CHRONIC TRAUMATIC ENCEPHALOPATHY
CHRONICKÁ TRAUMATICKÁ ENCEFALOPATIE

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ABSTRACT
Background: Chronic traumatic encephalopathy (CTE) is an illness mostly presenting in athletes that causes many severe health complications.
Objective: The objective of the overview study is to analyze chronic traumatic encephalopathy research studies from the perspective of diagnostic options.
Methods: For the analysis, selected research studies were used from scientific databases PubMed, Scopus, and Web of Science regardless of their publishing date. The search was conducted via key words: chronic traumatic encephalopathy, CTE, boxer syndrome, sport, dementia pugilistica, punch drunk syndrome. The results of the analysis show that the most common diagnostic method of CTE is the autopsy, less common are neuropsychological examinations, and using imaging methods – namely the PDDNP-PET (but only in one case).
Results: The study states that there is a causal link between CTE and the number of brain concussions where the higher the number of concussions, the higher the risk of developing CTE.
Conclusion: The quality of life of persons suffering from CTE is very low due to the health complications that usually lead to developing dementia. That is why it is crucial to focus on timely diagnosis of this illness.

Key words: Chronic traumatic encephalopathy. Boxer syndrome. Diagnosis. Overview study.

ABSTRAKT
Východiská: Chronická traumatická encefalopatie (CTE) představuje one-mocnění, které se týká především sportovců a způsobuje řadu závažných zdravotních komplikací.
Cíl: Cílem této přehledové studie je analyzovat výzkumné studie zabývající se chronickou traumatickou encefalopatií z hlediska diagnostických metod.
Metody: Pro analýzu byly použity vybrané výzkumné studie z vědeckých databází PubMed, Scopus a Web of Science, bez časového omezení.Vyhledávání probíhalo pomocí klíčových slov: Chronic traumatic encephalopathy, CTE, boxer syndrome, sport, dementia pugilistica, punch drunk syndrome.
Výsledky: Výsledky analýzy ukazují, že nejčastější diagnostická metoda CTE je pitva a v menší míře se využívají neuropsychologické vyšetření a využití zobrazovací metody, konkrétně FDDNP-PET, pouze v jednom případě. Studie uvádí, že existuje příčinná souvislost mezi CTE a počtem otřesů mozku, kdy od dvou otřesů signifikantně roste riziko vzniku CTE.
Závěr: Kvalita života osob s CTE je velmi nízká kvůli zdravotním komplikacím, které nejčastěji vedou k rozvoji demence. Z toho důvodů je důležité zaměřit se na včasnou diagnostiku tohoto onemocnění.

Klíčová slova: Chronic traumatic encephalopathy. Boxerský syndrom. Diagnostika. Přehledová studie

INTRODUCTION

In the Czech and Slovak professional envi-ronment, the set topic was not processed as a review article, for this reason, we focused on this disease, which is currently widely discussed. For the analysis, available research studies were gathered from the scientific databases PubMed, Scopus, and Web of Science. The research was conducted via the key words: chronic traumatic encephalopathy, CTE, boxer syndrome, sport, dementia pugilistica, punch drunk syndrome. The overview study analyzes research studies on the human level starting in 2005 until now that focus on chronic traumatic encephalopathy. However, according to the analysis, research was also conducted on the subhuman level.

Chronic traumatic encephalopathy

Chronic traumatic encephalopathy (CTE) is global brain damage that was described for the first time by H. S. Martland in 1928 in the scientific journal *Journal of American Medical Association* under the name “punch drunk syndrome” mani-festing itself via mild mental confusion, deceleration of muscle movements, or hand tremors within the case history of boxers (Cantu, 2007). It is however crucial to note that some authors, e.g. Tarazi et al. (2016), state that although “the punch drunk syndrome” can be understood as an older terminological synonym to CTE (especially due to the number of similarities in their clinical pictures), there is a number of differences, especially when it comes to the motor functions.

According to conducted studies, CTE most often occurs in athletes such as boxers or wrestlers (Omalu et al., 2010), or in American football/soccer players (Omalu et al., 2006; Hazrati et al., 2013; Spiotta et al., 2012) and hockey players (McKee et al., 2013). McKee et al. (2009) compared CTE in boxers, wrestlers, and American football players. They found out that box is most commonly connected to CTE. Boxers with long-term CTE often suffer from dementia (46 %), wrestlers from de-

pression and memory loss, and American football players only had mild CTE consequences. CTE was also noticed in army veterans (Omalu et al., 2011; Goldstein et al., 2012). All of these types of sports and other sports or contact activities increase the probability of repeatedly experiencing MTBIs.

Etiology

CTE is a neurodegenerative illness, similarly to Alzheimer's, Parkinson's, etc. The main pathological features of this illness are neurofibrillary tangles (NFTs), accumulation of hyperphosphorylated τ-protein, immunoreactive astrocytes, microvasculopathy (Daneshvar et al., 2015), and according to McKee et al. (2018) also the TDP-43 pathology. According to the authors of the study, one of the fundamental features of CTE is axonal damage and loss of myelin fibers – the extent of damage is connected to the level of neurodegeneration. The main risk factor of developing CTE are repeated mild traumatic brain injuries (MTBIs). Giza and Hovda (2014) state that for the abovementioned injury, the biochemical changes in the brain are the most important, such as slower intake of calcium, or increased level of potassium that when combined with sodium leads to the disruption of neural homeostasis, thereby contributing to the increased metabolism of glucose, and to the subsequent start of the so-called neurometabolic cascade. Already in 2001, it was proven that these differences between regular glucose supply and decreased supply during an MTBI leads to energy crisis of brain cells (Giza and Hovda, 2014). A specific feature is also the abnormal accumulation of the TAU protein (pTAU) that is not only typical for MTBIs but also e.g. for Parkinson's, which is one of the consequences of MTBIs (Tarazi et al., 2016). McKee et al. (2018) notes that the changes on the biochemical level were also discovered for TDP-43 protein as well, which regulates the RNA metabolism via its connections to DNA. The most visible changes happened on the frontal and temporal cortices, middle temporal gyrus, or the basal ganglia. Omalu et al. (2006) adds, that it will be necessary to also focus on neurofibrillary tangles and neuropil threads, as well as on coronary atherosclerotic diseases that were also present in all studied subjects. Rose et al. (2015) adds that 85 – 90 % of patients recover, however the remaining 10 – 15 % do not, and the consequences of the metabolic changes remain. Similarly, the brain is also impacted physically. E.g. Blumbergs et al. (1994) mentions malfunctions in microvascular integrity. Physical changes of the organism can also be seen in the changes in head turning (Sullivan et al., 2013). The overview study by Maroon et al. (2015), which was aimed also at the existence of genetic factors that could influence the development of CTE, shows that CTE when compared to the general population statistically does not increase the presence of APOE e4. This can however be a genetic predisposition to chronic neurological illnesses (Saigal, Berger, 2014). Despite the findings of the authors Marron et al. (2015), see above, authors Saigal and Berger (2014) discovered a correlation between the severity of TBIs and the existence of APOE e4. An interesting finding connected to the motor disability on the physical level is the so-called motor weakness that in most impacted patients surprisingly manifests in cognitive and behavioral symptoms (McKee et al., 2013). The term MTBI terminologically replaced the term post-concussion syndrome, which was studied by the NFL's Mild Traumatic Brain Injury Committee, which was founded in 1994 based on several professional NFL players retiring prematurely due to the post-concussion syndrome (Pellman, 2003). An MTBI has several symptoms, such as the alteration or loss of consciousness, feeling dazed or weak, or symptoms connected to the post-concussion syndrome – dizziness, memory loss, vertigo, ringing in the ears, blurry vision, etc. (Maroon, Bost, 2011; Pellman, 2003). Nevertheless, headaches are the most crucial symptom according to Penn and Chi (2018). According to the Center for Disease Control and Prevention, at least 1.7 million people in the US experience traumatic brain injuries (TBIs). Concussions or mild TBIs make up 75 % of all TBIs (Okonkwo et al., 2014). According to the results of the study by Tator and Davis (2014) (N=138), the average number of long-lasting symptoms of PCS or MTBIs was 7.6.

Clinical symptoms of CTE

Clinical symptoms of CTE can be divided into four categories according to Montenigro et al. (2014): *behavior, cognitive function, mood, and motor functions* (srov. Bailes et al., 2015). Damage of cognitive functions includes memory loss, attention disorder, lowered intelligence, as well as dementia, etc. Behavioral changes include disinhibited behavior, personality changes, loss of control, impulsivity, aggression, or physical or other violence.

Mood disorders within CTE include hopelessness, anxiety, fear, apathy, euphory, insomnia, suicidal tendencies. Motor function changes include ataxia, rigidity, shivers, or muscle weakness (Montenigro et al., 2014). According to Chudomel et al. (2019), CTE has two forms – behavioural and cognitive; the behavioural form is more common in young patients.

CTE DIAGNOSTICS

Tarazi et al. (2016) describes the need for so-called differential diagnostics and discuss developing classification including symptoms. Mayer et al. (2017) adds however that a differential diagnostics has its limits, e.g. the fact that until 2015, only two consiliary criteria were available in the DSM-IV-TR and ICD-10, and that the DSM-5 does not include e.g. the post-contact syndrome to the actual diagnosis. In 2015, Petraglia et al. also encouraged experimental research leading to better diagnostic measures and therapy approaches based on the better understanding of the anatomic and physiological levels. Turner et al. (2014) also demands at least partially outlining the techniques and analyses for dividing traumatic brain injuries. Critchley (1957) included into the symptoms of MTBIs shivers, walking ataxia, neurological disorders connected to pyramidal tract disfunctions, and in worse cases blindness or deafness. Roberts (1973) added symptoms of emotional lability connected to changes of personality, as well as memory loss and the development of dementia. According to Kuppermann et al. (2009), it is nowadays common to use CT to save costs, and to timely discover acute cases (e.g. subdural or epidural hematoma, etc.). Davis et al. (2015) also discuss the costs in connection with healthcare when it comes to brain injuries. Stein et al. (2009) stresses the importance of using CT according to Canadian recommendations only for GCS scores <15 lasting two or more hours. It is also recommended to use MRIs for differentiated diagnostics (Williams et al., 1990).

A CTE diagnosis is most often diagnosed according to a clinical history, or during the autopsy based on the typical feature of brain tissue damage with microscopically conclusive p-tau accumulation (McKee et al., 2018). Research in this area primarily focuses on retrospectively describing the consequences of MTBIs and on describing CTE. An extensive current study that focused on determining CTE postmortem is e.g. the Mez et al. (2017) study in which the authors based on the autopsies of 220 American football players neuropathologically diagnosed CTE in 177 of these players.

Less frequent method is the neuropsychological examination (f.e. Schatz et al., 2011), despite the fact that this type of diagnostic method is crucial for concussion management (Stone et al., 2014). cognitive function test (Esposito, 2017) and FDDNP-PET screening (Omalu et al., 2018).

DISCUSSION AND CONCLUSION

From an epidemiological standpoint, there is a lack of clear data about the natural progression of development of CTE alongside other risk factors such as: the length of returning to sports after an MTBI, repeated MTBIs, genetics, and life-style factors. Saulle et al. (2012) state that within the lifestyle of athletes, there are subjectively falsely induced feelings leading to more ruthless and more violent playstyle that can and often has fatal impacts on CTE. Gavin et al. (2015) note that the injuries impact the lifestyle even after the athletes are no longer actively playing. In their article, they discuss cognitive and mood changes especially in later age. Schatz et al. (2011) concludes that brain changes concern even young persons – a statement proven by their research of athletes with brain injuries who more often experienced more often sleep difficulties, as well as physiological and cognitive disorders in comparison with athletes without brain injuries. Using anabolic steroids is in this case also considered a risk factors, since in contact sports and sports in general, they are used on different levels, despite the results of study by Mills et al. (2001) stating that there is no statistically relevant relation.

A specific matter according to Alaranta et al. (2008) is using medication – a matter largely discussed by the NFL between 2011 and 2014. (e.g. Belson, 2011 or Miles 2012, etc.). The connection between MTBIs and anabolic steroids was also discussed by Mills et al. (2012) who states that anabolic steroids do not have a statistically relevant connection to APP axons. Sills (2015) adds that it is crucial to remember that opiate therapies significantly impact the brain. Putukian et al. (2014) summarizes that CTE patient care must be complex and that the personnel must be educated, that initial evaluation is crucial, as well as the evaluation of the development of the injury.

The results show that the diagnostics of the chronical traumatic encephalopathy focuses prima-

rily on autopsy. Less common methods are neuropsychological examinations and brain imaging methods, such as computer topography and magnetic resonance (only in one study). On the other hand, Okonkwo et al. (2014) state that this type of diagnostic methods is standardly being used to evaluate the return of athletes to training and matches. The authors also state that doctors usually focus in such cases on balance, history of concussions, and evaluating memory, and neurological examinations.

Currently, the Sport Concussion Assessment Tool (SCAT), or its updated version SCAT5 (Davis et al., 2017), is most commonly used to evaluate and diagnose athletes.

Currently, there is no medicament therapy for CTE, which is why prevention is crucial and effective (Fesharaki-Zadeh, 2019). Therefor we regard it as crucial to further focus on the topic in the future due to the fact that the interest in contact sports and an increasing number of younger and more at risk participants. Currently, it would be appropriate to create a system evaluating the risk of syndrome based on the number of concussions. It would also be appropriate to cooperate with trainers and focus on timely evaluation of risk consucussions when training or during matches, as well as to introduce sufficient breaks after such injuries. An ideal diagnostic tool is in our opinion the MMRI which is not being sufficiently used so far.

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