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# Introduction

Although millions of individuals suffer a traumatic brain injury (TBI) worldwide each year, it is only recently that TBI has been recognized as a major public health concern. There is growing recognition that a single severe TBI (sTBI) or repeated mild TBIs (rTBIs) can also induce insidious neurodegenerative processes, which may be associated with chronic traumatic encephalopathy (CTE) [1].

**Sports** 

The objective of a boxing match is to render an opponent temporarily unconscious through blunt head injury, with subsequent intermittent loss of consciousness (knockout, KO). Prolonged exposure to repetitive head trauma can result in chronic traumatic encephalopathy (CTE), a neurological syndrome characterized by progressive impairments in cognitive, behavioral, and motor function [2].

Mixed martial arts (MMA), sometimes called "ultimate fighting," is used to describe full-contact combat sport activities utilizing a combination of Oriental martial arts (karate, judo, jiujitsu, and taekwondo) and Western combat sports (boxing, Greco-Roman wrestling, and kickboxing) [3]. It is a combative sport between two athletes that has undergone considerable growth and expansion in the United States over the past 15 years [4]. Bouts typically are 5 min in duration and consist of 3 to 5 rounds. Winners often are declared by judges' decision, technical knockout (TKO), referee stoppage, submission, knockout (KO), physician stoppage, or disqualification [5].

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Kickboxing is a combat sport which involves two competitors directing full-force strikes with the hands, elbows, knees, shins, and feet at each other. It is one of the modern combat sports and requires athletes to achieve high thresholds of several aspects of physical fitness [6].

#### History

Martland introduced the term "punch drunk," in 1928, to describe neurological symptoms, like confusion, tremors, slowed speech, and the gait disturbances, seen in boxers suffering from repeated blows to the head [7].

Millspaugh coined the term "dementia pugilistica" to describe similar cases, in 1937 [8]. Courville introduced the term, "psychopathic deterioration of pugilists" [9]. In 1957, Critchley reported on 69 cases of progressive neurological disease in boxers and proposed "chronic progressive traumatic encephalopathy of boxers" [10].

The neuropathology of CTE was first described by Brandenburg and Hallervorden and later by Corsellis who found several characteristic areas of damage: septum pellucidum, adjacent periventricular gray, frontal and temporal lobes, substantia nigra, cerebellar scarring, and diffuse neuronal loss [11-13].

Although originally described in boxers, CTE is also found in other contact sports (football, hockey, wrestling), as well as in individuals suffering repetitive brain trauma who were not athletes [11, 12], such as military blast victims and people who suffered physical abuse and epilepsy [11].

# Pathophysiology

Catastrophic brain injuries refer to severe brain trauma associated with cerebral contusions or intracranial hemorrhage, and it can lead to long-term neurological sequelae or even death. The most common cause of death in sports-related



**Traumatic Brain Injury in Fighting** 

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TBI, especially in boxers, is subdural hematoma [14, 15]. Each year in boxing, about ten deaths occur, most of which following knockout or technical knockout [16]. Deaths are more common in lower weight classes in boxing.

A knockout is associated with concussion and loss of consciousness. Concussion occurs more frequently in professional boxing than in amateur boxing or other contact sports [17]. Concussion can also happen in other martial arts like karate [18], taekwondo [17], and kickboxing [19, 20]. The work of Koh and Cassidy [21] showed that in a Korean taekwondo tournament, the incidence of head blows and concussions was 226 – there were 2328 competitors. The younger participants had a higher the incidence of head blows and concussions [21].

Cognitive impairment often persists beyond the subjectively symptomatic time in boxers following mild TBI or a knockout, as revealed by the neuropsychological tests – it can be impaired for days following a knockout in amateur boxers [22].

Subconcussion refers to a mild head injury that causes these subtle subjective and objective neuropsychiatric deficits [23].

Rapid acceleration and deceleration forces, either linear or rotational, on the brain are the primary mechanism in which concussion and subconcussion occur. When subjected to these forces, the brain – including its neurons, glial cells, and blood vessels – is stretched. And that may disrupt their normal functions. Axons are particularly susceptible to stretching, which can lead to diffuse axonal injury [24]. Blows to the head by hook punches (rotational acceleration) in boxing results in concussion more often than linear acceleration caused by straight head blows and head contacts, common in other sports such as American football [25].

## **Acute Brain Injury**

The study of Matser et al. [26] evaluated 38 amateur boxers before and after a bout. Concussion was observed in 13 percent of cases after the fight. Porter (92) observed 281 amateur fights, and 12% of them ended in a knockout (KO) or in the intervention of the referee following blows to the head [26].

# **Chronic Brain Injury**

In 1969, Roberts examined 224 former professional boxers from the United Kingdom for neurological abnormalities. Signs of brain injury were found in roughly half the subjects. The study reported a CTE prevalence of 17%. Longer duration of exposure to sport (measured as the number of bouts), older age at retirement from boxing, and longer length of boxing career are important variables that can increase an individual's risk of developing CTE [27].

Eighteen former and active boxers were evaluated by Casson et al. [28]. They conducted neurological and neuropsychological tests and performed EEGs and computed tomographic (CT) scans. In 13 of the 15 professional boxers (87%), at least two of the four tests revealed abnormal findings, suggestive of chronic brain injury. All the professional boxers and the three amateurs boxers had abnormal scores in at least one of the neuropsychological tests [28].

Jordan et al. [29] performed brain CT scans in 338 active professional boxers. Definite abnormalities were observed in 7% (25 boxers) and possible abnormalities in over 49% of the sample (75 boxers). There was no difference between boxers with clear abnormalities and the rest of the group in terms of age, in terms of number of bouts fought, won or lost, or in terms of type of EEG abnormality. Of the boxers with defined CT abnormalities, 68% suffered one or more KOs, compared with 49% of people with possible abnormalities and only 37% of those without abnormalities [29]. Jordan et al. [30], in another study, tested 30 professional boxers using neurological and neuropsychological evaluations. Chronic abnormalities of a mild to severe nature were observed in 19 of the subjects (63% of the sample). The severity of the abnormalities was related to the number of bouts [30].

#### **Biomarkers**

In lumbar cerebrospinal fluid (CSF) in boxers 4–10 days after a bout and in boxers who have not been knockout total tau protein levels are elevated and the level normalize within the 8–12 weeks if the boxers are not subjected to further bouts [31, 32].

In amateur boxers with mild TBI after a bout, levels of neurofilament light polypeptide (NFL) in lumbar CSF are also raised [31, 32]. NFL in lumbar CSF is probably the most sensitive biomarker of axonal injury and represents the susceptibility of long myelinated axons to mild TBI [33]. Exposure to head trauma – including number of blows to the head – is correlated with NFL levels in lumbar CSF in amateur boxers [31, 32].

## Chronic Traumatic Encephalopathy in Boxing

CTE includes a latent period of 8–10 years followed by onset of behavioral disturbance, characterized by impulsivity and depression. Cognitive symptoms include disturbance of attention and memory [34]. Post-traumatic parkinsonism is also related to extensive boxing exposure [35]. Advances in brain imaging provide an opportunity to characterize in vivo neurodegeneration in athletes. The findings of frequent magnetic resonance imaging (MRI) in professional boxers include hippocampal atrophy, cavum septum pellucidum, dilated perivascular spaces, indications of diffuse axonal injury (DAI), pituitary gland atrophy, and ventricular enlargement [36].

Diffusion tensor imaging (DTI) is an advanced MRI technique that measures the microstructural integrity of brain tissue using metrics such as fractional anisotropy (FA) and apparent diffusion coefficient (ADC). FA measures, indirectly, white matter microstructure by assessing the tendency of water molecules to move parallel to structural components of axons (anisotropic diffusion) that act as barriers to diffusion rather than across them. Higher FA is commonly associated with a structural environment characterized by higher fiber density and organization, homogeneity of the direction of the fibers, axonal diameter, and degree of myelination. ADC assesses how freely water moves inside the brain tissue (isotropic diffusion or diffusivity) and is usually negatively correlated with the components of the structural environment described above. Moderate and severe traumatic brain injury (TBI) frequently results in decreased FA and increased ADC in the chronic stage [37, 38]. In acute mild TBI, the directionality of FA has been reported as elevated in some studies and reduced in others, and the reason for that is not clearly understood [39]. DTI is of great importance because it can detect changes in white matter tracts that are not observed on conventional MRI, including potential DAI associated with CTE [34].

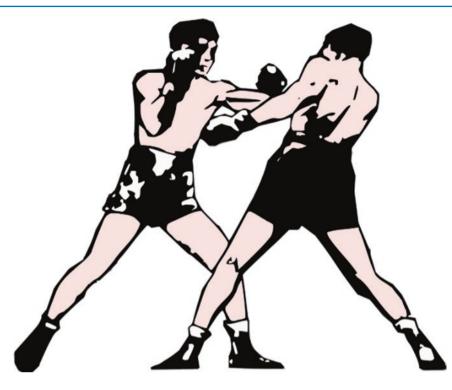
Previous DTI studies on the chronic effects of boxing showed lower FA and greater diffusivity in professional boxers in comparison with a control group [40–42].

Chappell and colleagues compared DTI in 81 professional boxers with 12 control subjects using a voxel-based analysis, and the analysis revealed regions of white matter that presented lower FA and increased ADC, including the midbrain, medial temporal lobe, lower fronto-occipital fasciculus, inferior longitudinal fasciculus, and cerebral peduncles [40]. Zhang and colleagues [42] found lower FA in the genu, splenium, and posterior internal capsule of boxers who also had greater diffusivity in the anterior and posterior limbs of the internal capsule, and for that they used a DTI region of interest (ROI) analysis. However, the comparison groups of these studies were composed of healthy individuals and did not control participation in sports.

Researchers also examined subject variables and boxing history in relation to DTI. Chappell et al. [40] found that diffusivity in subcortical structures increased with age in both boxers and the control group, but the correlation between diffusion parameters such as ADC or mean diffusivity and age in boxers (mean age of 28 years) was significantly higher than in the control group [40]. This indicates that although diffusion parameters generally increase with age, they do so at a higher rate in boxers, possibly suggesting a neurodegenerative process. The exposure to boxing is frequently estimated by the number of boxing matches and years of boxing. Shin and colleagues studied the relationship between AF, diffusion measures, and knockouts (KOs) in boxers. These researchers found a positive correlation between KOs and diffusion and a negative correlation between KOs and FA in the corpus callosum, isthmus of the cingulum bundle, pericalcarine region, precuneus, and amygdala [43].

It is important to emphasize that most DTI studies have imaged professional boxers [40–42]. Even though several studies using conventional MRI suggested that amateur boxers also exhibit chronic and neurobehavioral effects of repetitive head trauma [44, 45], an investigation of boxers and amateur boxers who have recently become professionals reported negative MRI scans and neurobehavioral findings that did not differ from a control group of athletes engaged in contactless sports [46]. In addition, the rate of chronic traumatic brain injury among amateur boxers has been viewed as insignificant [35]. The gaps in the boxing literature include sparse DTI-related data and MRI imaging for cognitive performance and history of exposure. In addition, not all studies included a comparison group with similar demographic characteristics and participation in noncontact sports.

Davis et al. [47] studied the effect of the rules change in 2013 on amateur boxing strategy, technique, and safety. Pre-2013 and post-2013  $3 \times 3$  min elite-level amateur boxing was compared from video footage of 29 Olympic (pre-2013) and 50 World Championship bouts (post-2013), totaling 99 male boxers. They found that several techniques that were dominant pre-2013 were used less post-2013, including total punches thrown, rear hand punches, and hook rear hand, while defensive movements were higher post-2013. Boxers have increased their foot movement by 20%, post-2013, to move in and then away from their opponent, combined with long-range punches and deliberate defensive movements. Pre-2013, 1.7% of bouts did not last the full duration due to referee stoppage, while post-2013, this increased to 4.2% as a result of two knockouts and eight technical knockouts. An increase in skin splits and technical knockouts is apparent. It is likely that boxers believe head guard removal has made them more prone to knockouts [47].



Fonte: Pixabay

## **Mixed Martial Arts**

The review of Lystad et al. [48] revealed that the head was the most commonly injured anatomic region, ranging from 66.8% to 78.0%. The most common type of injury was laceration/ abrasion, ranging from 36.7% to 59.4%, followed by fracture, ranging from 7.4% to 43.3%, and concussion, ranging from 3.8% to 20.4%. There is a very high proportion of head injuries in MMA and professional boxing where punches to the bare head are allowed. The high proportion of head injuries in MMA is a cause for concern, since continued repetitive head trauma is associated with degeneration in brain structures such as the bilateral hippocampi, basal ganglia, and thalamus, which can lead to cognitive impairment [48].

Published rates of injury are similar between boxing (17– 25%) and MMA (24%), and therefore many studies assume that MMA injury patterns will be similar to other combat sports such as boxing and wrestling, but given the different components of each one used in MMA, it may not be possible to extrapolate exactly that data. In fact, a review of the MMA literature reveals considerable variation in observed injury patterns, limiting the generalization of boxing and wrestling analysis to this population. A notable difference is that the lighter gloves used in MMA (4–6 oz) versus boxing (16 oz) serve only to protect the hands of competitors and do not decrease attack forces compared to wearing no gloves at all [49, 50]. Some of the available studies reviewed video evidence to evaluate head trauma but it is complicated to determine the incidence of concussion on the basis of video evidence of head trauma alone.

The study of Buse (2006) revealed (after he reviewed video footage of 1284 men competing in 642 matches from 1993 to 2003) that the proportion of matches ending by head trauma was higher in MMA (28%) compared with boxing (9%) and kickboxing (8%). An important limitation of Buse's review was that it was simply a video review of televised matches [51].

Ngai observed severe concussion – a loss of consciousness resulting from a KO – as an injury in 3.3% of matches. He reported this incidence to be similar to what has been demonstrated in taekwondo competitions [52]. The study of Scoggin evaluated 116 bouts in Hawaii, and he reported that 11 of the 55 injuries were concussions. Of the 55 fighters, 7 who had concussions had loss of consciousness, 4 had retrograde amnesia, and 5 reported facial injuries. Concussions occurred in 4.7% of exposures, and facial injuries occurred in 2.2% of exposures [53].

Heath and Callahan studied a sample of MMA athletes (n = 19) that reported concussive symptoms, training routines, and medical histories through an online survey. Almost 15% of the MMA athletes reported history of a knockout, and nearly one-third reported a technical knockout [54].

#### Kickboxing

Chronic TCE can be caused by knockout (KO) with loss of consciousness or by the cumulative effect of punching or kicking the head. Kickboxers with long experience or kickboxers with limited defense skills who repeatedly suffered heavy blows are at the highest risk of developing this condition [20]. Kickboxing is associated with chronic repeated chronological trauma that can cause brain injuries [20, 55], unconsciousness, and neurological abnormalities, mainly hypopituitarism [65]. Some studies have investigated pituitary function in amateur kickboxers and demonstrated that kickboxing is a cause of TBI, and growth hormone (GH) deficiency and insufficient adrenocorticotropic hormone (ACTH) were also very common (22.7% and 9.1%, respectively) among the 22 amateur kickboxers [56]. Consequently, Tanriverdi et al. [57] reported that GH is the most common hormone lost after TBI, followed by ACTH, gonadotropin (luteinizing hormone (LH) and follicle-stimulating hormone (FSH)), and thyroid-stimulating hormone (TSH). The mechanisms responsible for pituitary dysfunction after BIT are not entirely clear, but genetic predisposition and autoimmunity may play a role.

As in Muay Thai, all body targets are permissible in both amateur and professional kickboxing except for the groin [19]. Thus, the head, arms, and trunk would be expected to be the primary targets/injury sites for kickboxers [20, 58]. Head injuries were found as the second most frequent injury in amateur and professional kickboxers [59]. Zazryn et al. [20] reported that the head, neck, and face, followed by the lower extremities, were the most common body regions injured. The latter authors also reported that Australian kickboxers suffered more head injuries than those in the United Kingdom and the Netherlands (51.6% vs. 42.5%) but fewer lower extremity injuries (39.8% vs. 53.4%).

### **Boxing x Martial Arts**

In the study of Lee et al. [60], a conventional 3 T RM image was used to evaluate 499 fighters (boxers, mixed martial artists, and martial artists) and 62 controls for nonspecific white matter changes, cerebral hemorrhage, cavum septum pellucidum, and cavum vergae. The prevalence of non-specific white matter changes was similar between the groups. Fighters had a prevalence of cerebral hemorrhage (4.2% vs. 0% for controls, P = 0.152) and a higher prevalence of cavum septum pellucidum versus controls (53.1% versus 17.7%, P < 0.001) and cavum vergae versus controls (14.4% versus 0%, P < 0.001). The lengths of the cavum septum pellucidum plus the cavum septum pellucidum for the septum pellucidum length ratio (P = 0.009) were higher in the fighters than in controls. They found that the number of combats was slightly correlated with the length of the septum of the cavum septum pellucidum plus cavum vergae (R = 0.306; P < 0.001)



and the length of the cavum septum and pellucidum (R = 0.278; P < 0.001). When the fighters were subdivided into boxers, mixed martial artists, and martial artists, the results were similar to those of the whole-group analysis. Although brain microhemorrhages were greater in fighters than in controls, this finding was not statistically significant, possibly due in part to insufficient study [60].

## Conclusion

The objective of fighting sports, like boxing, kickboxing, and mixed martial arts, is to render an opponent temporarily unconscious through blunt head injury, with subsequent intermittent loss of consciousness (knockout, KO). Prolonged exposure to repetitive head trauma can result in chronic traumatic encephalopathy (CTE), a neurological syndrome characterized by progressive impairments in cognitive, behavioral, and motor function. Increasing data supporting the link of repetitive TBI and long-term neurodegenerative consequence has had significant implications in sports which is leading to changes in the sports' rules.

Conflict of Interest There is no conflict of interest to declare.

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