stops the kind of whiplash injury when a player gets knocked down backwards, so that can reduce concussions. And also some of the manufacturers are developing better protection around the jaw area because many of you know when you think about boxers getting punched in the jaw, the side of the jaw, that's where most concussions originate, that's where people get knocked out that twisting motion of your head causes many people to lose consciousness.

The problem is we don't address sub-concussive blows and I think what's going to have to happen in the future is a change in a way we tackle and that's something is definitely being addressed and you can see those behaviors changing in high schools that have been involved in these research programs. When the data is shown back to them, to the coaches, to the players and to the parents, they start to implement changes in the way they tackle so that the students are no longer using their heads to tackle anymore. They're going back to more of the rugby style tackle where they use their arms and shoulders more than their heads, and I think that's a good thing.

I think we've got a further our education efforts; coaches, players and parents are all beginning to realize what an important issue this is. And there's actually a movement afoot on doing impact camps where the helmets are rigged up to look at how hard the impacts are and to count the number of impacts and after a certain amount of hits to the head are recorded over a certain G-Force, then the player has to be pulled from the game. So this would be similar to a pitch count in baseball where the pitcher can only pitch a certain amount of innings before he'll damage his arm and they pull him out the game. So I think this is a great idea, I think right now it's based purely on guesstimate, we don't know what those numbers are and we're just trying to err on the side of caution.

I think we also need to educate more on the symptoms of a concussion, most people are just looking for somebody who is knocked out cold and that's not really what you're supposed to be looking for, we need to really educate, and the other players as well to notice when their teammates are having some issues out in the field and get them out of the game.

The single most important thing after a concussion is recovery. The brain needs time to heal and if you get a second hit to the head before the brain has fully recovered, then that's going to do a lot more damage then if you had that same impact after the brain was fully recovered. And a startling fact about repeat concussions is that we know that the average recovery takes about 7 days, usually you get full recovery within about 10 days after a sports-related concussion and of course there are outliers to those numbers. But we know that 75% of repeat concussions are happening in sport athletes within the first 7 days. That means that these players were put back on the field before they were ready to be back out there and they got a second hit, they don't have the right balance, they don't have the right faculties about them and they suffer a second concussion. And stunningly 92% of all repeat concussions happened within a 10-day window after the first concussion. So even a simple thing of pulling a player from a game and making sure they're out for 10 days would get rid of 92% of those second concussions which is an amazing statistic.

So that's all I have for my prepared remarks, I'd like to thank you all for joining me on this call today and I'm more than happy to take any of your questions, if I haven't address any of your questions up to now. Thank you.

George Vradenburg: Thank you very much Dr. Burns for really quite an interesting discussion.

Reminder to everyone, if you have a question during the call please press *3 on your phone. By pressing *3, you'll be placed into the question queue. Please have a question ready to share briefly with a member of our staff and we'll try to get you live on the air as soon as possible.

I've got a couple of questions, I mean in both the boxing example, and football examples, you indicate that basically the same trauma to the head of two different people might have differential results. There are boxers who box for a long period of time and don't get these diseases. What do we know about what may be in the brains of many people that is protective in character, I mean is it physical or is it genetic, is it something else, that is potentially protecting most brains even when they get concussions?

Dr. Mark Burns: I think it's an excellent question and it has been examined and the first one is actually, the better the boxer, the less likely he seems to be to get this disease. And what they've tied that back to is that the better boxer managed to keep their heads protected longer, their bouts with other boxers are shorter, they're knocking out their opponents quicker. So this does seem to be a dose response, so the more hits to the head you get, the more likely you are to get the disease. And then they also seem to have found as well the longer your career in boxing or football or anything else that you continue to be hit on the head, the more likely you are to get the disease in later life. But there are also genetic factors involved as well, and for those of you who followed the Alzheimer's disease literature the term ApoE4 won't come as a huge surprise to you. So this is a risk factor for the development of Alzheimer's disease and we see a lot more people who have this gene, that go on to develop Alzheimer's disease it's quite a strong risk factor for the disease. And this gene also appears very strongly in both types of trauma I was talking about today—the single moderate to severe trauma or the repeat concussions. Again the ApoE4 gene is playing a role that people who have that gene and who have the repeat concussions are more likely to get this disease than people without it. So there's definitely a genetic factor involved as well.

George Vradenburg: And one other question, what is it that the brain is doing in the 7 to 10 days that it's self-repairing and is there some intervention that's being explored that would reinforce or accelerate that repair mechanism?

Dr. Mark Burns: I think that's a good question and that's something that my lab is actively working on to try and figure out. And when I first went into this, when we first saw that even a mild traumatic brain injury would cause this wide spread loss of connectivity in the brain, that the neurons stop communicating with each other. We thought, okay this is going to be very exciting if we can prevent that from happening, what we might be able to do is get people back to work quicker and return to function quicker as well. The longer I'm working on this, the more I begin to think that this really is the brain is trying to protect itself, it's withdrawing itself and withdrawing its connections because it needs time to get its balance back again. Because when we have a trauma we get this shock wave that goes through the brain and it causes the release of factors within the neuron that usually we keep lock up quite tightly that it's actually simply calcium, but calcium is so important to keep tightly balanced within the cell. But when we release our calcium it tells the neuron that we've got too much in the cell and it's time to stop communicating with the other neurons as well. So we think it's pulling back those connections in order to let all the neurons just heal themselves to lock back up their calcium again to get its house back in order and then it re-establishes those connections they are not permanently lost, it can reconnect again.

So I'm beginning to change the way I think about this to think that this is something we don't want to stop happening, this is something that if we can let the brain do what it's supposed to be doing in a timely basis then that would probably be better off in the long run. Unfortunately, when we're dealing with things like football or boxing, we don't have time. You can't stop every time you are punched in the head and say okay I need to sit down for seven days before we have the next round of boxing. So I think that's what makes those athletes much more susceptible to long-term issues after this. But I think for your average everyday Joe, who has a concussion that is by far the safest thing that you can do. I do think there is a problem with those patients that have symptoms that go on for longer than 7 to 10 days, I think it then becomes unfeasible to have them just recovering. And that's something we don't have a model of that. So we don't understand why these patients are taking much longer than other patients to recover and until we can model these diseases, including the repeat concussion model we're basing everything we know on a postmortem brain. So, brains that we can get from these patients when they die and we really need to look earlier on. And of course you can't get a concussion brain if the patients don't die from a concussion. So we don't have any signals and we don't have any data that really tell us what's happening inside their brains, which was what makes modeling very important in the lab.

George Vradenburg: Take a sport like soccer, which by the very nature of the game involves headers, involves use of the head with a pretty hard ball as part of the game. Is there any research into whether those headers are increasing concussions and whether those concussions are in fact leading to later dementias?

Dr. Mark Burns: I think that's a good question, and being a European of course I refuse to believe that soccer could be anything but great for your body and soul. But there is data out there that has looked at soccer players and there are soccer players that have had Chronic Traumatic

Encephalopathy. It is a lot rarer than in football players, it is not something that it's commonly seen. I think what usually happens when you deliberately head the ball is that you tighten up those neck muscles, you're preparing yourself for the impact of that ball. I think it would be naive to think a shock wave isn't still going through your head and you are getting some impact to the head. But the data is not conclusive, so there are a lot of researchers now that are building accelerometers that can be worn throughout the soccer games so we're beginning to collect more data now. It will help give us the answer of how many G-Forces these players are experiencing. But I wouldn't be too surprised, especially things like prolonged heading drills that they might do in training where you're just continually heading the ball for up to 20 minutes at a time. That might need to be looked at more carefully once more data is in. But right now from the postmortem data there are soccer players who'd have had this disease but they're very few and far between as far as we know.

George Vradenburg: We have a question from Annette Guidry. Annette, you're live and please ask your questions. Annette?

Question: Hello? Yes. This is Annette. My question is what does severe psychological trauma? Is there any research on severe psychological trauma such as having taken part in a war, being party of an accident, recurrent psychological trauma and the depression that happens after severe psychological trauma and is it related to Alzheimer's. Is there an increased risk?

Dr. Mark Burns: Thanks very much for your question, Annette. I think that's a really important question because what we're beginning to understand, especially if you watch those soldiers coming back from war is that there is a lot of comorbidity between traumatic brain injury, post traumatic stress disorder and long term problems after that. I think that the very quick answer is that we don't know yet. Post traumatic stress disorder and the risk of Alzheimer's disease, that data is really not available. Unfortunately it's hard to decouple in a lot of the patients what the role of traumatic brain injury versus the role of post traumatic stress because quite often those events have happened at the same time especially when you're talking about a soldier coming back from war. But to my knowledge there is no evidence to say that post-traumatic stress disorder is causing the same kind of physical stress on the brains that you're seeing after traumatic brain injury that can be causing these disorders.

George Vradenburg: We have a question here from Meryl Comer. She mentions that brain games, I think you answered this question in your talk but Meryl if you've got a further elaboration on that, we'd loved to hear the question.

Question: Yes, thank you. Doctor Burns, you did mention the use of brain games as a potential therapy after trauma. But there is great controversy about the games themselves and whether or not just the repetitive nature of the games, you get a practice effect rather than it really being a repair function or increasing on-going brain function and capability.

Dr. Mark Burns: I think that's a good point that if you continue to play the same games, are you just going to be strengthening the same set of synapses that you've already built? And that's not a bad thing. At least you're using your brain; at least you're strengthening those synapses. But I would agree that diversity is key like doing lots of different things that make you think, something outside of your comfort zone, is always going to be a good thing for your brain. That making new synapses and making new connections can only be a good thing and struggling with new problems, with new issues. When the brain get stimulated it starts to make growth factors and something called neurotrophins that really help strengthen your brain. And so all of that can only be a good thing in my opinion to do. But just like anything we can find, I mentioned about education being protective, the more education you have. But of course I know lots of people who have PhDs, MDs brilliantly clever people who still come down with this disease as well. So we do talk in terms of risk factors and unfortunately nothing is ever guaranteed to work for this. The best thing we can do is prepare ourselves.

Question: Thank You

George Vradenburg: Are there other behavioral things that can be done to repair or help restore brain function after concussion? I'm thinking of diet or exercise or other mechanisms - behavioral mechanisms or lifestyle mechanisms that have been shown to be helpful in this regard.

Dr. Mark Burns: There are a lot of studies going on right now. I mean most of the data that's out there has focused on the moderate to severe traumatic brain injury. The work on concussions has been so difficult to do, that until recently when everybody got interested in it again, it's been overlooked. But there is definitely evidence out there on the more moderate to severe TBI's that diet is important. Again that, what's always been striking to me is the similarities between what we see in the traumatic brain injury field and what we see in the Alzheimer's disease field. So we talk about omega-3 and 6 fatty acids being important. Somebody had a question about flax oil and whether that was a good thing and flax oil is very rich in omega-3 and 6 fatty acids and these are things that are the essential building blocks of your neuronal membranes. So when you have any damage to these neuronal membranes, having these good diets rich in beneficial oils can only be a good thing. So quite often you'll see that being recommended to patients as well improving their diet, getting lots of fatty acids and things that would be the essential building blocks for neurons in your brain. So anything you've heard essentially for the treatment of Alzheimer's disease also seems to be beneficial for the treatment of traumatic brain injury.

George Vradenburg: One last question from Marilyn Flint. Marilyn would you like to ask your question?

Question: Yes, it's related to what you just spoke about, hemp oil from the hemp seeds is a perfect balance of essential fatty acids, omega-3 and 6 and they are finding that it actually reduces the amyloid plaques in the brain. And as you probably know, hemp has no psychoactive THC in it unlike marijuana. I'd like you to comment about that.

Dr. Mark Burns: Actually that is what I meant, not flax, I did mean to say hemp when I was answering that question. But that's exactly right; the hemp oil is rich in the Omega-3 and 6 fatty acids, exactly as you said. It doesn't contain any psychoactive ingredients and so we already know from dietary studies that a good diet, that a Mediterranean diet or a diet rich in fish, that the incidents of Alzheimer's disease is a lot less in people in countries that have that diet as their primary lifestyle. So again, I will always be a little skeptical that these dietary supplements, none of them will reverse this disease once it starts. These are changes and lifestyles choices that I believe have to be many decades in the making but also again we're talking about risk. You can have someone highly educated that has the perfect diet that exercises everyday, who has a healthy heart, and they will still come down with this disease. So I think, just making sensible choices about lifestyle is always going to be beneficial for no matter what the condition we're trying to treat is and treating your body with respect, but unfortunately most of us don't tend to do that over time. But yeah, I think that hemp oil sounds very much like the data that we've heard before from other omega-3 and 6 fatty acids rich diet. So it looks like it would be a good thing.

George Vradenburg: Thank you Marilyn. Thank you again to Dr. Mark Burns for his work in this area, for something you do everyday, but also for taking the time to speak with us today.

We've had people on this call from 25 states, the Virgin Islands and the Ukraine. And I would repeat what you said and thank Shawn Taylor who is a board member of USAgainstAlzheimer's Network for introducing us to you and for generously supporting this call and all of our work.

Thank you all again for participating in Alzheimer's talks in about a week we'll have a copy of the recording and a transcript on our website for you to share with friends. As always please stay on the line if you would like to leave us a message with a question or comment. But thank you very much for joining us today. It's 3:00 on the nose and we look forward to hearing from all of you when we convene this Alzheimer's talk again next month. Take care and have a good day all.