

REVIEW ARTICLE

Boxing—Acute Complications and Late Sequelae

From Concussion to Dementia

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SUMMARY

Background: Boxing has received increased public attention and acceptance in recent years. However, this development has not been accompanied by a critical discussion of the early and late health complications.

Methods: We selectively review recent studies on the acute, subacute, and chronic neuropsychiatric consequences of boxing.

Results: Cerebral concussions (“knock-outs”) are the most relevant acute consequence of boxing. The number of reported cases of death in the ring seems to have mildly decreased. Subacute neuropsychological deficits appear to last longer than subjective symptoms. The associated molecular changes demonstrate neuronal and glial injury correlated with the number and severity of blows to the head (altered total tau, beta-amyloid, neurofilament light protein, glial fibrillary acidic protein, and neuron-specific enolase). The risk of a punch-drunk syndrome (boxer’s dementia, dementia pugilistica) as a late effect of chronic traumatic brain injury is associated with the duration of a boxer’s career and with his earlier stamina. There are similarities (e.g. increased risk with ApoE4-polymorphism, beta-amyloid pathology) and differences (more tau pathology in boxers) compared with Alzheimer’s disease.

Conclusion: Protective gear has led to a remarkable reduction of risks in amateur boxing. Similar measures can also be used in professional boxing, but may decrease the thrill, which does appeal to many supporters.

► Cite this as

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Boxing matches were added to the Olympic games in 688 BC. The athletes boxed without any breaks until one of the opponents was not longer able to defend himself. The Greek boxers wrapped leather straps around their fists, while from 150 BC Roman boxers wore gloves that were reinforced with iron and lead. The British boxer Jack Broughton introduced the use of padded boxing gloves (mufflers) for training and exhibition matches after killing an opponent. In 1742 Broughton codified a set of rules that were later named in his honor: a break in the fighting after a knockdown and no blows below the belt. The Queensberry Rules were published in 1867 and their use became widespread towards the end of the 19th century. They stipulated:

- the wearing of boxing gloves
- a round of three minutes’ duration with a one-minute rest period
- counting to ten after a knockdown.

Although rules in professional boxing vary around the world, in amateur boxing measures to protect boxers have become increasingly uniform since 1946 (1, 2) (www.aiba.org). These protective measures include:

- the wearing of a head guard
- more heavily cushioned gloves each weighing 284 g (10 ounces, 8 ounces in professional boxing)
- shorter and fewer rounds (4 x 2 minutes for men, 3 x 2 minutes for women)
- stopping the bout in accordance with the “out-classed rule” if the point difference becomes too large (>20)
- the option for a boxer to interrupt the bout himself
- the option for the ringside doctor to intervene (only the referee may intervene in professional boxing).

Amateur boxers undergo regular medical examinations once a year and prior to matches (including ECG, eye and laboratory tests). Professional boxing matches are staged without these extensive protective measures. This has possibly stimulated the public’s interest with the result that for several years these matches have been broadcast on public television networks during prime time.

In this review article we describe the results of the most comprehensive studies conducted in the last decade on the acute, subacute and chronic medical complications of boxing.

Methods

A PubMed search in April 2010 using the keyword “boxing” retrieved more than 1000 research articles, of which 303 were published within the last 10 years. We selectively describe the essential material from the most recent and comprehensive original and review articles from the last decade on the acute, subacute and chronic neuropsychiatric consequences of boxing and quote these in the brief list of references. Older research articles and case reports were not separately specified. In the case of multiple publications by the same authors or research groups on closely related topics, the most recent research article was quoted in the reference list. Relevant search results on related topics such as similar combat sports, recurrent traumatic brain injury or neurodegeneration are only briefly mentioned.

Acute consequences

Mechanism

The objective of a boxing match fought according to the rules is to render an opponent unable to defend himself, for example, by inflicting a blunt head injury with subsequent intermittent loss of consciousness (knockout, KO). The speed of the fist upon impact with the head can be 10 m/s or greater. The force increases with the weight class to up to more than 5000 Newton resulting in translational acceleration of the opponent’s brain of more than 50 g (3, 4). Rotational acceleration of the brain has a critical effect on the outcome of matches. Shearing forces result in compression, strain and functional lesions in the central pathways in the upper brainstem (5). Acceleration and impact of the brain hemispheres against the roof of the skull may cause coup and contrecoup lesions as a result of punches to the head or the head striking the ring floor. These injuries generally occur in professional boxing without head guards.

Other injuries

As well as a legitimate knockdown, other injuries to the head and face are often observed in boxing matches (6). In 907 matches fought by 545 professional boxers aged 18 and 43, 214 other injuries were registered (24%) (7). In 17% of 524 professional boxing matches fought between September 2001 and August 2003 in Nevada, such other injuries were inflicted of which 51% were to the facial area, 17% to the hands, 14% to the eyes and 5% to the nose (knockout was not considered an injury) (6). The injury rate was 17.1 per 100 boxing matches or 3.4 per 100 rounds (3.6 per 100 rounds for men and 1.2 per 100 rounds for women; $p < 0.001$). Ninety percent of the professional matches were fought by men and significantly more knockouts were recorded for men than women ($p < 0.001$). The risk of sustaining such injuries was significantly increased among the losers (odds

ratio 2.5; confidence interval (CI) 1.7–3.7) and was approximately four times higher after defeat due to knockout (8). In one study of 956 Italian boxers (55% professional boxers) reported injuries to the conjunctiva, cornea, lenses, vitreous bodies, retina or pupils in 41% of the study participants although only 6% proved to be serious (9).

In amateur boxing, data from 5 Olympic Games and 10 World Championships indicate that up to the year 1984, 13.6% of the matches had to be stopped due to a knockout or other injuries. After the introduction of head guards this was still the case in 9.5% of matches up to 1996 and after switching from three 3-minute rounds to four 2-minute rounds in only 2.2% of matches up to 1999. After the introduction of the “out-classed rule” no matches were stopped up to 2004 (1). The risk of sustaining injuries not covered by the rules in a match increases with the number of matches fought and the age of the boxer (6, 7).

Acute deaths

Records kept since 1890 about boxing matches fought according to various rules have documented about 10 deaths every year. A comparison revealed that none of the statistics are complete (10) (Boxing Fatality Collection, www.ejmas.com; www.boxrec.com). The absolute numbers must therefore be higher.

An evaluation indicated that only 4% of the fatalities occurred in championship matches (www.ejmas.com). Two-thirds of those killed were professional boxers; three-quarters of the boxers died in the ring itself.

The causes were:

- cardiac complications
- tears to the liver or spleen
- head and neck injuries (more than 80%) such as
 - ruptures or thromboses in larger brain vessels
 - epidural hemorrhages
 - subdural hematomas
 - other injuries.

A comparison of the decades between 1890 and 2000 revealed a slight downward trend in the number of deaths reported (103—94—127—191—155—116—146—113—95—67—78; according to www.ejmas.com). Recent numbers are not available. Potential risk factors for increased mortality are:

- age
- pre-existing brain changes
- somatic diseases (hypertension, diabetes, bleeding diathesis)
- medication (antihypertensives, anticoagulants, steroids, erythropoietin)
- dehydration
- pronounced weight loss
- a large number of punches striking the head during the match
- “second impact syndrome” with incomplete recovery after a recent injury (www.boxrec.com).

Video analyses of matches that ended in fatalities have—as expected—shown that the total number of punches thrown by both contestants and the number of

the punches that landed were related to the outcome of the match; these indices could possibly be used to stop a match before a fatality occurred (10).

Subacute consequences

Subjective symptoms

A questionnaire of 632 Japanese professional boxers (11) revealed that on the day after a knockout almost half of the athletes continued to suffer from persistent symptoms such as:

- headaches
- tinnitus
- forgetfulness
- impaired hearing
- dizziness
- nausea
- impaired gait.

Approximately 10% of these active boxers reported constantly suffering from forgetfulness, headaches and other symptoms.

Neuropsychology

Cognitive deficits after sports trauma last measurably longer than the subjective perception of the problems (12). Many active boxers develop at least mild cognitive disorders which can be easily detected using simple tools. Computer-based neuropsychological testing (ImPACT™) showed that delayed recall was limited in amateurs even after training matches while wearing head guards (sparring) (3). Male boxers had more obvious and longer lasting deficits (initial value 0.80 ± 0.06 ; immediately after the boxing match 0.73 ± 0.14 , $p < 0.05$; 24 hours later 0.75 ± 0.14) than female boxers ($0.79 \pm 0.07/0.74 \pm 0.09$, $p < 0.05/0.76 \pm 0.08$). This study revealed no significant changes in the immediate recall, working memory and reaction time (3). A comparison of 82 amateur boxers revealed that those who had been knocked out performed significantly worse in visual-spatial and mathematical exercises in the following two days (12). A prospective study of amateur boxers whose matches had to be stopped were significantly slower in simple reaction tests and multiple choice exercises afterwards (13). Eighteen professional boxers still had significantly impaired performance in information processing and verbal fluency compared to the baseline results one month after a knockout. Cognitive function declined depending on the total number of preceding matches (14). The time required for cognitive recovery is strongly age-dependent as indicated by a comparison of college and high school students, that is, of age groups well below 30 years of age (15). There are also indications of adverse neuropsychological effects in other sports. A study of amateur and professional footballers revealed a statistical correlation between reduced cognitive performance and the number of headers and traumatic brain injury (16).

Biochemistry

Traumatic brain injury induces the formation of significantly more beta-amyloid, the primary consti-

tuent of Alzheimer plaques, within 24 hours. Fourteen Swedish amateur boxers volunteered to have a lumbar puncture about one week and three months after a boxing match (17). The one-week values for total tau protein, neurofilament light protein, and glial fibrillary acidic protein were significantly higher than the three-month values and this was more obvious the more and harder the punches sustained by a boxer. Serum levels of neuron-specific enolase was still elevated after a two-month hiatus (18). These results indicate acute neuronal and astroglial cell lesions.

Chronic consequences

Neuropsychiatry

Ten to 20% of professional boxers suffer from persistent neuropsychiatric sequelae. The following are the most serious consequences of chronic recurrent traumatic brain injury in professional boxers with longer careers (19, 21):

- motor skills: tremor, dysarthria, Parkinson's disease, ataxia, spasticity
- cognition: slowing, memory disorders, dementia
- experience and behavior: depression, irritability, aggression, criminality, addiction.

The frequency of the individual symptoms cannot be systematically determined.

Similar risk factors were found for dementia pugilistica (punch drunk syndrome, chronic traumatic encephalopathy) as had been found for the acute complications of boxing: age (>28 years), duration of career (>10 years), number of matches, and poor defensive reflexes. Additional factors include frequent knockouts, lengthy sparring sessions, "good staying power," and carrying the apolipoprotein E4 genotype (19). However, an evaluation of 36 studies of amateur boxers did not yield any higher grade evidence for clinically serious long-term disorders (20).

Neuroradiology

Conventional methods for structural imaging only show clear chronic-pathological changes in a small percentage of boxers but do reveal an increase in the incidence of anomalies such as cavum septi pellucidi (22). A recent series found structural anomalies in only 7 of 49 professional boxers examined, specifically white matter changes (5x), chronic subdural hematoma (2x) and cavum septi pellucidi (1x), however, the boxers had increased diffusion coefficients and reduced diffusion anisotropy compared to healthy adults, which may indicate microstructural lesions (23). These changes are pronounced in the posterior white matter. An earlier study by the same group of authors revealed a correlation between these diffusion variables and the number of hospital admissions resulting from boxing matches. Microhemorrhages were found in 3 of 42 amateur boxers taken from a heterogeneous sample (24). Almost half the boxers had a deficit in growth hormones at the end of their careers and all of them had reduced hypophysis volumes (25). The same group of authors elsewhere described an increased risk of post-traumatic

hypophyseal insufficiency in boxers with the ApoE4 genotype.

Neuropathology

The primary histological features of chronic traumatic encephalopathy in boxers are increased tau phosphorylation and patchy distribution of neurofibrillary tangles, particularly in the upper layers of the frontal and temporal lobes (21). Amyloid plaques are also found. Animal experiments have demonstrated that the post-traumatic accumulation of amyloid involves the same molecular mechanisms as Alzheimer neurodegeneration (presenilin 1, gamma-secretase, BACE1) (e1). The neurodegenerative process in boxer's dementia is increased by apolipoproteinE4 polymorphism just as in Alzheimer's disease (19). Cell biology experiments found indications of a more than additive effect of repetitive trauma (e2); repetitive trauma accelerated the formation of neurofibrils in transgenic mice models of tauopathy (e3). In agreement with these neurobiological findings, the epidemiological evidence for a correlation between traumatic brain injury and Alzheimer's disease is increasingly compelling (e4).

Discussion

Our review can be summarized as follows:

- Along with legitimate lesions sustained by competitors, for example as a result of cerebral concussion (knockout), there is a considerable risk of acute injuries to the head, heart, and bones in competitive boxing. Every year, several boxers die in the ring.
- Neuropsychological deficits last longer than most subjectively experienced consequences of blunt traumatic brain injury beyond the acute phase. Tests conducted on cerebrospinal fluid (CSF) verify previous nerve damage.
- Repetitive brain trauma over a lengthy career may result in boxer's dementia having neurobiological similarities to Alzheimer's disease.

Overall, there is a significant difference between professional and amateur boxing in terms of acute complications and neuropsychological and neurodegenerative risks, although the greater protection worn by amateurs cannot avert the considerable dangers inherent in boxing. Along with many other contact sports, trampolining, American football, soccer, rugby, equestrian sports, diving, climbing, gymnastics, skiing and cycling are all associated with health risks, although these are not caused intentionally by an opponent.

From a medical and scientific point of view the question arises of whether the sequelae of boxing can be recognized and prevented—similar to early diagnosis of Alzheimer's disease—by prospective studies (2, 10). Such programs could include:

- regular neuropsychological testing, possibly including determination of the cognitive reserve
- magnetic resonance imaging, possibly including determination of the diffusion parameters
- CSF analysis with measurement of total-tau, phospho-tau and beta-amyloid₁₋₄₂

- genotyping including apolipoprotein E.

Because medical examinations are carried out in many sports and are financed by the German Olympics Sports Confederation, it should be demanded that these usually annual examinations focusing on internal medicine and orthopedics be supplemented by neuropsychological testing. In addition, attempts should be made to specify criteria that enable qualified ringside doctors to recognize potential acute dangers for boxers more reliably and earlier and to avert these if possible.

The risks—not only in competition, but also during preparation for matches—may only be successfully reduced by an integrated care approach in which the health of the sportsman is central rather than victory at any price. The training required to meet the great demands of boxing is particularly intense and varied. High levels of endurance as well as strength, speed and coordination are all necessary.

The World Medical Association (WMA) recommended a general ban on boxing in 2005 because of the underlying intention to inflict physical harm on the opponent. The British Medical Association protested against the first matches of mixed martial arts in the United Kingdom in 2007. In the Federal Republic of Germany no such discussions are being held amongst doctors although professional boxing has become an important, actively advertised part of the television programming of public broadcasters (for example: <http://sport.ard.de/sp/boxen/>; <http://boxen.zdf.de>).

Limitations of this review

The following limitations apply to the current review:

- Despite the long tradition of boxing only a few systematic studies of the neuropsychiatric consequences have been conducted. This may be due to the reticence of athletes and doctors to be involved in ongoing studies of the subject and on the difficulty of defining control groups (battered wives, victims of torture?).
- Ethical questions—for example, about the acceptance of boxing by the public, specific advertising in the media, the dubious function of boxers as role models, or boxing projects for rehabilitation of vulnerable adolescents—were not addressed in the current review.

Conflict of interest statement

Prof. Förstl has received financial support from Eisai, General Electric Lundbeck, Pfizer, Merz Janssen, Novartis, AstraZeneca, BMS, GSK, Lilly, Nutricia, Sanofi, Aventis, Schwabe, Servier, and other companies.

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KEY MESSAGES

- Only in boxing is the knockout—i.e., intentionally causing acute traumatic brain injury in an opponent—accepted as a legitimate objective of a competition.
- There is also the risk of other acute, sometimes life-threatening, complications as well as subacute neuro-psychological consequences.
- Neurobiological findings have revealed a similarity in the neurodegenerative changes that occur in boxer's dementia and Alzheimer's disease.
- Regular screening tests to diagnose cognitive and physical risks to protect boxers are both sensible and possible.
- There have been few medical and ethical conflicts due to the problematic nature of boxing, despite the current popularity of boxing.

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