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Effective Lifestyle Modifications Pro Football Players Utilize to Prevent Future Complications of Chronic Traumatic Encephalopathy

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Abstract

The National Football League (NFL) is a billion-dollar entertainment industry that values itself on the physical and gritty sport of football. Even though these athletes are revered for their physical prowess and durability, at some point in their professional football careers these players are likely to sustain some variation of head injury—if not multiple. Each of the 22 players on the gridiron must physically wear out their matchup with tackles, stiff arms, bullrushes, rip moves, and any illegal hits the referee may not be able to see. The repeated blows these players sustain over the course of their career often causes a condition known as Chronic Traumatic Encephalopathy (CTE). CTE causes brain degeneration which can impede mental, emotional, and physical function. This type of traumatic brain injury (TBI) is responsible for many venerable, community-serving NFL players to murder, abuse, and self-harm, which is how the enigma of CTE was initially discovered and studied. Furthermore, CTE is neither curable nor detectable over the lifespan, and is only discoverable during autopsies. The CTE scare has prompted numerous NFL players to end their careers prematurely to prevent the acceleration of CTE, and to hopefully prevent the afore-mentioned negative outcomes. Through a review of the literature and a proposal for further study, the goal of this thesis is to find out techniques professional football players--both active and retired--can employ to reduce risks for CTE.

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Introduction

Chronic Traumatic Encephalopathy (CTE) is a degenerative brain pathology that causes radical, negative outcomes in its victims. Often times, these victims succumb to suicide, domestic abuse, homicide, depression, and anxiety (Aldag et al., 2019). Individuals contract CTE via repeated blows to the head of any intensity, big or small (Aldag et al., 2019). In other words, an individual can have no history of a concussion or severe head trauma and still contract CTE. While CTE cases occasionally occur in car accident survivors and martial artists, CTE plagues the National Football League (NFL) as its notorious health concern, and may be to blame for the controversies affiliated with the players. Ex-NFL player Aaron Hernandez is most notorious for his multiple offenses to the law, which included being charged and arrested for his connection to two murders and for his conviction of first-degree murder ("Aaron Hernandez," 2018). Hernandez' life came to an end when he committed suicide in his jail cell ("Aaron Hernandez," 2018). A recent study focusing on CTE and the pro football population found "Duration [playing professional football] was significantly associated with odds of CTE at death, with odds increasing 30% every year, doubling every 2.6 years, and increasing by < 10 fold every 9 years" (Mez et al., 2019). Unfortunately, CTE is diagnosable only during an autopsy and impossible at this point in time to diagnose during an individual's life (Alosco et al., 2021). So, the purpose of this study is to uncover healthy lifestyle modifications active NFL players should incorporate into their lives to prevent future CTE complications or to slow down the progression of CTE.

Problem Statement

National League Football's entertainment value of big hits and physical play provides thousands of jobs and revenue for the cities each team represents. Football is also part of American culture, for the pride it brings to the cities and for the holiday-like event of Super Bowl

Sunday. While CTE would be less prevalent if football was no longer played, it is an unrealistic expectation to ban football for its impact on the communities that enjoy it. So, how can CTE be prevented in these football players without taking away the sport? CTE is responsible for hospital visits, psych ward admissions, jail time, and violence. This has caused controversy to surround the NFL and the culture of football. Further research on CTE can hopefully minimize the stigma of these individuals while simultaneously improving chronic health of pro football players. CTE is still a newly discovered chronic condition with no effective screening tool, and effective prevention techniques have no long term reliability and no long term data (Alosco et al., 2021). This creates risks for doctor's, who may improperly misdiagnose a patient with a mental disorder and not consider if the patient has CTE from football. This then trickles down onto nurses who help with patient education and treatment, which can result in the nurse providing ineffective nursing interventions which can worsen a patient's condition. Unfortunately, there are no proven medical interventions at this time that either prevent CTE progression or lower CTE risk for active NFL players. So, later on in this paper a research proposal will focus on finding out this missing information.

Research Questions

What healthcare practices can NFL players utilize to reduce their risk of CTE or to control CTE-related symptoms? How can we screen for CTE? What are the most common symptoms of brain injuries? How do brain injuries occur?

Literature Review

To explore the current research on the topic, a review of the literature was performed. Each study, included in this review, will answer and/or expand on one or more of the research questions. The databases used for finding these articles were PubMed and PubMed Central, and

the search terms included: CTE, Traumatic Brain Injury, Chronic Traumatic Encephalopathy, Head Injury, and Head Trauma. Six articles related to the research questions were chosen for inclusion in this review.

The literature review is organized into two categories: Animal (Mouse) Research (one article) and Human Research. See the Appendix at the end of this thesis for a literature review table, summarizing each study.

Animal Research

The first research article to review is Kahriman's "Mouse closed head traumatic brain injury replicates the histological tau pathology pattern of human disease: characterization of a novel model and systematic review of the literature." This study subjected mice to daily instances of head trauma with the goal of monitoring mental acuity (Kahriman et al., 2021, para. 4). These mice would then be put down and autopsied anywhere from one week to four months after being studied. Specifically, the study included 50 gram weights being dropped onto the head of a mouse once daily for five consecutive days (Kahriman et al., 2021, para. 9). Upon inspection for mice that sustained one week of trauma, the cerebral cortex appeared intact with no plaque buildup. However, at four weeks and beyond, tau buildup, an indicative factor of CTE prevalence in humans, became apparent via the staining process the study utilized (Kahriman et al., 2021, Table 1). What this potentially means is that CTE in humans may occur faster than scientists initially proposed. If CTE accumulates that fast in humans, discovering effective medical interventions for this disease becomes a dire necessity. While these NFL players have years of experience playing football and have likely contracted CTE due to the nature of their profession; kids and teenagers are populations now at risk for CTE if this study with mice contracting CTE in four weeks translates to humans. A big limitation of this study is that the

research was conducted on mice, which means results and the collected data may not fully translate to human research (Kahriman et al., 2021 para. 4). Though this limitation exists, the researchers made a robust argument that the data may be transferable because the buildup of tau in mice appeared in the same anatomical structures in humans (Kahriman et al., 2021 para. 46). Because the researchers believe this pathological similarity is not unique between species, future research on TBI and CTE could utilize mice as an ethical and more efficient alternative to human participants.

Human Research

The second research article to review is "Interventions to evaluate fitness to drive among people with chronic conditions: Systematic review of literature" by Marino et al (2012). This article's goal is to see if the results of mental acuity tests correlate to driving capabilities as well as interventions used to improve outcomes related to driving and driving assessments. The inclusion criteria for the review included individuals over 18 years old with a chronic disease including Alzheimer's disease, Parkinson's diseases, TBI, CVA, Sleep apnea syndrome, narcolepsy, multiple sclerosis, and hepatic encephalopathy (Marino et al., 2012). This research utilizes a study design revolving around randomized control trials, cohort analytic studies, interrupted time series, and controlled before and after studies (Marino et al., 2012). This study's design utilized multiple tests to determine driving capabilities. These tests included behind the wheel driving test, memory tests, visual tests, and simulations (Marino et al., 2012 para. 38). The study found that Stroke Drivers Screening Assessment, Adult Memory and Information Processing Battery, and Stroop test are the most effective screening tools to determine driving fitness levels in TBI. (Marino et al., 2012 para. 66) While CTE has limited research, TBI is a well-documented and studied condition with many similarities and outcomes similar to CTE.

Since the researchers' study on TBI found the Stroop Test, Adult Memory and Information Processing Battery, and Stroke Drivers Screening Assessment determine driving capabilities, these three TBI-focused screening methods may apply towards CTE and screening for symptoms or conditions. While the limitations of the article mention that screening TBI may not reliably assess driving fitness, the tools can be studied and repurposed to analyze other activities of daily living in patients with brain injuries to gain more understanding of diseases like CTE.

The third research article is "Advanced biomarkers of pediatric mild traumatic brain injury: Progress and perils" by Mayer et al (2012) This systematic review talks about screening options for detecting traumatic brain injuries in children, with 43 studies conducted on pediatric patients in clinical settings. The researchers reviewed various types of imaging used to detect brain injuries in pediatric patients like metabolic imaging, hemodynamics, and magnetic resonance imaging in cross-sectional studies and convenience samples (Mayer et al., 2012, para. 47). The researchers found MRIs to be the most effective imaging for these pediatric brain injuries (Mayer et al., 2012, para 50). However, MRIs were the most commonly used technique for imagining brain injuries and researchers had the most data about that technique. They had less data about the other imaging techniques and reported that they could not adequately assess the other techniques (Mayer et al., 2012 para 50).

The researchers found that the imaging techniques they studied could only detect sub-acute brain injuries, leaving injuries like CTE completely undetected. (Mayer et al., 2012) Furthermore, the researchers struggled with obstacles outside of the imaging itself. (Mayer et al. reported that "Patients were more likely to receive an MRI if they had a prior concussion, were still participating in the activity that caused the concussion or had cephalic or emotional symptoms on the day they visited the clinic" (Mayer et al., 2012, para. 23). It was also stated in

the research that "...ambulatory [TBI] patients were less likely to seek follow-up care after discharge and were less likely to have positive imaging findings" (Mayer et al., 2012, para. 23). Considering the findings and limitations of this systematic review, future research should consider including more representation for screening techniques other than the MRI. If the research had included equal representation for all of the screening options instead of focusing on MRIs, the results might have been different.

The fourth research article is Perry's "Association of traumatic brain injury with subsequent neurological and psychiatric disease: a meta-analysis" (Perry et al., 2015). This analysis focused on finding out if a previous brain injury diagnosis could affect the chances of developing another psychiatric condition. The participants included adults over 18 who had a psychiatric disorder diagnosed, with 57 studies being reviewed. (Perry et al., 2015). This statistical meta-analysis was organized to separate individuals who had TBI diagnosed in the last 12 months from individuals who did not have a TBI diagnosed in the last 12 months to see if one population was more likely to be diagnosed with another psychiatric condition when compared to the other. (Perry et al., 2015). This was one of this research's strengths: simplicity. By having only two main groups, the research avoided deviating from the purpose while remaining easy to follow along with. This design led to the researchers finding that individuals with a previous TBI "...had higher odds of Alzheimer's disease, Parkinson's disease, mild cognitive impairment, depression, mixed affective disorders, and bipolar disorder [ ] compared to those without TBI" (Perry et al., 2015). While the verdict on how to treat CTE is still undetermined, the diseases the research mentions like Alzheimer's Disease and Parkinson's Disease treatment plans shown to slow disease progression and to control symptoms. Perry's research potentially means that a

treatable condition like Alzheimer's could remain undiagnosed because of a missing diagnosis of CTE (2015).

The fifth research article is Lal's "The Effect of Physical Exercise After a Concussion: A Systematic Review and Meta -Analysis" (2018). This meta-analysis researched studies that compared Post-Concussion Symptom Scale Scores (PCSS) between individuals who exercised and individuals who did not exercise throughout the recovery period of a concussion. The 14 studies utilized a mix of randomized controlled trials, propensity score matching studies, cohort studies, and before and after studies (Lal et al., 2018). The major finding of this study was that exercise decreased PCSS score in patients with symptoms of concussion, with specific improvements in the reaction time and Immediate Post-Concussion Assessment and Cognitive Testing components of the PCSS (Lal et al., 2018). One limitation to this study was that that only 5 out of 14 studies utilized randomized control trials, which may have affected the outcome. Despite this, the findings on positive outcomes on exercise for concussed patients could potentially become a lifestyle modification for individuals with CTE. (Lal et al., 2018) Without enough data on effective interventions for CTE symptoms and progression, the correlation between exercise and improved concussion scores could be researched to determine if the same idea applies to CTE.

The sixth research article is "Dual vulnerability of TDP-43 to calpain and caspase-3 proteolysis after neurotoxic conditions and traumatic brain injury" by Yang and colleagues (2014). This research delves into the pathophysiology of conditions like CTE, and how TBI may cause a release in a debilitating protein called "TDP-43" that causes ALS and dementia (Yang et al., 2014). The study was conducted on human post-mortem brains affected by TBI with conditions including but not limited to Huntington's Disease, Alzheimer's Disease, and Pick's

Disease (Yang et al., 2014). To study the brain, the researchers stained and mixed various chemicals in the brain to see how the cerebral fluids and chemistry react, and to hopefully identify structural anomalies associated with TBI (Yang et al., 2014).What Yang discovered was that TDP-43 causes cell necrosis in the brain that can lead to conditions like ALS and dementia (Yang et al., 2014). Professional football players are already a highly at risk population for CTE, a condition that can affect these players long after they retire. Yang's findings demonstrate that these retired football players are at an increased risk of further future health complications because the research correlates TBI to the aforementioned chronic conditions.

Literature Review Conclusion

The literature review raised many questions regarding the limited data on CTE. The limited data on CTE exacerbated the process of finding appropriate articles, which led to the topic often leading to "TBI" rather than CTE. Despite the difficulty of finding articles, much of the same findings the researchers found on TBI's can be applied to CTE. One common theme in the literature was the difficulty with screening brain injuries. The articles talking about this focus struggled with finding consistent means of detecting any sort of brain injury, let alone CTE. This could be because of the sensitive nature of the brain and the difficulty of studying it in both live subjects as well as deceased subjects. Because the brain regulates all of the human body's life-sustaining functions, there is an ethical dilemma surrounding any sort of studying or experimentation of the brain. This ethical debate has prompted human studies and any experimentation to be regulated to undergo multiple review boards to protect human participants as well as the integrity of research, meaning studies on the brain will take longer in exchange for following an ethical practice of research.

Research Study Proposal

Theoretical Framework

The theoretical framework this research utilizes is the Qualitative Grounded Theory (Glaser & Strauss, 1967), which is a tool that will guide my data analysis towards drawing comparisons between all aspects of research including its participants and the data collected (Chun et al., 2019). Given that I did not find extensive research specifically investigating CTE in professional football players, the purpose of using Grounded Theory is to develop theory surrounding this phenomenon (Glaser & Strauss, 1967. While grounded theory often uses interviews for data collection (Qualitative Research Guidelines, 2008), I will focus on using open-ended survey questions that players can easily fill out online.

Ethical Considerations

Before beginning field research, this study's plan must first be approved by an institutional review board to ensure all participants are fully informed of the data to be collected, as well as how the data will be collected. The participants' confidentiality will be strictly maintained to help ensure truthfulness in each response. No personal data, such as name or address will be collected. Potential participants will be informed that they may stop answering any questions and discontinue the survey at any time. Submitting the survey constitutes participants' consent to use their answers for the study.

Since the literature review concluded that the research showed similar for cases of TBI and CTE, distinguishing between symptoms could be a problem for players who choose to submit their surveys for analysis. To help alleviate potential confusion in distinguishing between these two related conditions, the questions in the survey will ask about symptoms of TBI or CTE (so players do not necessarily need to make the distinction)

Research Question

What are the experiences of symptoms of and possible remedies for TBI and CTE of California professional football players?

Design

This thesis' research study design will focus on a qualitative approach, specifically exploring what interventions may be more effective than others. An online survey with open-ended questions will be employed to help answer the research questions.

Sample

The population to be surveyed are active NFL players from the Chargers, 49ers, and Rams. Up to twenty total participants will be surveyed from a combination of the three California teams, with at least three participants coming from a single team. This restriction is put in place because teammates will have the same trainers and potentially have similar experiences when it comes to rehabilitation and health maintenance. The inclusion criteria for this population will be players who play the specific positions of running back, lineman, and linebacker.

Enrollment

In order to get into contact with the appropriate participants, I will first present my study to the National Football League Players Association (NFLPA). The NFLPA is an organized player’s union that strives to uphold the rights and health of its constituents. With CTE being an ongoing controversy for the NFL, the ethical way to get into contact with these players is through their union, for which the data collected will be beneficial towards understanding CTE and generating more positive outcomes for those with it or for those who are at risk. A convenience sample will be used participation will be voluntary.

Methodology

To best answers to the research questions, it is important that the NFL players surveyed play these specific positions: running back, lineman, and linebacker. These positions require the most physicality to play, and these positions are at risk for sustaining the most physical ailments of all the NFL positions. These players are more likely to experience CTE symptoms due to the repeated blows to the head that players in these positions often sustain, which means that these players may be more likely to seek treatment and be active in their health maintenance.

After the study is explained to the union representative, an announcement about the survey will be provided to players. Players who are interested will be able to go to an online link to complete the survey. I will limit my survey to demographic questions, including age, ethnicity, number of years playing football, and number of years as an NFL player, and five open-ended questions to avoid survey fatigue and to focus on the recipient's response.

My first question is: "Considering you are an NFL player and thus at risk for brain injuries, what do you know about these types of injuries?" This question is important to ask as a first question because this measures the patient's education level and will help inform the answers the participant gives for the next two questions. This also gives the participant an incentive to ask questions and seek more information about brain injuries in the future, if the individual realizes he is not well informed on the subject. For this question I am expecting responses mentioning how playing football is a risk factor for brain injuries, statements about how brain injuries can have both physical and mental presentations, and statements talking about football's protective equipment utilized by its players. While I do think these football players will have at least a basic understanding of brain injuries, this question must be asked in case participants do not have background information on the topic. General knowledge of brain

injuries is needed to answer the next two questions, so education will be provided to the participant as needed.

My second question is: “What brain injury-related symptoms (depression, anxiety, headache, memory loss, aggression) do you experience in daily life?” Symptoms are the closest indicator to diagnosing CTE, so this data will provide an estimate to how many players in the NFL might have CTE. The next questions are related to this second question.

The third question asks: " What remedies have you used to help alleviate the TBI or CTE symptoms you've experienced?

The fourth question is in two parts: " Which remedies have you found most helpful for reducing symptoms of brain injury, if any, and what recommendations do you have for others who experience TBI or CTE symptoms? These last two questions will help distinguish what interventions may be effective for treating symptoms.

The fifth and final question is: “What medical practices. alternative therapies and/or rituals do you participate in to prevent or reduce risk of brain injury?”

While I hypothesize that all the participants will report symptoms of brain injury, I do not expect each participant report to be the same. Some participants may report anxiety, depression, mood swings and forgetfulness while another participant may just have anxiety. Each participant’s response will be documented and all participants will have their reported symptoms examined carefully to see what was most common and least prevalent.

Analysis

The data collection on the medical and alternative health practices question will be presented the same way: players will provide information about their brain health maintenance

routine and each response will be examined based on what action was the most commonly used and what was the least used.

Descriptive statistics will be used to describe the demographic data. After collecting survey answers from the participants, the process of constant comparison analysis, described by Glaser & Strauss (1967) will be employed to analyze the data. After carefully reading through and examining participants answers, the data will be analyzed at three levels of analysis. First, similar words and frequently used phrases will be identified and grouped together in categories. Next, the categories will be explored and organized into groups. Lastly, the categories will be organized and themes that describe the understanding of the football players experiences will be presented.

The data is expected to show what symptom are most common amongst players and the medical or alternative intervention are most used by players. By identifying the participants' most popular interventions, further research can be conducted to determine if the intervention's success can be replicated consistently. If further studies provide evidence that the interventions are successful, then NFL players can have tools to help, potentially, with long term control over CTE. By finding out more about the types of and interventions for symptoms NFL players experience, nurses, athletic trainers, and doctors can gain more insight on what to look for regarding TBI and CTE. This data also has potential to opens up more research opportunities for medical interventions that already exist but have not been used for TBI. An example is how benzodiazepines are used to treat anxiety. If an NFL player who has had a TBI and who possibly has CTE, presents with anxiety, research can be conducted to determine if benzodiazepines could be effectively used in long-term treatment. Lastly, this research design can be easily replicated and conducted at either the same scale or larger due to the design's simplicity in its

implementation and data collection. The analytical comparison method provided by (Glaser & Strauss) offers an opportunity to further develop the theoretical groundwork for successful research.

Proposal Limitations

While health is not a one size fits all--which I consider a limitation on its own--CTE has very few studies regarding effective interventions. What may work for one individual may not work for another. Limitations to this design include the limited pool of teams and focus on specific positions. The three teams to interview are all from California, a state known for its medical professionals and investment in pro sports. These individuals are more likely to be educated on the topic and to receive effective medical treatment for their injuries compared to other states with a smaller market and less medical prestige. Another limitation of this study are the varying levels of NFL experience each participant has. NFL veterans are more at risk of exhibiting symptoms of CTE compared to rookies, and often invest more time and effort into maintaining their body evident in their prolonged tenure in the NFL. Lastly, twenty participants may not be enough to gather data. Because the design requires comparisons, more participants would mean more comparisons and thus more meaningful results.

Conclusion

Chronic Traumatic Encephalopathy is a debilitating disease professional football players develop over their careers that causes depression, anxiety, aggression, and suicidal thoughts, as documented in the review of the research literature. Because the disease has only recently been discovered, it is currently untreatable and diagnosable only after death. The presented research proposal suggests that in order to prevent negative outcomes associated with CTE in the NFL player population, it is imperative to first review with a small sample size and survey what

interventions, medical or alternative, work for each player. Ultimately, the research proposal offers more benefits than drawbacks, especially since CTE has limited data in all aspects of the disease. Football players are likely to participate in the survey because these players are at risk of losing their job due to TBI and because of the potential health advancements from which they and others may well benefit. Regardless of the results of the survey, the world will be one step closer to unraveling the enigma of CTE.

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Appendix: Literature Review Table

Author/ Citation	Purpose/ Objective of Study	Sample - Population of interest	Study Design/ Objective	Study Methods	Major Findings	Strengths	Limitations
Kahriman, A., Bouley, J., Smith, T. W., Bosco, D. A., Woerman, A. L., & Henninger, N. (2021). Mouse closed head traumatic brain injury replicates the histological tau pathology pattern of human disease: characterization of a novel model and systematic review of the literature. Acta neuropathologica communications, 9(1), 118. https://doi.org/10.1186/s40478-021-01220-8	Replicate the pattern of concussive blows on a mouse to further study behavior and neural degeneration.	Adult male mice from Jackson Laboratories	1 daily TBI for 5 consecutive days and conditions were monitored at 1, 4 , and 24 weeks.	Mouse affect was studied at 1, 4, and 24 weeks, and mice autopsies were conducted to monitor the brain chemistry, fluids, and structure.	Tau buildup, onset, and prevalence was similar to humans. Brain chemistry and structure was also similar.	Tau buildup was present in similar anatomical structures between mice and humans. Studies on mice can produce a faster solution to CTE than studies over lifetimes with humans.	These are mice and not humans and the ideas may not translate.

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Lal, A., Kolakowsky-Hayner, S. A., Ghajar, J., & Balamane, M. (2018). The Effect of Physical Exercise After a Concussion: A Systematic Review and Meta-analysis. *The American journal of sports medicine*, *46*(3), 743–752. https://doi.org/10.1177/0363546517706137	Post-Concussion Symptom Scale Scores comparison between individuals who exercised and individuals who did not exercise while effects of concussion still present.	adults with a current concussion diagnosis.	Longitudinal, Observational, systematic review, meta-analysis	A search of 5 databases from the earliest available date to September 30, 2016, and a hand search of a few articles were performed. Trial registries were reviewed, and authors of multiple studies were contacted to find additional published or unpublished studies. Randomized controlled trials (RCTs), cohort studies, and before and after (pre-post) studies evaluating the effect of physical	exercise decreased PCSS score in patients with concussion symptoms. Reaction time and Immediate Post-Concussion Assessment and Cognitive Testing components of the PCSS improved.	Major finding is related to the thesis focus, longitudinal and observational aspects add reliability.	only 5 out of 14 studies utilized randomized control trials.

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				exercise, compared with control, in patients with a concussion or mild traumatic brain injury were included.			
Marino, M., de Belvis, A., Basso, D., Avolio, M., Pelone, F., Tanzariello, M., & Ricciardi, W. (2013). Interventions to evaluate fitness to drive among people with chronic conditions: Systematic review of literature. *Accident; analysis and prevention*, *50*, 377–396. https://doi.org/10.1016/j.aap.2012.05.010	Evaluate if certain individuals should drive with their chronic condition.	Patients with Alzheimer's and Parkinson's diseases, TBI, and encephalopathy.	Systematic Review	Utilize clinical and neuropsychological tests to determine if the individual would be a safe driver.	Clinical and neuropsychological tests did not determine driving literacy.	This may mean that clinical and neuropsychological tests for CTE may not be effective.	The review had unequal amounts of focus in different chronic diseases. Alzheimer's, Parkinson's and TBI had different amounts of studies.

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Mayer, A. R., Kaushal, M., Dodd, A. B., Hanlon, F. M., Shaff, N. A., Mannix, R., Master, C. L., Leddy, J. J., Stephenson, D., Wertz, C. J., Suelzer, E. M., Arbogast, K. B., & Meier, T. B. (2018). Advanced biomarkers of pediatric mild traumatic brain injury: Progress and perils. *Neuroscience and biobehavioral reviews*, *94*, 149–165. https://doi.org/10.1016/j.neubiorev.2018.08.002	What type of technology can be used to identify subconcussive brain injuries before death?	Population is pediatric patients in clinical settings; 43 studies.	Systematic Review Monitor consistency with brain monitoring systems to predict what may come next in regards to imaging subconcussive and concussive brain injuries in adults.	Review of the various types of imaging like metabolic imaging, hemodynamics, and MRI's	The injuries that were picked up in imaging were only done so because of the acute nature of the injury and the type of injury that is more traumatic. Subconcussive blows were not imaged. MRI's were superior to other forms of imaging in general.	Human brain injuries can sometimes be imaged before an autopsy, which is good considering CTE is only diagnosable at an autopsy. Reviews the brain at a more delicate stage that may be harder considering the growth of a child compared to an adult.	Included descriptive and cross-sectional studies deemed to provide weak evidence.

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Perry, D. C., Sturm, V. E., Peterson, M. J., Pieper, C. F., Bullock, T., Boeve, B. F., Miller, B. L., Guskiewicz, K. M., Berger, M. S., Kramer, J. H., & Welsh-Bohmer, K. A. (2016). Association of traumatic brain injury with subsequent neurological and psychiatric disease: a meta-analysis. *Journal of neurosurgery*, *124*(2), 511–526. https://doi.org/10.3171/2015.2.JNS14503	Are brain trauma and psychiatric disorders correlated?	English speaking adults over 18 who had a psychiatric disorder diagnosed at least 12 months after a recorded TBI, 57 studies reviewed.	Statistical meta-analysis that reviews the type of traumatic injury and its components (LOC, memory loss, other psychotic symptoms) with the amount of time that surpassed before a psychotic disorder was formally diagnosed.	Organize different types of TBI's like concussions, or injuries that include LOC. Organize the type of psychiatric disorders and the severity and components. (measure anxiety, self harm, violence)	Disorders amongst the older population like Alzheimer's and Parkinson's diseases were found to be a common occurrence. Even ALS, which may be considered a physical condition, was found to be consistent with TBI. Anxiety and depression have many varying factors, and proved inconclusive in occurring alongside a TBI.	Not only will mental affect worsen with TBI, but a physically degenerative condition like ALS is a serious issue that may be caused by TBI. It is still being extensively researched like CTE because of what little is still known about ALS.	Meta analysis assesses a group of studies retrospectively and does not necessarily generate "new data."

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Yang, Z., Lin, F., Robertson, C. S., & Wang, K. K. (2014). Dual vulnerability of TDP-43 to calpain and caspase-3 proteolysis after neurotoxic conditions and traumatic brain injury. *Journal of cerebral blood flow and metabolism : official journal of the International Society of Cerebral Blood Flow and Metabolism*, *34*(9), 1444–1452. https://doi.org/10.1038/jcbfm.2014.105	Study of how TBI may cause a release in the protein that causes ALS and dementia (TDP 43).	Post-mortem brains who were affected by TBI and with conditions including but not limited to Huntington's, Alzheimer's, Pick's.	Study in vitro the brain's structural anomalies.	The brain is to be stained and mixed with various chemicals to see how the cerebral fluids and chemistry react.	TDP-43 causes cell necrosis in the brain, TDP-43's presence comes from TBI. TDP-43 causes dementia and ALS.	Chemical understanding of how TBI chronically damages the brain and no conflicts of interest.	Number of impacts or subconcussive impacts is unknown in this context.