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CLINICAL FEATURE
PERSPECTIVE

Determining brain fitness to fight: Has the time come?

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Abstract

Professional boxing is associated with a risk of chronic neurological injury, with up to 20–50% of former boxers exhibiting symptoms of chronic brain injury. Chronic traumatic brain injury encompasses a spectrum of disorders that are associated with long-term consequences of brain injury and remains the most difficult safety challenge in modern-day boxing. Despite these concerns, traditional guidelines used for return to sport participation after concussion are inconsistently applied in boxing. Furthermore, few athletic commissions require either formal consultation with a neurological specialist (i.e. neurologist, neurosurgeon, or neuropsychologist) or formal neuropsychological testing prior to return to fight. In order to protect the health of boxers and maintain the long-term viability of a sport associated with exposure to repetitive head trauma, we propose a set of specific requirements for brain safety that all state athletic commissions would implement.

Keywords:

Concussion, traumatic brain injury, dementia, boxing, return to play

History

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Introduction

Professional boxing is associated with a risk of chronic neurological injury. Chronic traumatic brain injury (CTBI) encompasses a spectrum of disorders that are associated with long-term consequences of brain injury, including chronic traumatic encephalopathy, dementia pugilistica, post-traumatic parkinsonism, post-traumatic dementia and chronic postconcussion syndrome. In 1927, Osnato and Giliberti described 100 cases of concussion where individuals did not return to their pre-injury baselines, coining the term "traumatic encephalitis" [1]. Dementia pugilistica, or the "punch drunk" syndrome, was first described in the medical literature by Martland in 1928, when he described a 38-year-old retired boxer with advanced Parkinsonism, ataxia, pyramidal tract dysfunction, and behavioral changes [2]. This syndrome is the long-term cumulative neurologic consequence of repetitive concussive and subconcussive blows to the head. Recent studies have estimated 20–50% of former boxers have symptoms of chronic brain injury [3]. As a result of this prevalence and the relatively long latency to symptom onset, CTBI remains the most difficult safety challenge in modern-day boxing.

Boxers are on the receiving end of thousands of blows to the head over a typical career; the type and severity of brain injury that occurs with each blow is a complex mixture of the force applied, head movement induced, and neurophysiological state at the time. One study determined that the force of a punch from a professional boxer could be compared with being struck by a 13 lb bowling ball swung at 20 mph [4]. The essential feature of a concussive force is that it is sufficient to provide both linear and rotational acceleration of the skull (and the brain within) [5]. The element of fatigue accumulating over the duration of a fight can also increase the risk of brain injury due to the relaxation of cervical muscles. The decreased resistance provided by impaired neck musculature results in an increase in translational and rotational accelerations with each additional punch [6]. Furthermore, there may be a period of time after sustaining a concussive blow that the brain is physiologically more vulnerable to be injured again at a lower threshold. Better identifying those higher risk fighters could facilitate primary prevention efforts, such as reducing the risk of reinjury (secondary prevention), and providing access to appropriate interventions that

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may reduce associated personal and societal costs (tertiary prevention) [7].

Understanding the precise threshold of damage required for the production of both acute and chronic neuropathology remains elusive; thus early detection and appropriate management of neurological injury in professional boxing is imperative. In order to reduce chronic morbidity after acute injury, most amateur and professional-level sports organizations now adhere to various return-to-sport guidelines after concussion [8-10]. These guidelines generally restrict symptomatic physical activity and recommend cognitive rest in athletes until the symptoms of concussion have improved. Ultimately they require a return to neurocognitive baseline prior to the resumption of contact risk activities. In boxing and mixed martial arts (MMA), medical suspensions are generally required after a technical knockout (TKO) or knockout (KO). During a restricted period, the athlete is prohibited from sparring and competitive fighting but not from conditioning. These suspensions range from 30 days to 180 days, but vary greatly in uniformity and regulation by the various athletic commissions [11-14]. Furthermore, due to the lack of federal oversight, countless fighters who are precluded from boxing in a state due to a medical condition often apply to fight in a state which does not have such stringent requirements in place [15].

Because the sport encourages deliberate blows to the head, participants are at risk of head injuries that may be cumulative and even fatal. Much of the world's medical community has spoken out against boxing, including the American, British, Canadian, Australian and World medical associations; and the American Academy of Pediatrics [16-21]. The current authors, however, suggest that such arguments fall short recognizing the benefit of active medical involvement in the context of combat sports. Clinicians should emphasize the inherent risks, insist on safety precautions, and even discourage participation on certain medical grounds. We remain wary, however, of opposing this sporting genre en masse, due to other associated factors, such as socioeconomic background and the benefit of structure/self-discipline/exercise.

Safety issues in boxing

Issues regarding brain health in boxers can generally be divided into three categories: 1) pre-participation assessment of neurologic status, 2) determination of return to fight from concussion, and 3) assessment of ability to continue participation in the sport ("when do you hang up the gloves?").

The effects of concussive injuries have been increasingly recognized due to a number of factors, including greater media coverage, educational outreach, and position statement papers on injury management from various medical organizations. With this improved awareness, numerous policies now exist to decrease the risk of morbidity/mortality following injury. Most major professional sports leagues in the United States, including the National Football League (NFL), National Basketball Association (NBA), National Hockey League (NHL), Major League Baseball (MLB), Major League Soccer and Ultimate Fighting Championship (UFC) have a formal concussion policy in place. Since 2009, the NFL has required clearance from an independent neurological consultant prior to RTP after concussion. The NBA and NHL require that each diagnosed concussion be reviewed by the independent neurologist or neuropsychologist overseeing their formal concussion programs, respectively [22,23]. In 2011, MLB created a seven-day disabled list for players with concussions, in addition to the normal 15-day disabled list for other injuries. It also mandates baseline neurological testing for players joining a new club, as well as every player during Spring Training [24]. In July of 2014, the National Collegiate Athletic Association (NCAA) released new guidelines for concussion safety, including limiting live contact football practices to two per week during the season [25]. The guidelines address contact at football practices, independent medical care for all athletes, and best practices to diagnose and manage concussions. The UFC requires a MRI or CT scan of the brain following a KO loss. A mandatory medical suspension is also levied, banning the fighter from contact drills in practice for a specified length of time as directed by the specific athletic commission [26]. The UFC is currently reviewing concussion guidelines that have been used in other professional sports.

The return to fight approach, however, in professional boxing, remains much less standardized. Traditional guidelines used for return to sport participation after concussion are inconsistently applied, dependent upon specific jurisdiction. Furthermore, few athletic commissions require either formal consultation with a neurological specialist (i.e. neurologist, neurosurgeon, or neuropsychologist) or formal neuropsychological testing prior to return to fight. The transient nature of boxers also provides a significant challenge in delivering "best practice" medicine. Many boxers travel between states or internationally for bouts, thus complicating attempts to track fighters between contests.

In addition to acute injury, chronic neurological impairment is also a major medical concern in modern-day boxing [27,28]. It has long been recognized that certain individuals exposed to repetitive head trauma develop persistent and in some cases progressive neurological impairment even with the cessation of exposure to head trauma (Table 1) [29]. The natural history of this disorder is not known nor are there any specific diagnostic tests that can reliably identify those who are afflicted during life [30]. Without any objective measures, a vexing problem for athletic commissions is determining when the cumulative exposure a fighter has sustained has reached a point where the fighter should no longer be allowed to participate in sanctioned competitions. It is possible that serial neuropsychological testing may help objectively identify those with chronic progressive

Table 1. Chronic traumatic brain injury.

Long term consequences of traumatic brain injury	
Chronic traumatic encephalopathy	Dementia pugilistica
Chronic postconcussion syndrome	Chronic neurocognitive impairment
Posttraumatic dementia	Posttraumatic cognitive impairment
Posttraumatic parkinsonism	Persistent posttraumatic headache

Data taken from [29].

neurocognitive impairment; however many challenges exist in the practical application of these tests in combat sports.

Current state of affairs

There is little uniformity with regard to the medical regulation of professional boxing in the United States. Boxing remains the only major professional sport in America that does not have a national and/or unified commission. Unlike other professional or even elite amateur sports (NCAA, United States Olympic Committee) that are organized at a national level, professional boxing lacks a single major governing body to enforce its rules. Yet, fighters frequently fight in different states throughout their career.

For states that sanction professional unarmed combat events, the responsibility for regulation of these sports, and protection of the participants, falls to the state athletic commission. Each state has developed its own requirements for licensure of combatants and those associated with the sport (e.g. trainers and officials). From a practical standpoint, the commission would like to determine if the fighter already has evidence of a neurological deficit (either clinically or by imaging) that puts them at higher risk of acute injury if they fight or are showing signs or symptoms of neurological impairment that may indicate onset of a potentially progressive process. The problem, as depicted in (Table 2), is that no two states have the same exact requirements, particularly as it pertains to the evaluation of neurological status and many commissions have no specific requirements for neurological assessment [31,32].

Evaluation of brain "fitness" to fight generally has included three primary domains: brain imaging, neurological examination, and cognitive testing [33,34]. A number of states have requirements for brain imaging, though the specifics range from a single initial MRI/MRA to the need for periodic testing ranging from every 3–5 years [31]. The main purpose of the imaging is to uncover a structural lesion such as a subdural hematoma, vascular malformation or aneurysm, or large arachnoid cyst, which may increase the risk of intracranial hemorrhage [29]. The decision regarding the significance of an MRI finding is usually left with the state commission's medical advisor or officer. Thus, a fighter may be excluded from competing in one state due to a structural lesion, yet be allowed to fight in a different state. There is no data regarding what frequency of MRI imaging is optimal to help reduce serious brain injury; however, neuroimaging performed immediately post-bout is sometimes indicated to rule out acute hemorrhage and/or evidence of diffuse axonal injury in cases of high clinical suspicion.

Whereas most states require a physical examination that presumably includes evaluation of the neurological system, few states mandate a neurological examination by a neurologist or neurosurgeon. It is certainly likely that the detail of the evaluation, even among neurologists, varies between examiners; the determination of what is a significant finding is subjective indeed. No state utilizes an instrumented evaluation tool to assist in the neurologic assessment of fighters.

It is a rarity for state commissions to require formal assessment of cognitive function, despite the fact that cognitive impairment is a common symptom from repetitive head trauma. The few states that require cognitive testing have variable requirements, ranging from an abbreviated mini-mental status examination embedded in the neurological exam to no specific instrument designated.

Once licensed by a particular state, the fighter is usually required to renew yearly with similar testing, with the exception of repeat brain imaging. Certain states do mandate more extensive testing based on age or number of rounds fought. However, these criteria are not evidence-based; it has not been demonstrated that there is a relationship between a particular age or specific number of rounds and risk of brain impairment.

An unpublished 2014 survey completed by 27 state athletic commissions highlighted these disparities between states [32]. Specifically, 8 respondents required "evaluation by a neurologist or neurosurgeon" prior to obtaining licensure, 6 required similar evaluation after a TKO or KO loss, and 12 required said evaluation in high risk and/or older fighters (*A high risk fighter is any fighter who has suffered 6 consecutive losses, lost more than 25 total fights, has a career of more than 350 rounds, has suffered a concussion or difficulty in a match where the physician has requested additional testing, and/or has been inactive for more than 30 months* [31]). Similarly, on the question of required neuroimaging exams (either MRI brain or CT head), 10 required this prior to obtaining initial licensure, 6 after a TKO or KO loss, and 13 commissions reported this mandate in high risk and/or older fighters.

Formal recommendations

As mentioned above, the goals of any required neurological assessment would be to identify those disorders that would place the fighter at increased risk of serious acute injury (e.g. intracranial hemorrhage) during competition or indicators of cumulative brain injury that could significantly affect athletic performance or predispose to progressive neurological impairment.

On June 18, 2012, Senator John McCain introduced the Professional Boxing Amendments Act of 2012, co-sponsored by Harry Reid. Its stated goal was to better protect professional boxing from "ineffective regulation that has plagued the sport for too many years, and that has devastated physically and financially many of our nation's professional boxers" [35]. This legislation aimed to establish the United States Boxing Commission, providing a unified regulatory body for professional boxing in the United States. Despite these efforts, the resolution was ultimately defeated. Since the 103rd Congress in 1993, there have been no fewer than 19 failed attempts at establishing a national commission for professional boxing through legislation [15].

Given the inability to establish a national commission for boxing (and more broadly, unarmed combat sports), we recommend the incorporation by state athletic commissions of a uniform set of minimum requirements for brain safety that would be available and shared between states. Each state could add more requirements as they saw fit.

In developing these (or future) minimum recommendations, there were several logistical factors to be considered

Table 2. State-to-state athletic commission variability.

State	Neurologic Exam	Specifics	Radiological Exam			Consistent with State Commission Website	Comments	Additional Requirements
			Type	Renewal	Specifics			
Nevada	N		MRI or MRA w/o contrast	N		Y	There is no separate neurological exam, however, reflexes are noted in the physical exam	If have not fought in last 36 mo or has fought over 425 professional rounds, then must submit comprehensive physical exam
California	Y	Valid for 15 mo	MRI w/o contrast (GRE technique)	Y	Valid for 5 yrs	N	The length of time the medical exams are valid are not specified on state commission website	
Arizona	N		N			Y	There is no separate neurological exam, however, reflexes, speech, and memory/judgement are noted in the physical exam	applicants over 36 years of age must get special permission from commission; LICENSE EXPIRES ANNUALLY (DEC 31ST)
Illinois	N		N			Unclear	No clear guidelines were listed on the state commission website	
Texas	N		N			Y	There is no separate neurological exam, but the physical exam has neurological subset (gait, finger to nose, bicep jerks, brudzinski, rhomberg, knee jerks, babinski, and cranial nerves)	
New York	N		MRI w/o contrast	Y	Valid for 3 yrs	N	Unable to access any medical forms aside from Medical Information Release; Unable to find statement of MRI requirement or renewal	Fighters with 6 consecutive losses, fighters with 3 consecutive KO or TKO losses, or being idle for > 1 yr may require additional testing
Connecticut	Y*	Valid for 3–4 yrs	MRI or CT scan*	Y	Valid for 3–4 yrs	Unclear	*Fighter has a choice of MRI, CT scan, or Neurological exam	
Florida	N		N			Y	Must contact commission if interested	
New Jersey	N		MRI w/o contrast or CT	Y	Within 3 years of event/licensure	Y	There is no separate neurological exam, but the physical exam has neurological subset (gait, finger to nose, bicep jerks, brudzinski, rhomberg, knee jerks, babinski, and cranial nerves)	
Ohio	Y*	Valid for 5 yrs	MRI w/o contrast and MRA*	Y	Valid for 5 years	Unclear	*Neurologic exam: req'd for fighters who have multiple losses, KO's, TKO's, or are 35 yrs old and older; *Radiological Exam: ≥ 35 yrs-MRI w/o contrast required; ≥ 39 yrs-MRA and MRI w/o contrast required	

Abbreviation: TKO: Technical knockout.

including availability and reliability of the measures and the financial burden they may impose. Recognizing that fighters commonly train in areas far from where they will compete, any recommended testing should be widely available or at least able to be completed at the venue the day before the competition. Moreover, the measure must be reliable and have adequate test/re-test properties with minimum practice effect. Finally, the cost of the required testing must not place a financial burden to the fighter, as they often incur the cost of testing and licensing.

Our initial recommendations include

Standardized neurological testing

Arguably, the most crucial component for assessment of both return to play from acute injury and for long-term monitoring of neurological function is a standardized neurological examination. This type of testing should include measures of cognitive and motor function. Because of inherent variability between different examiners in the clinical neurological examination, an instrumented approach may be preferable. Systems that can be performed on tablet or even smartphone devices which assess processing speed/working memory, postural stability, and dynamic visual acuity, are currently available and have been used in other contact sports. *A baseline evaluation should be performed as part of the standard pre-licensing evaluation with follow-up testing administered prior to each bout.* This allows an objective comparison should that athlete sustain a concussion during a fight and would hopefully prevent the fighter from returning to competition until back to their neurological baseline. Any return to competition following symptomatic head trauma should follow the same recommendations as outlined in the 2012 Zurich Consensus Statement on Concussion in Sport (Table 3) [10]. Boxers exhibiting signs or symptoms suggestive of chronic neurologic impairment should be withheld from further contact exposure until more extensive neurological evaluation can take place. Moreover, longitudinal testing of a fighter may also be able to detect cumulative brain injury which is a risk factor for CTBI.

Though not part of the minimum requirements, states may consider requiring a clinical neurological evaluation by a neurologist for those fighters who have sustained a KO, TKO, or "hard" fight prior to being approved for their next competition.

Table 3. Return-to-play guidelines.

Steps	Activity	Functional Exercise
Step 1	Rest	Symptom limited physical and cognitive rest
Step 2	Light aerobic exercise	Walking, stationary bike, swimming, elliptical (no resistance training) *Keep HR < 70% maximum predicted
Step 3	Sport-specific exercise	Running drills, heavy bag training, etc. (no head impact activities)
Step 4	Non-contact training drills	Progress to more complex training drills. May incorporate progressive resistance training
Step 5	Full-contact practice	Participate in normal activity/training/ sparring (following medical clearance only)
Step 6	Return-to-play	Cleared to compete without restriction

Adapted with permission from [10].

Neuroimaging

Neuroimaging may be useful in protecting the health and safety of the boxer and virtually every sort of imaging modality, ranging from pneumoencephalography to positron emission tomography has been studied in boxers. Surveillance pre-bout neuroimaging at times (though not often) has proven beneficial in detecting preexisting brain lesions that may predispose boxers to catastrophic brain injury [36]. In addition, a number of reports in the literature indicate imaging changes associated with cumulative exposure to head trauma [37,38].

Despite these associations, the application of what we know through evidence-based practice regarding imaging in boxers remains limited [39-42]. There is a paucity of data from well-designed studies to determine the utility of information in making decisions on fitness to fight or the value of these measures in protecting fighter safety. Most published imaging studies are cross-sectional and do not include a clinical outcome, so the significance of any one finding in predicting clinical change is unknown. In addition, the composition of the samples studied is usually not random, which may result in a bias of having more clinically symptomatic individuals participate.

For these reasons, we recommend use of neuroimaging in the initial licensing process to exclude any structural lesions that may place the fighter at risk, acknowledging that the yield of finding an abnormality is small. With longitudinal studies of fighters underway, this initial scan also may serve as a baseline which could be used for comparison in the future. The MRI of the brain should be performed without contrast on a 1.5 or 3.0 Tesla Magnet, including T1 weighted images, T2 weighted images, Gradient Echo or Susceptibility-Weighted Imaging (SWI), Diffusion-Weighted Imaging (DWI), and Fluid-Attenuated Inversion Recovery (FLAIR). These sequences are useful in detecting vasculature and other structural lesions or anomalies that should preclude further participation in competitive boxing including: large arachnoid cyst; arteriovenous malformation; intracranial aneurysm; evidence of underlying hydrocephalus; symptomatic Chiari-I malformation; evidence of subdural hematoma or previous intracranial hemorrhage. The significance of a microhemorrhage present only on gradient echo/susceptibility weighted images has not been established. The risk this lesion presents to a fighter needs further study; the finding should be integrated with other clinical and imaging information in making a decision about fitness to fight.

It is recommended that the imaging be repeated if the fighter shows objective decline in their neurological testing or are felt to be at high risk based on a risk index (see below).

High risk fighters

The mainstay of preventing chronic neurological sequelae in boxing is appropriate identification of those participants

who may be at increased risk. Many states require more comprehensive evaluation of certain fighters based on age (often 35 years or older) or number of rounds they have fought. Repeated exposure to head trauma over time is the most important risk factor for the development of chronic neurological impairment. Information from the Professional Fighters Brain Health Study suggests that simply using criteria of age or number of rounds fought did not strongly identify those individuals who were performing worse on tests of cognitive function [43]. Rather, a Fight Exposure Index was proposed that combines several factors including age, number of professional fights, average fights per year, and number of KOs. This formula which is based on readily available information, significantly correlated with performance on cognitive measures. Thus, *we would recommend using a risk index to identify those fighters at highest risk of impairment for closer evaluation including MRI brain imaging and instrumented and clinical neurological evaluation.* Further testing, such as functional MRI, PET imaging, or a formal neuropsychological battery may be requested at the discretion of the attending neurologist or neurosurgeon.

The role of biomarkers

The significance of Apolipoprotein (Apo4, ApoE promoter gene), tau polymerase and other genetic markers in the management of sports concussion risk or neurologic outcome is unclear at this time. APOE e4 has been associated with an increased severity of chronic neurological impairment in high-exposure boxers (i.e. boxers with more than 12 professional bouts), suggesting there may be a genetic predisposition to the untoward effects of a long boxing career [44]. In addition, biochemical serum and cerebral spinal fluid biomarkers of brain injury (including S-100B, neurofilament light chain (NFL), neuron-specific enolase, myelin basic protein, glial fibrillary acidic protein, and tau) have been proposed as a means by which cellular damage may be detected if present [45-50]. *There is currently insufficient evidence, however, to justify the routine use of these biomarkers clinically.* Further investigation will hopefully prove beneficial with guiding sports medicine physicians in the medical counseling of fighters and long-term risk discussions.

Conclusion

Unfortunately, acute and chronic brain injuries are the most common injuries sustained by boxers. The sport has long been regulated by state commissions, but currently these governing bodies vary greatly in providing for the neurologic health of boxers. Many states lack best practice medical requirements and enforcement varies widely, which leads to forum shopping by the boxer until a favorable fighting venue is located. State regulation of boxing also results in conflicts of interest because stringent regulation by a state may lead to lost revenues when a bout is scheduled elsewhere. Boxing remains the only major sport in this country that lacks a central regulatory organization. Concussion and lasting brain damage is an especially significant risk for boxers, as the goal of the sport is, in fact, to deliver a concussion to the opponent. With studies estimating that up to half of all boxers will suffer from chronic traumatic brain injuries, the time has come for the development of uniform minimum requirements for brain safety that all states incorporate. The health of boxers and the long-term viability of the sport both depend on it.

Declaration of interests

There were no sources of material support provided for this manuscript. T Seifert is a member of the Kentucky State Boxing Commission and has served as a consultant for the United States Department of Defense. He has received personal compensation as a speaker for the National Headache Foundation and the American Headache Society. C Bernick receives funding for the Professional Fighters Brain Health Study from UFC, Top Rank Promotions, Golden Boy Promotions, Bellator/Spike TV, Haymon Boxing, Lincy Foundation/UCLA Dream fund. B Jordan is the Chief Medical Officer of the New York State Athletic Commission, an Unaffiliated Neurotrauma Consultant for the National Football League, and is a Medical Advisory Physician for the National Football League Players Benefits. He also receives compensation from expert legal opinion. A Alessi is a consultant to the National Football League Players Association and is a member of the NFL/NFLPA Accountability and Care Committee. He also serves as ringside physician for the Mohegan Tribe Department of Athletic Regulation, Mashantucket-Pequot Tribe Athletic Commission, and the Connecticut State Athletic Commission. J Davidson is an independent medical consultant to the Ultimate Fighting Championship as well as The Ultimate Fighter. R Cantu receives compensation from the National Football League (NFL) as Senior Advisor to the Head Neck and Spine Committee, from the National Operating Committee on Safety of Athletic Equipment (NOCSAE) as Chairman of the Scientific Advisory Committee, and from Sports Legacy Institute (SLI) as Co-founder and Medical Director for some talks given and research conducted. He receives royalties from Houghton Mifflin Harcourt and compensation from expert legal opinion. C Giza is a member of the California State Athletic Commission and receives grants/research support through the NIH, NCAA, DoD, NFL-GE, Today's and Tomorrow's Children Fund, UCLA BIRC, and the UCLA Steve Tisch BrainSPORT program. He is a consultant in medicolegal cases for Pearson PLC, Alcobra. He serves on the Speaker's Bureau of the Medical Education Speakers Network. M Goodman is the President and Board Chairman of the Voluntary Anti-Doping Association. She is the former Medical Advisory Chairman of the Nevada State Athletic Commission. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

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