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Chronic Traumatic Encephalopathy and Its Future in Potential Immunotherapy-Based Treatment

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ABSTRACT

In the annals of medical history, few conditions have captured the world's attention and spurred a race for effective treatments quite like Chronic Traumatic Encephalopathy (CTE). Chronic traumatic encephalopathy (CTE) is a condition rarely studied and is quite a serious neurological disorder that is progressively debilitating. However, the reason why chronic traumatic encephalopathy is rarely studied is because only repeated concussions or traumatic brain injuries (TBIs) can cause CTE. As it so happens to be, many athletes who play close contact sports such as football, hockey, and rugby are at the most risk of developing this disorder. Although there is no definitive way to diagnose CTE during life (it can only be categorized as "probable" CTE), and can only be confirmed postmortem, scientists have identified the criteria and specific potential brain and blood biomarkers associated with CTE such as total tau (t-Tau), phosphorylated tau (p-Tau), neurofilament light chains (NfL), and amyloid-beta (Aβ), etc. These biomarkers could potentially help diagnose CTE while the individual who is suspected to have the disease is living. Furthermore, scientists have been researching immunotherapy, a new potential treatment for CTE. Throughout the following sections, this research article will navigate CTE and its clinical manifestations, pathology, and its implications on individuals and society. Subsequently, this article will discuss immunotherapy, uncovering the fundamental principles that underlie this approach, while highlighting its success in revolutionizing medical treatments for cancer, and the possibility of its future in treating chronic traumatic encephalopathy.

Introduction

In the annals of medical history, few conditions have captured the world's attention and spurred a race for effective treatments quite like Chronic Traumatic Encephalopathy (CTE). According to recent statistics conducted by Boston University's CTE Center, CTE has become a significant public health concern, particularly for athletes and military veterans (Moran, 2017; Mann, 2023; "Criteria Set For Diagnosing…", 2021). Among athletes, research has shown that playing close-contact sports such as rugby, football, basketball, and even hockey increases the risk of developing CTE as athletes who play these sports may be exposed to repeated TBIs or concussions, which are associated with being the cause of CTE (Mckee, Abdolmohammadi, Stein et al., 2018). Every year approximately 42 million people worldwide have mild traumatic brain injuries (MTBI) or concussions (Gardner, Yaffe, 2015), however, this does not mean that if an individual gets diagnosed with a concussion, they automatically have CTE. Even still, chronic traumatic encephalopathy is quite a serious consequence of the absence of enforcement of rules when it comes to concussions or head injuries. And CTE is not the only scary disease that is caused by repeated TBIs, sporadic Amyotrophic Lateral Disease (sALS), Alzheimer's disease (AD), and Parkinson's disease (PD) can also be caused by them as well, which are just a few diseases among others that have not been researched quite as much (Vanltallie, 2019). Depending on the number of head injuries, the severity of them, the age of the person, and other factors, an individual's risk of developing CTE increases (Mez, Daneshvar, Kiernan et al., 2017). A study from 2017 shows that in the UNITE Brain Bank (the world's biggest tissue repository focused on CTE), over 99% of the brains of NFL players were diagnosed with CTE postpartum (Mann, 2023; Moran, 2017). Even more seriously, the number of individuals who played high school sports and were diagnosed with CTE is on the rise (Mann, 2023). In the state of Texas, many high schools are

now required to report the concussions of athletes that were sustained when participating in UIL activities to a registry ("Largest Texas high schools…", 2019). Without proper diagnosing techniques, this condition leaves many affected individuals, especially those who play sports, and their families to deal with its devastating consequences. However, in recent years, a shimmer of hope has presented itself—immunotherapy. This type of treatment uses the immune system, which can be used in different ways (or subcategories) to combat life-threatening diseases, and it holds the promise of transforming the way we perceive and manage CTE (Breen, Krishnan, 2020).

Because of the devastating symptoms of CTE, more research needs to be conducted in the future, not only to find better treatments for the disease but also to find better methods to diagnose and alleviate those symptoms as well. Since so many in the United States play these types of contact sports, it is crucial to find better ways to help these people, and with expanded research that is available and accessible to the public, will come rules that better protect athletes that put in so many hours of effort just to entertain us.

Clinical Manifestations & Diagnostic Criteria

The most recent definition of chronic traumatic encephalopathy is "a progressive and fatal brain disease associated with repeated traumatic brain injuries (TBIs), including concussions and repeated blows to the head" ("Chronic Traumatic Encephalopathy…", n.d.; Breen, Krishnan, 2020; D'Ascanio, Alosco, Stern, 2018). Although this disease is difficult to diagnose because it can only be confirmed postmortem, symptoms or conditions may present themselves such as trouble organizing thoughts, paying attention, problems with memory, balance, and motor skills, personality changes, and erratic behavior such as aggression, depression, and suicidal thoughts ("Chronic Traumatic Encephalopathy…", n.d.; "Chronic Traumatic Encephalopathy…", 2016). It's important to note that not every scientist agrees with the prior list, but CTE has been strongly associated with its symptoms. To resolve this, a relatively new study called, an 8-year ongoing research project has given us the first expert consensus criteria for traumatic encephalopathy syndrome (TES), a condition medically associated with CTE ("DIAGNOSE CTE", n.d.; Alosco, Mariani, Adler, 2021). The very first "NINDS Consensus Workshop to Define the Diagnostic Criteria for TES" was in April 2019 in Phoenix, Arizona. A group of 20 interdisciplinary clinician-scientists attended it as well as 7 educated observers from establishments from across the country, all of whom had a thorough education in areas of study related to the brain and the human body ("Criteria For Developing…", 2021). Led by Douglas Katz, after eight months, the board achieved a consensus with a "provisional level of certainty" for criteria to diagnose individuals with TES & CTE. Individuals can only receive a traumatic encephalopathy syndrome (TES) diagnosis if they have experienced repetitive head trauma while engaging in activities such as contact sports, military service, or similar pursuits ("Criteria For Developing…", 2021). It is imperative to note, however, that the individual must have spent a specific period participating in the activity that led to the brain injury before being considered for TES. Additionally, the individual must exhibit a progressive decline in cognitive function, including "episodic or 'short-term' memory and/or executive functioning, such as planning, organization, judgment, and multi-tasking", and/or neurobehavioral dysregulation ("Criteria For Developing…", 2021; "DIAGNOSE CTE", n.d.). Neurobehavioral dysregulation encompasses explosiveness, violent outbursts, impulsivity, and emotional lability, rage (Tarter, Kirisci, Mezzich et al., 2003;). The criteria for diagnosis also specify that other health conditions, whether neurological or psychiatric, cannot be fully attributed to these clinical problems, even though these conditions can be diagnosed concurrently with TES ("Criteria For Developing…", 2021). The list of criteria will be updated and revised as newer and better research is shared among the medical community. All that being said, it's crucial that doctors or providers not make a clinical diagnosis based on the conditions or symptoms of an individual.

Epidemiology & Risk Factors In Sports

CTE In Football (American)

Since chronic traumatic encephalopathy cannot be diagnosed, only suspected during a person's lifetime, the epidemiology of CTE is unclear. However, in a study conducted by Boston University's CTE Center in 2018 on NFL players' brains, 345 out of 376 players (91.7%) were diagnosed with CTE. In an alternate research project, when the brains of non-NFL players were donated to the same center and studied, only 1 out of 164 brains (0.6%) showed signs of CTE (Moran, 2017; Mez, 2017). That single brain belonged to an individual who played college football. Dr. Anne McKee, who directs the Boston University CTE Center and the UNITE Brain Bank, has stated that "Every 2.6 years of football at any level doubles your risk for CTE, and the longer you play and the higher level that you play, the greater your risk". The study was done in 2018, and even still, five years later, Dr. McKee still warns that even though they have more brains to study, they "...are still seeing that more than 90% of NFL players are affected" (Mann, 2023). This shows that because there is so minimal evidence, many major contact sports leagues will not properly enforce concussion policies unless there is more research done on how the disease can be confirmed.

CTE In Ice Hockey

Football is not the only known sport associated with risks of CTE. Hockey, while not seeing as high rates of chronic traumatic encephalopathy in their players, is still one of the few sports with the highest concussion rates. After they studied CTE in football, Boston University's CTE Center once more opened a study to determine a link between ice hockey and CTE. They found that the risk of developing the disorder may increase by 23% each additional year that an individual plays ice hockey. Of the 74 brains donated, 40 (54%) of the donors were diagnosed with CTE, and each of the donors played at various levels (professionally, in college, youth, etc.). However, this research is only at a preliminary stage, so it may not represent the general population of hockey players, only more research can show more precise results ("Additional Years of Ice Hockey…", n.d.).

CTE In Rugby

Additionally, rugby is another sport that is very similar to American football and also has one of the highest concussion rates ("What Sport Has the Most Concussions…", 2018). Former rugby player Nick Fozzard was diagnosed with early-onset dementia and probable CTE. Many other rugby players have reported this as well, and have conditions and symptoms ranging from dementia, Alzheimer's, mood disorders, and more which again, are the hallmark symptoms of CTE. Recently, 100 former RFL players have formally launched legal action against the Rugby Football League, claiming that the organization was negligent and did not enforce regulations that would have helped protect them from brain injuries and concussions (Bower, 2023). Some of the athletes who are fighting in this legal battle even report having been diagnosed with probable CTE due to the many concussions that they have received during their careers, and the blame for this is now falling upon the RFL. This is a prime example of why there should be stricter rules when it comes to concussions or even any injury in close-contact sports. When the number of people who have chronic and debilitating injuries starts to rise, no more can the Western world ignore the dangerous risks of unenforced concussion and injury rules and procedures.

Neuropathology of CTE

Macroscopic Changes

When looking at the gross pathology of CTE, it is very important to note that many years may pass before symptoms even show the early stages of it often do not show any identifiable changes (Georges, Das, 2022), and if there are any changes presented at all, they will most likely be either or both cavum septum pellucidum (a cavity at least 1 millimeter wide in between the septum pellucidium, or the middle of the brain) and a small expansion of the frontal and temporal horns of the lateral ventricles, which are both very common traits of CTE and are also common abnormalities seen in other neurological diseases (Mckee, Abdolmohammadi, Stein et al., 2018; Breen, Krishnan, 2020; Das, Dossani, 2023). However, it is essential to note that early CTE is only preclinical pathology. Sometimes the condition could be asymptomatic, or can even be linked to extended post-concussive symptoms, therefore it doesn't necessarily mean that the symptoms are advancing (Breen, Krishnan, 2020). In advanced stages, changes may include atrophy or a lowering in the weight of the brain, the reduction or lessening of gray and white matter, and the increase of space and the deposition of p-tau in between the cortical sulci (or the overlapping folds) of the brain (see figure 1), typically seen in the frontal and anterior temporal lobes (Mckee, Abdolmohammadi, Stein et al., 2018; Murray, Osterman, Bell el al., 2022). In addition to the atrophy of the hypothalamus (which regulates heart rate, blood pressure, body temperature, hormones, and hunger) and the thalamus (essentially the sensory "traffic directory" of the brain), in severe cases the atrophy of the mammillary bodies (MB), which are small, round nuclei brain stems located on the posteroinferior facet of the hypothalamus, may also be present (Mckee, Abdolmohammadi, Stein et al., 2018; Peterson, Reddy, Mayes, 2021). Mammillary bodies are especially important because they have a direct connection with major components of memory circuitry, including the hippocampus, and its atrophy has also had a link established with Alzheimer's Disease (AD) and memory loss (Emfietzoglou, n.d.; Tao, Pan, Myslinski, 2021). Other changes that are seen in the intermediate to advanced stages of CTE are the enlargement of the lateral and third ventricles, septal fenestrations, thinning of the isthmus of the septum corpus callosum (the corpus callosum controls movement, cognitive function, and vision), discoloration of the locus coeruleus and substantia nigra, which are both neurotransmitters which regulate behavior and emotion (Mckee, Abdolmohammadi, Stein et al., 2018; Breen, Krishnan, 2020; Prasuhn, Prasuhn, Fellbrich et al., 2021; Goldstein, Covington, Mahabadi et al., 2023). Late-stage CTE may be asymptomatic in some cases and in some macroscopic changes may not even be present, but most times, it is associated with sudden mood swings and aggressive behavior (Breen, Krishnan, 2020).

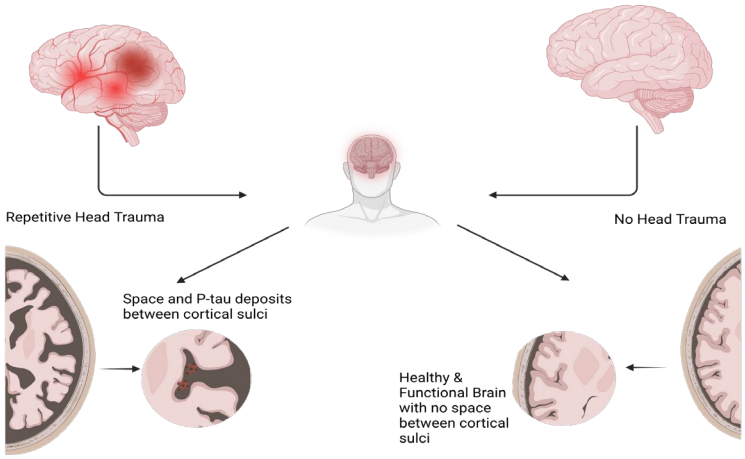

Figure 1: Atrophy or shrinkage of the brain, can be seen in the brain that has CTE (left) because there is space between the cortical sulci, in which there also can be p-tau deposits at the bottom of them; usually, a healthy brain (right) would not have so much space between the folds of the brain (Mckee, Abdolmohammadi, Stein et al., 2018; Murray, Osterman, Bell el al., 2022; Zhou, Thompson, Toga, 1999)

Microscopic Changes

In normal brain cells, a protein called tau helps to stabilize the microtubules of neurons and keep them from disintegrating (as seen in figure 2). In most cells, the microtubule is used for cell division. (Bass, Matamoros, Leo, 2016) Because cell division does not happen to most neurons, unlike most cells that use microtubules for mitosis, neurons use them as more of an architectural support, as they are needed to support and develop the axons and dendrites of neurons ("Tau Topic Sheet", n.d.; Bass, Matamoros, Leo, 2016). The microtubule is able to act as an internal skeleton for neurons because of the tau protein, which helps stabilize it by spurring tubulin production, making it able to carry substances that are essential to the survival of neurons (Bass, Matamoros, Leo, 2016). While that is the main function of tau in neurons, tau possibly contributes to the integrity of genomic DNA, changing the movement of materials needed for the axon, and therefore helps to provide necessary materials to help the neuron function (Hill, Wall, Moffat et al., 2020). However, in CTE the microtubule degenerates by a process called hyperphosphorylation, which causes tau to be turned into p-tau (Gong, Iqbal, 2008; Breen, Krishnan, 2020; "Tau Topic Sheet", n.d.; Mishan, Kanavi, Shahpasand, 2019). Hyperphosphorylation occurs because of a few etiologic factors, which can be the dysregulation of the phosphorylation/dephosphorylation system of tau (which kinases and phosphates are responsible for), brain glucose metabolism that is weakened, and corrupted amyloid-beta (Aβ) peptides (Gong, Iqbal, 2008; Noble, Hanger, Miller et al., 2013). Additionally, neurofibrillary tangles can eventually form over years and years after concussions (see figure 3), after hyperphosphorylation of tau, p-tau undergoes a process called oligomerization, which turns the pathogenic tau monomers into bigger molecules called tau oligomers (Schaefur, Grimes, 2018; Gong, Iqbal, 2008; Breen, Krishnan, 2020). These are unwanted structures that eventually group and form neurofibrillary tangles (NFTs), and the neurotoxicity caused by the build-up of Aβ plaque and neurofibrillary tangles is what leads to neuron death because the microtubule starts to degenerate, and is very similar to what is seen in Alzheimer's (Gong, Iqbal, 2008). Another aspect that causes tau to turn pathogenic is the isomerization of *trans* to *cis* tau. Also seen in AD, the isomerization of tau by one of the peptidyl-prolyl isomerases, Pin-1 causes *cis* tau, which cannot stabilize the microtubule, to turn into *trans* tau, which is the normal tau found in the brain (Butterfield, Abdul, Opii et al., 2006). However, under stress or lack of oxygen, Pin-1 can revert trans tau back to *cis* tau.

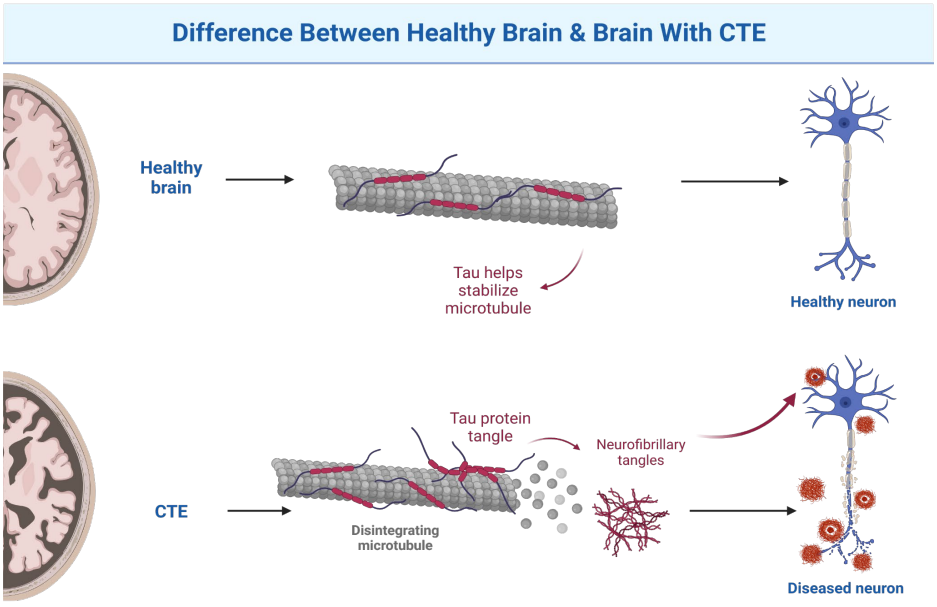

Figure 2: The microtubule is able to act as an internal skeleton for neurons because of the tau protein, which helps stabilize it, making it able to carry substances that are essential to the survival of neurons (Bass, Matamoros, Leo, 2016; "Tau Topic Sheet", n.d.).

While that is the main function of tau in neurons, tau possibly contributes to the integrity of genomic DNA, changing the movement of materials needed for the axon, and therefore helps to provide necessary materials to help the neuron function ("Tau Topic Sheet", n.d.; Bass, Matamoros, Leo, 2016; Hill, Wall, Moffat et al., 2020). However, when p-tau starts to form oligomers and then starts to form into neurofibrillary tangles (see figure 3 for more detail), the microtubule loses its stability and starts to disintegrate, which is what leads to a diseased neuron (Schaefur, Grimes, 2018; Gong, Iqbal, 2008; Breen, Krishnan, 2020).

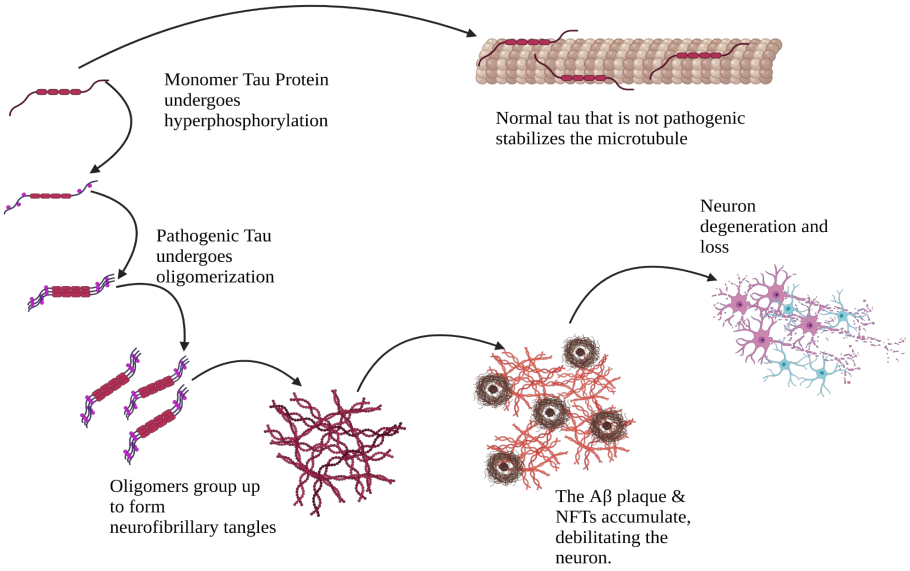

Figure 3: This figure shows how NFTs form, and what tau usually would do in the microtubule; its main role being stability ("Tau Topic Sheet", n.d.; Bass, Matamoros, Leo, 2016). After hyperphosphorylation of tau, p-tau undergoes a process called oligomerization, which turns the pathogenic tau monomers into bigger molecules called tau oligomers; unwanted structures that eventually group and form smaller neurofibrillary tangles that later form into a bunch of tangles that have amyloid-beta plaque build-up in them (Schaefur, Grimes, 2018; Gong, Iqbal, 2008; Breen, Krishnan, 2020). The neurotoxicity caused by the build-up of Aβ plaque and neurofibrillary tangles is what leads to neuron death because the microtubule starts to degenerate, and is very similar to what is seen in Alzheimer's (Gong, Iqbal, 2008).

Biomarkers of CTE

When looking at the diagnostic tests of CTE in the long run, evolved neuroimaging tests that corroborate the disease along with tests that look for its biomarkers would sustain more evidence of CTE rather than falling back on only biomarker tests. However, because there is no imaging machinery to confirm CTE in individuals before death, biomarkers that are tested via cerebrospinal fluid (CSF) could potentially be the key to spotting and diagnosing the probability of the disease in individuals who are high risk or have had multiple TBIs and concussions before (Gerges, Chalhoub, Atallah, 2023; Alosco, Culhane, Mez, 2021). Biomarkers of chronic traumatic encephalopathy are CHL1, a protein that plays many important roles in keeping neurons alive, and excessive KIF2A; its dysfunction also relates to cortical dysplasia (Ge, Guo, Li, 2022). Some others include higher levels of neurofilament (NfL) light chain proteins which are found in plasma, miR-1183, and miR-287 that is found on the surface of the neuron, both of these are also markers for many other neurological diseases of varying severity (Dickstein, Gasperi, Sosa et al., 2020; Ge, Guo, Li, 2022). Since tauopathy is a key aspect of CTE, elevated levels of total and pathogenic tau are considered as well (Dickstein, Gasperi, Sosa et al., 2020). The biomarkers for CTE are quite similar to the ones found in Alzheimer's,

because their tauopathies, which is a hallmark of both diseases are also immensely similar as well (Dickstein, Gasperi, Sosa et al., 2020; Turk, Gaeda, Alvarez et al., 2022). In fact, until around six years ago, the biomarkers between the two were previously indistinguishable, but now, there are certain subtle differences (Turk, Gaeda, Alvarez et al., 2022). More recently, scientists including Dr. Ann Mckee, who is the director of Boston University's CTE Center, have found a specific biomarker of CTE, CCL11, that is not shown when compared to normal brains and brains with AD (Cherry, Stein, Tripodis et al., 2017; Rimer, 2017). Of course, in the future, doctors would have to take into account the patient's medical history, concussion record, and symptoms to form a diagnosis even with tests that show specific CTE biomarkers.

Immunotherapy In Cancer

Immunotherapy is a type of cancer treatment that aims to boost the inborn immune system (Zhang, Zhang 2020), different from chemotherapy, which is a widespread treatment drug that has powerful chemicals in it to kill cancer cells ("What is Chemotherapy", 2022). However, much more research has been done on chemotherapy, even though it is known to have many side effects, some being mild and others being incredibly hard to manage. So what is the difference between immunotherapy and chemotherapy if the same side effects may show up in either treatment? Chemotherapy works to destroy cancer cells when they divide, which is why this treatment can also cause the destruction of any tissues that have cells that take part in the division cycle ("How chemotherapy works", n.d.). Unlike chemotherapy, which makes the immune system weaker, immunotherapy makes an individual's immune system stronger and functions at a higher level than a normal immune system would ("Immunotherapy Side Effects", n.d.). Another aspect that is different from chemo is that this new type of therapy can teach the immune system how to spot and target cancer cells and eliminate them effectively ("Immunotherapy Side Effects", n.d.). There are many types of immunotherapy, such as adoptive cell transfer, cytokine therapies, cancer vaccines, and immune checkpoint inhibitors, but oncolytic virus therapies have been the most studied and used in clinical practice (Zhang, Zhang 2020). Oncolytic virus therapies have been used for over a century, its central concept being that enhancement of the immune system could be caused by bacterial or viral infections. As time and research progressed, scientists found ways to genetically modify viruses to infect cancer cells, so that the advanced immune system would better target them (Zhang, Zhang 2020). Specifically, an oncolytic virus that has shown much progress and promise in treating advanced melanoma is talimone laherparepvec (T-VEC), which is based on a modified type 1 HSV, or herpes simplex virus, the way it has been modified is the deletion of two genes of the original virus. It has also proven itself to be safe, with symptoms of the virus ranging from chills and muscle pain to a mild fever (Andtbacka, Kaufman, Collichio, et al., 2015). Other types of immunotherapy treatments such as cancer vaccines, which use tumor-specific antigens, show extremely high promise in treating cancer as well (Zhang, Zhang 2020). Of course, even more research has to be conducted for immunotherapy to be used as a sole treatment for cancer, and more knowledge being available on different types of immunotherapies may lead it to eventually treat other diseases as well.

Immunotherapy in CTE

Although currently there is no cure for chronic traumatic encephalopathy, there is the possibility of using monoclonal antibodies (mAB), or immunotherapy, in treating the disease. Because tau is important in the neuron, especially in microtubule construction, the antibodies would only have to target pathogenic forms of tau to be considered effective in curing CTE and safe to treat people with (Zhang, Zhang 2020). To understand how this works in humans, scientists use mouse models to explain how immunotherapy works to combat tauopathy (Alipour, Tebianian, Tofigh et al., 2022; Gonçalves, Wijesekara, Fraser et al., 2020). In mice, this type of immunotherapy has been proven very effective. In several studies, scientists mimic the type of forces at play when humans get concussed in mice, and the severity of it

would depend on its velocity and direction, among other aspects. These forces include stereotaxic forces, which involve vertical impact on the mice while restraining the head, and rotational forces, in which the body of the mouse is laying flat and is restrained while there is a horizontal impact on the head (Zhang, Zhang 2020). The mice were then exposed to the impacts over again to induce tauopathy so that scientists could test the treatment on them. In a very similar but different study, mice were injected with the immunotherapy and within close to an hour, the antibodies had entered the brain (Sigurdsson, 2018), which is a major breakthrough considering that the blood-brain barrier (BBB) is something that has hindered the progress of immunotherapy for neurodegenerative diseases for a very long time (Zhang, Zhang 2020). The study also showed that the cognitive function of mice also improved, as well as the improvement of mice when participating in motor tests (Sigurdsson, 2018). In theory, because of the transition of tau from trans to cis tau by Pin-1, a better alternative to monoclonal antibody therapies would be isoform-specific antibodies that target the cis tau since pathogenic tau is often marked by the cis version of tau (Zhang, Zhang 2020). In fact, isoform-specific antibodies have blocked the advancement of cis pathogenic tau in experimental trials in vitro and mice (Kondo, Shahpasand, Mannix, et al., 2015). Even still, there are some factors that scientists still have to bypass to make the use of mABs effective. For it to effectively work, the therapy needs to target and cleanse both intracellular tau and extracellular tau. However, the human chimerization of the antibody reduces its binding, therefore reducing its efficiency, when compared to an unmodified antibody (Congdon, Chukwu, Shamir, et al., 2019; Zhang, Zhang 2020). As mentioned before, BBB permeability has been a challenge, and to solve this, scientists are researching unilateral focused ultrasounds (FUS), and by using it scientists can create openings for a short amount of time by inducing the enlargement of microbubbles in the blood-brain barrier (see figure) so that antibodies can go through it, and demonstrations of this have already been done in vivo (Hynynen, McDannold, Vykhodtseva, et al., 2001; Conti, Kamimura, Novell et al., 2020; Breen, Krishnan, 2020). Although no experiments have been done specifically for chronic traumatic encephalopathy, the tauopathy is astonishingly similar to that of Alzheimer's disease, so treatments to treat AD would also cover the tauopathy of CTE, which is its main hallmark (Breen, Krishnan, 2020). Through the advancement of technology and treatments related to CTE, new challenges will arise in due time, but there will be a way to overcome challenges. As of now, immunotherapy may be the best possible solution to CTE, and in the future, it could revolutionize the treatment of many neurodegenerative conditions if harnessed in the right ways.

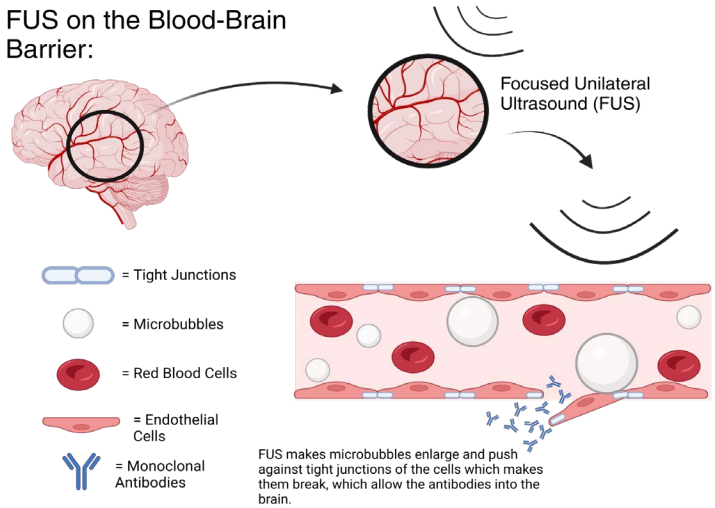

Figure 4: This model shows how focused unilateral ultrasounds allow isoform-specific antibodies into the brain through the blood-brain barrier (Breen, Krishnan, 2020), which may be a very critical method for treating CTE in the future, as the BBB is impermeable to many things (to protect the brain), including the modified antibodies. The FUS makes microbubbles in the BBB enlarge, which then pushes on its endothelial cells to make their tight junctions (which hold them together), break apart (Conti, Kamimura, Novell et al., 2020). This allows the antibodies to go into the BBB and the brain (Conti, Kamimura, Novell et al., 2020; Breen, Krishnan, 2020).

What To Do If You Suspect CTE

If an individual that has dealt with multiple concussions and thinks they might have chronic traumatic encephalopathy as a result, there is always still hope. As mentioned before, while there is no cure for CTE, there are medications that could possibly help people with probable CTE and its symptoms live a fuller and better life ("Chronic Traumatic…", n.d.). Usually, patients with this neurodegenerative disease should see, but are not limited to the following symptoms: a progressive and slow decrease of cognitive function, such as problems with memory, problem-solving skills, reasoning, erratic and aggressive behavior that is out of character, as well as motor decline ("Criteria Developed…", n.d.). This means that slowly, people with the disease will lose their ability to take care of themselves, and at some point will need care and emotional support, not just from family, but also from a medical team ready to cater to their needs ("Living with CTE", n.d.).

Looking For Doctors

When seeking out treatments for the symptoms of CTE, it is very important to note that seeing a doctor who is familiar with neurodegenerative diseases such as AD and specializes in treating CTE would help the individual get the care that they deserve; many generalized practitioners would not be able to effectively help manage the disease due to its complexity. Doctors who will be able to provide efficient outcomes would be doctors who are in specialties such as neuropsychiatry, cognitive neurology, and neuropsychology. This would be separate from a doctor who only specializes in traumatic brain injuries ("CTE Treatments", n.d.). Another thing to consider when looking for a specialist is for a patient to ask themselves if the specific doctor listens to them and does an in-depth examination of their past medical history and current health problems, instead of jumping straight into a treatment plan, as doing the latter could be quite dangerous and could cause serious implications ("CTE Treatments", n.d.).

Helpful Daily Tips

Although at times being a person who has CTE seems impossible, several lifestyle changes can help those suffering from the disease. Of course, when needed, it is crucial to reach out to get help for dealing with the mood swings and disorders that come with CTE, some serious symptoms being anxiousness, depression, and suicidal thoughts ("Chronic Traumatic…", n.d.). However, a daily routine that takes one task at a time step-by-step can help regulate anxiousness and put people in a better mood, and this tactic even works for people who do not suffer from chronic traumatic encephalopathy but suffer from crippling nervousness because it helps to provide a stable environment ("Living with CTE", n.d.). On that note of anxiety, regulating emotions is key, and calming exercises would be highly useful in the long run. This can include yoga, meditation, breathing exercises, as well as sleeping and eating well. In the mild to late stages of CTE, writing things down can substantially help with remembering basic tasks ("Living with CTE", n.d.), such as drinking water, eating, showering, etc. Lastly, having a support system to help with tasks and daily life is important as well, especially in the later stages of life.

Research Programs

Since research on CTE is still in its infancy, more brains must be donated to conduct studies on the disease. Such generous donations of people's brains have brought CTE research to new heights, and more research is needed now more than ever. Research programs like the one at the UNITE Brain Bank will save many lives in the time to come and could lead to new advancements not just in CTE, but in other neurodegenerative diseases that affect different populations too ("Brain Banks", n.d.; "Brain Donation", n.d.). These new advancements could even be the key to becoming the cure for chronic traumatic encephalopathy in the near future.

Conclusion

Through the advancement of research in chronic traumatic encephalopathy, scientists have found many breakthroughs such as the disease's symptoms, pathology, mechanisms, and biomarkers. Even though there is still so much that is unknown about CTE, research has come a long, long way from where it was before. Now that researchers such as Dr. Ann Mckee know the neuropathology, mechanisms of the disease, such as how tau turns pathogenic, and what parts of the brain atrophy as a result of the disease, scientists have formed the basis of diagnostic tests and find biomarkers such as NfLs and other proteins, and know what biomarker separates AD from chronic traumatic encephalopathy. They have also helped scientists learn that there is a way to prevent tauopathy through immunotherapy and isoform-antibodies that stop CTE from progressing. However, preventing CTE in athletes and people who serve in the military is always better than having to treat them after multiple brain injuries, and protecting athletes and veterans by enforcing safer protocols would also help eradicate the disease. And even though what is learned from past and current studies is invaluable for future development, so too is making decisions based on the needs of patients with CTE, such as medication specifically for the disease that treats its symptoms.

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