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**Athrofa Prifysgol Cymru, Caerdydd**

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**SCHOOL OF SPORT, P.E. AND RECREATION**

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## **CHRONIC BRAIN INJURY IN BOXING**

# UNIVERSITY OF WALES INSTITUTE, CARDIFF

Athrofa Prifysgol Cymru, Caerdydd

## Examination for the M.Sc. Sport & Exercise Medicine

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This work is dedicated to Michael Watson,  
whose courage has been an inspiration.

## **ABSTRACT**

This study evaluates the available data on chronic brain injury in amateur and professional boxing, using the Scottish Intercollegiate Guidelines System (SIGN). Recommendations are made in terms of screening and supervision of the boxer.

The available literature has been divided into five research areas:

Histopathology;

Neurophysiology;

Radiology;

Physical examination;

Neuropsychometric assessment.

The existing evidence indicates that amateur boxing does not cause a clinically recognisable syndrome of chronic brain damage. Some professional boxers develop a triad of motor, cognitive and neuropsychological dysfunction, which at its most profound has been called the “punch drunk” syndrome. The level of exposure to head trauma appears to account for the difference between the two codes.

Histopathological examination of professional boxers brains show distinct patterns of damage, the bulk of this evidence being from a small cohort of boxers who fought 50-100 years ago.

Neuroradiological studies suggest that trauma may result in development or enlargement of a cavum septum pellucidum.

Physical examination demonstrates evidence of dysfunction in some professional boxers related to the length of the career and number of bouts fought.

Neuropsychometric assessment may give a dynamic representation of chronic brain damage in evolution.

Electrophysiological studies are of little value as they analyse areas of the brain not directly related to boxing neurotrauma.

Genetic testing for the presence of apolipoprotein E (APOE)  $\epsilon$ 4 genotype may provide some indication of predisposition to detrimental effects of head trauma.

This study concludes that the sport of amateur boxing does not lead to the development of a chronic brain syndrome, whilst some professional boxers display evidence of such impairment. There is no predictive test that will indicate which boxer may develop brain damage, though neuropsychometric testing carried out in a serial manner may demonstrate impairment in evolution, providing a superior means of monitoring boxers.

## **INTRODUCTION**

In October 1993 the British public was captivated by the heavyweight boxing contest between Lennox Lewis and Frank Bruno. Bruno was seen as the people's champion, and Lewis, who despite being the titleholder, was the pretender. Many who had never watched boxing were fascinated by the prospect of an all-British championship; as such the glorified bravery of these athletes became a focus of intense media interest. Counsel as to who would win was offered from many quarters, and the polarisation of public opinion and media attention involved the outcome alone, with little mention of the dangers inherent in the sport of boxing.

Only two years prior to this, following a similar all British title fight between Chris Eubank and Michael Watson, opinion had been dramatically divided for a different reason. The end point of this fight was a knockout suffered by Watson, within the legitimate and legal rules of this sport. Thereafter, Watson developed an acute sub-dural haematoma, requiring two emergency craniotomies and a prolonged period of ventilatory support on intensive care. Thirteen years later there remains a profound residual disability as a result of this sporting encounter.

The argument consequent upon this highly publicised incident was clearly divided. The protagonists saw boxing as a noble art form, which exemplified all that was good in man. The abolitionists viewed it as a barbaric throwback to a bygone age (Lundberg, 1983), having no purpose other than to brutalise and maim the opponent, with the specific intent being to inflict brain damage.

A third school of thought may also have existed, encompassing those who really did not care one-way or the other.

Although each point of view in this polarised discussion carried with it much emotion, both sides of the argument purported to have scientific evidence that would attest to the correct nature of their particular stance. This was perhaps best exemplified by the Panorama television debate (Humphries, 1995) wherein eminently qualified medical practitioners defiantly and passionately argued both for and against a ban on boxing. The debate still goes on, and the entrenched opinions remain mutually incompatible.

Scientific evidence and personal accounts which demonstrate the dangers of boxing with particular reference to brain damage are countered with similar reports and anecdotes attesting to the safety of the sport. The margins of scientific exactitude are blurred on all sides by statements that have been repeated over a period of time such that they have become accepted as medical fact. A major area of concern is the separating of the factual basis for either argument from the philosophical (Fiore, 1996).

There are many that would argue the medical profession has no place in advising as to whether a sport such as boxing should be allowed to continue in its present form, or be abolished. The belief exists that such testament is outside the jurisdiction of the medical profession, as it is a purely moral contention. Doctors can provide scientific facts in an unbiased manner, which can then be used by the general public to make an informed choice.

In reality, boxing exists for two reasons alone. People want to box, and people want to watch them box. The fact that boxing as a sport is condoned is witnessed by the viewing figures for major fights, which attract tens of millions worldwide.

For many, boxing occupies the outer limit of morally acceptable behaviour. The intent to injure the opponent is to them abhorrent. If we as a society accept that boxing occupies this outer limit of what is morally acceptable, then it must be of equal concern to ask what would happen if boxing were banned. In time another sport would take its place at the edge of morality. Should this next sport then be banned for the same reasons? If we are to continually draw in the limits of moral acceptability then where do we stop? Ultimately society will decide that a given number of sports are acceptable in terms of risk, danger and moral probity. This is not a theoretical point in the future it is the situation now. Society has drawn the limits, and boxing falls within.

Having stated that the medical profession appears to have no place in advising on moral issues, there is a historical link that places physicians at the forefront of the debate which allows the sport of boxing to continue as a legal endeavour. A sport that encourages the striking of the opponent's head, in an attempt to render them unconscious, would

contravene the offences against the person's act 1861, Sections 47, 20 and 18, concerning the causation of actual bodily harm (Swarbrick, 2005).

There would also appear to be a contravention of the Criminal Justice Act 1988 in respect of common assault and battery. The sport of boxing by definition of its rules would seem to be outside the law, as every bout would be a breach. The anomalous situation allowing boxing to continue appears to be the result of evidence given in the Central Criminal court in November 1866, by a house surgeon from Charing Cross hospital in London (R. v Young). In the last round of an organised boxing match between two men, one of them fell, striking his head on a post. Five hours after admission to hospital the subject died. The admitting house surgeon, Dr George Airey, showed that death was due to a brain haemorrhage, caused either by a blow or a fall. In answer to specific questions posed from the court, opinion was expressed that sparring in the manner as described by other witnesses might be dangerous to human life, but death would be very unlikely. The defence argued that the charge of manslaughter was unsubstantiated, as the death had occurred in the exercise of a lawful sport. Defence counsel cited 'East's Pleas of the Crown' wherein it is argued,

*"If death ensue from such sports as are innocent an allowable the case will fall within the rule of excusable homicide" (East, 1803)*

In summing up, the judge placed great emphasis on the medical evidence as provided by Dr Airey,

*"But the medical witness here had stated that this sparring with gloves was not dangerous and not a thing likely to kill."*

The defendants were found not guilty. In consequence boxing appears to be removed from the offences against the persons act, and this court case would seem to be a pivotal point at which time the close relationship between medicine and boxing became established.

Since Dr Airey expressed an opinion regarding the safety of boxing, many others have done the same. There is now a body of literature that discusses the effect of boxing on the

human brain. There is evidence of the cumulative nature of brain damage, and the detrimental effect it has, though other studies appear to question such a link. There exists a very real need to clarify the evidence in respect of brain damage in the sport of boxing. Personal opinion and conjecture must be removed allowing only purely scientific facts to be presented, thereby empowering the individual to make an informed choice, based on current best practice. There is a variation in practice as witnessed by the dichotomous views of the medical profession as a whole. This affects patient outcome, as the protagonists view would have the sport continue in its present form, whereas abolition would be the end point for the antagonists. The boxer is essentially a patient and the benefit to this individual is clear. If the literature shows no evidence of significant risk of long-term injury, then the sport should be allowed to continue. An evidence base that shows long-term chronic damage to the brain may allow changes; either to the rules or the law, so reducing this harm. Overall the boxer will benefit, as a systematic review of the literature will separate the science from the philosophical, moral and ethical considerations, allowing reasoned and informed choice. Current best practice suggests we empower our patients by providing them with the information that allows the individual to make such a choice. The same holds true for the sport of boxing.

Boxing may be divided into amateur and professional codes. This classification may be less important for acute injury, but is valid in respect of chronic changes, as the rules and regulations of amateur and professional boxing are so different as to introduce a clear cut distinction in terms of exposure to the presumed damaging agent, the head punch.

The main differences between amateur and professional boxing are summarized in table (1). The length of competition during which the head is exposed to punches is a maximum eight minutes in senior professionals (4 x 2 minute rounds), and 36 minutes in professionals. (12 x 3 minute rounds). Amateur rules and regulations are uniform throughout the world, unlike the professional code, which has numerous sanctioning bodies and local regulating authorities. The lack of uniformity within the professional code has resulted in variable medical requirements in terms of licensing. For example the British Boxing Board of Control (BBB of C) require Magnetic Resonance Imaging (MRI) of the brain with angiogram prior to

issue of the first licence, and annual MRI scan thereafter. There is no such prerequisite in any other jurisdiction throughout the world.

There is provision made within the amateur code, to protect a boxer who is thought to be in danger. The standing eight count is implemented when a boxer appears in difficulty. This allows a referee to intervene and prevent further punches being delivered. If the referee feels the boxer has recovered, the bout will be allowed to continue, if not the 'referee stops contest' (RSC) rule may be invoked, or 'referee stops contest due to excessive head punches' (RSC(H)). Computerised scoring systems present at many amateur tournaments will keep a running total. If one competitor is 20 points ahead in a male senior bout (15 points for junior and female) in all but the last round, the bout is stopped, and the decision is 'referee stops contest, outclassed' (RSCOC).

No such provision exists in the professional code, and as such the referee can only stop a bout if one boxer is knocked out, or deemed unable to defend himself. Such decisions are final, unlike the standing eight-count after which the bout may continue.

The purpose of amateur boxing is to score points by hitting with a designated part of the glove in a given target area incorporating the head and torso. No points are awarded for knocking the opponent down. Whilst a similar scoring policy is in operation throughout the numerous sanctioning bodies in professional boxing, aggression will score more points, and a record of knocking out opponents will enhance the earning potential of a professional boxer. The head is thus very much more of a target in professional boxing.

Further division into acute and chronic injury is equally valid as the pathophysiological processes that are thought to lead to brain damage in each case are essentially different.

**Table 1 Differences Between Amateur and Professional Boxing**

ASPECT	AMATEUR	PROFESSIONAL	SAFETY IMPLICATION
<b>Rules</b>	Uniform in all 186 affiliated Amateur International Boxing Associations.	Variable according to location, jurisdiction and governing body.	Uniform rules result in uniform standards in amateur code
<b>Rounds</b>	3 rounds of one minute up to a maximum of 4 rounds of 2 minutes.	4 rounds of 3 minutes up to maximum 12 rounds of 3 minutes	Longer bouts increase exposure to head trauma
<b>Gloves</b>	10 ounce gloves for competition White area over knuckle denotes striking surface for point scoring	8 or 10 ounce. No striking surface marking.	Lighter gloves thought to be associated with higher rate of knockout
<b>Headguards</b>	Compulsory for all competition since 1984	Prohibited	Headguards reduce facial cuts and external ear injuries
<b>Singlets/tops</b>	Mandatory for Male and Female	Prohibited for males	Allows gloves to be cleaned. Prevents rope abrasion
<b>Standing eight-count</b>	Given to boxer in difficulty. Three counts in one round, or four in total the bout is stopped	No standing eight count	Protects the boxer. Allows referee to assess boxer, and implement RSC rule (see below)
<b>Duties of referee</b>	To protect the boxer by enforcing rules	To protect boxer by enforcing rules. May be required to score contest as well.	Variable rules and regulations may not always protect boxer.
<b>RSC - outclassed</b>	RSC = Referee stops competition. If a boxer is overmatched and is having difficulty against a superior opponent, the contest is stopped by referee	No such rule	Allows Amateur referee to intervene prior to serious injury or knockout. No such provision in professional code
<b>Objectives</b>	To win on points by landing more correct scoring blows on the opponents target area. Knockdowns do not gain extra points. Knockouts are accidental and not an objective.	Objective is to score points by striking target area. Points also awarded for aggression. Variable rules depending on sanctioning body and jurisdiction. Knockout rate will enhance earning potential.	Encourages professionals to aim for head. Amateurs score from striking head and torso.

## **METHODOLOGY**

In examining chronic brain damage, further classification into the following areas allows a more reasoned and systematic approach:

1. Histopathological examination;
2. Neurophysiological/electrophysiological tests;
3. Neuroradiological imaging;
4. Neurological/physical examination;
5. Neuropsychometric assessment.

This study will review the evidence currently available.

For any literature review to be scientifically valid, the elements of bias and subjectivity must be eliminated. In order to achieve this, a set protocol must be adopted for the systematic analysis of each and every journal article. The methodology used to assess each individual article must be comparable to any other in the series under review.

For the purpose of this study the Scottish Intercollegiate Guidelines Network (SIGN) system of assessment and grading has been used.

SIGN was formed in 1993 and in 1998 the system for evaluating guideline evidence and grading recommendations was further refined (Harbour and Miller, 2001). The objective of the SIGN protocol was to improve the quality of healthcare for patients in Scotland, by standardising practice and outcome, through the development and dissemination of national clinical guidelines, containing recommendations for effective practice, based on current evidence.

For a topic to be suitable for development of a SIGN guideline, there must be evidence of variation in practice which affects outcome, and a strong research base providing evidence of effective practice (SIGN, 2004). The potential benefit to patients must be sufficient to justify the resources invested in the development and implementation of such a guideline. The methodology whereby SIGN guidelines are developed can be applied to the scientific literature in respect of brain injury in boxing.

In order to identify the best available evidence, a systematic review of the main study types must be undertaken. A systematic review is defined as

*“... an efficient scientific technique to identify and summarize evidence on the effectiveness of interventions and to allow the consistency of research findings to be assessed and data inconsistencies to be explored.”(SIGN, 2004)*

These study types and sources of evidence can be sub-divided into the following headings:

1. Existing guidelines, meta-analyses, systematic reviews;
2. Randomised controlled trials;
3. Observational studies (such as cohort studies);
4. Case control studies;
5. Diagnostic studies;
6. Economic evaluations;
7. Non Analytical studies (case reports/case series);
8. Expert opinion.

To minimise bias and ensure appropriate and adequate coverage of the relevant literature, the literature search must cover a range of sources. For the purpose of this study three main reference libraries were used Ovid, Medline and the Cochrane library.

The initial search utilised the key words “boxing” and “head injury” in a combined search. For both Medline and Ovid this generated of 36 articles, thereafter it was decided to broaden the search to “boxing”, which resulted in 699 articles. Where available the abstracts were read and assessed for their suitability and relevance. Where only title and summaries were available these were reviewed in the same manner. The two lists generated by Ovid and Medline were cross-referenced, compared and combined to produce a single list of 368 references.

Only articles pertinent to head injury in boxing are contained therein. This list has been added to periodically with contemporary publications. Articles that precede the limits of the

electronic database search have also been included. These additional articles have been obtained by systematically reviewing the reference lists of the earliest publications from the Ovid and Medline databases. Relevant articles were then obtained by hand from library sources. The process of reviewing the reference list was repeated until 36 additional articles were obtained, dating back to the 1928 work by Martland, which appears to be the first to describe the “*punch drunk*” syndrome of chronic brain damage in boxers (Martland, 1928) Sixty-one publications were printed in foreign languages, translations of which could not be obtained, and as such they have been excluded.

The database of the Cochrane library provided no additional information.

Each article has been read, assessed, and graded according to the guideline developers handbook methodology checklist as outlined in the SIGN protocol (SIGN, 2004). The grading system assigns a score from 1 ++ to 4, for highest and lowest levels of evidence. (Table 2).

Grades of recommendation can be specified based on the scores attained by individual papers within a given area of research (Table 3).

The grading does not relate to the importance of the recommendation, but to the strength of the supporting evidence, and in particular to the predictive power of the study designs from which the data has been obtained.

For each chapter a table has been provided summarizing the relevant studies, their classification and the respective SIGN score accredited to each one. The discussion pertaining to individual papers contained within each table is included in the relevant chapter. Publications that did not add any additional information, such as a number of SIGN grade 4 personal opinions have not been included in the tables, as they refer mainly to comments on the subject of boxing as a whole, rather than the individual sub-headings under discussion, and do not add anything to the discussion.

Scrutiny of the available scientific data will provide objective information regarding brain damage caused by boxing. It may then be possible to appraise the predictive value of any given area of research, with the potential for future recommendations, consequent upon evidence-based science.

**Table 2 Revised SIGN grading system**

<b>SIGN GRADING</b>	<b>LEVEL OF EVIDENCE REQUIRED</b>
<b>1 ++</b>	High quality meta analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias
<b>1+</b>	Well conducted meta analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
<b>1 -</b>	Meta analyses, systematic reviews of RCTs, or RCTs with a high risk of bias.
<b>2 ++</b>	High quality systematic reviews of case – control or cohort studies. High quality case control or cohort studies with a very low risk of confounding, bias, or chance, and a high probability that the relationship is causal
<b>2+</b>	Well conducted case control or cohort studies with a low risk of confounding, bias or chance, and a high probability that the relationship is causal
<b>2-</b>	Case control or cohort studies with a high risk of confounding bias or chance, and a significant risk that the relationship is not causal.
<b>3</b>	Non analytical studies, e.g. case reports and case series
<b>4</b>	Expert opinion

**Table 3 SIGN Grades of recommendation**

<b>SIGN GRADE</b>	<b>REQUIREMENT</b>
<b>A</b>	At least one meta analysis, systematic review, or randomized control trial (RCT) rated as 1++, and directly applicable to the target population; or a systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results.
<b>B</b>	A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 1++ or 1+
<b>C</b>	A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or extrapolated evidence from studies rated 2++
<b>D</b>	Evidence level 3 or 4; or extrapolated evidence from studies rated as 2+

There are limitations to this present study. There may be important information contained within the foreign literature that has not been translated. Also, despite the guidelines issued by SIGN, there is an element of subjectivity and the potential for bias to be introduced. For non-analytical studies such as case reports, case series and 'expert opinion' there are no methodological checklists, and the reader assessing each article is required to make a subjective analysis of the paper or report. The inclusion of additional article outside the electronic database search also introduces the possibility of subjectivity. This criticism is valid; however, only articles thought to be relevant to the discussion have been included.

**CHAPTER I**  
**HISTOPATHOLOGY**

In his treatise of 1835 Gama stated,

*“Fibres as delicate as those of which the organ of mind is composed are liable to break as a result of violence to the head” (Gama, 1835).*

An appreciation of the damage caused to such structures will in reality only be possible by direct visualisation of suitably prepared histopathological specimens, either from biopsy during life, or post mortem. The majority of specimens examined in relation to boxing fall within this second group, and existing material appears to be extremely limited. The availability of appropriate staining techniques further constrains the information derived from these specimens. In simple terms, profound and distinctive patterns of cellular damage may be present within a given histopathological slide, but the absence of specific staining techniques will render them invisible.

In an original paper, Martland (1928) suggested that the occurrence of neurological symptoms in almost 50% of fighters,

*“seems to be good evidence that some special brain injury due to their occupation exists”.*

Contemporaneous theories of concussion allowed speculation as to aetiology, though in suggesting multiple concussion haemorrhage as a possible cause, Martland stated,

*“This theory, whilst quite alluring, is unsusceptible of proof”.*

Edward Carroll (1936) published a synonymous paper, which concluded,

*“Little information is available concerning the actual anatomic changes in punch drunk, and the explanation of this syndrome must be based on analogy and conjecture”.*

Subsequent attempts to define the pathological changes were hampered by lack of suitable material, relying on pathology unrelated to boxing, augmented by isolated case reports.

Brandenburg and Hallervorden (1954) published one of the earliest histopathological studies citing a boxer with evidence of encephalopathy. Histology demonstrated senile plaque formation with neurofibrillary tangles identified in the cortex, basal nuclei, and to a lesser extent the cerebellum. The presence of senile plaques revealed by staining techniques available at this time, in this isolated case, raised the possibility that the dementing illness was in fact Alzheimer's disease. This point will be expounded later in the chapter.

Strich described 20 cases of closed head injury, in two publications (Strich, 1956, Strich, 1961) Most had been involved in motor vehicle accidents, wherein they were rendered unconscious immediately. Injury was uncomplicated by laceration of the brain, intracranial haematoma or raised intracranial pressure, with clinical recovery leading to a state of extreme dementia in all cases. Post mortem examination revealed a normal macroscopic appearance of the brain. The histopathological picture was one of diffuse degeneration of the white matter with haemorrhage into the Corpus Callosum. The degenerative changes were neither due to cortical cell loss/infarction nor laceration of brain substance, but suggestive of nerve fibres having been stretched or torn by rotational shearing forces at the time of trauma. The true pathogenesis could not be determined, only speculated upon. This work pertains to victims of road traffic accidents, and a theory of how pathological changes may have occurred. It has been cited as relevant to the pathological changes that may take place in a boxer's brain (BMA, 1993).

The rotational nature of trauma following a punch to the head may account for similar pathological changes seen in some boxers; however, Strich's work describes one end of a traumatic scale and though relevant to an understanding of brain injury, may not readily be extrapolated to boxing.

Payne (1968) reported the histological findings in a group of six professional boxers, comprising enlarged ventricles, scarring of the grey matter, focal myelin degeneration of the

white matter, areas of proliferation of the cortex, particularly in the gyri of the posterior cerebrum. A cavum septum pellucidum was present in all cases, with fenestration in three of six. The presence of a cavum septum is demonstrated in many of the pathological and radiological studies on professional boxers and appears to be a significant finding. Payne stated that small scars collectively reduced competent brain function, but there was no means of correlating the degree of clinical disturbance of brain function, with the number of scattered small lesions in the brain. Of the six subjects, two were chronic alcoholics; a third received a significant head injury in a traffic accident, and also suffered with malignant hypertension. Such confounding variables, coupled with small sample size diminish the relevance of this study in respect of brain damage related to boxing.

Animal experiments have been used in an attempt to understand how the biomechanics of head injury relate to subsequent histopathological changes. In a series of experiments, Unterharnscheidt (1970) described two types of impact trauma. Translational trauma involved linear forces passing straight through the center of gravity of the skull, rotational trauma involved forces that spin the skull about this point. Investigation of the types of brain damage caused by these two different forces was undertaken using animal models. Live animals' heads were subject to linear impact forces of 200-400G, and rotational forces of 100,000 to 400,000 rad/sec<sup>2</sup>, with increasing forces resulting in more marked and widespread pathological changes. Post mortem microscopic analysis, showed widespread ischaemia and necrosis, with neuronal loss and glial proliferation in the cerebrum, accompanied by reduction of Purkinje cells in the cerebellum. The histopathological changes observed in these animal studies have been used to illustrate the potential damage that could be caused by boxing. If the biomechanical basis of these experiments is examined, the link suggested by the author between these animal models and boxers appears somewhat remote.

The maximal force of a boxing punch as demonstrated by Atha And Yeadon (1985) in controlled clinical conditions was 53G. This was from a straight punch thrown unopposed by a world heavyweight champion against a static accelerometer. Subsequent studies recorded similar findings (Smith *et al.*, 2000). Unterharnscheidt (1972) suggested a boxer could generate a force of 100G, but this supposition is based on flawed science. In an

experiment using two students “*unskilled in boxing*”, forces generated by 12 ounce gloves were measured, using accelerometers bandaged to the subjects heads. The maximal force generated by a punch was 25G. Thereafter it was reasoned that by using 6-ounce gloves, the force would be 50G, and skilled professionals could generate even higher values. A graphical representation in another publication extrapolated this figure to 100G, (Unterharnscheidt, 1995a) but with no scientific explanation as to how this figure is calculated. The animal models used by Unterharnscheidt utilized even greater forces between 200 and 400G. Extrapolating the histopathological findings in these animal experiments to boxers lacks precision.

The most comprehensive study to date is that of Corsellis *et al* (1973). Detailed histopathological analysis was performed on the brains of fifteen ex-boxers, twelve professional and three amateurs. Psychiatric social workers interviewed relatives to determine a retrospective profile of each boxer’s life. Hospital records and those obtained from boxing periodicals augmented this information, building a clinical picture of each subject. Cases 1 to 11 were professional boxers and all 11 demonstrated clinical symptoms in keeping with organic brain damage. Case 12 was alleged to have boxed, but no record could be found. He died “*active and mentally alert*” at the age of 90, and may be considered as an outlier. Cases 13, 14 and 15 were amateurs. Case 13 had head injury outside boxing, 14 and 15 displayed no features of note suggesting brain dysfunction.

The significant histopathological findings were as follows:

**i) Abnormalities of the septum pellucidum;**

The septum pellucidum forms the medial wall of the anterior horn of the lateral ventricle. It consists of two thin sheets of nervous tissue, running in the sagittal plane from the undersurface of the corpus callosum, with its dorsal limits at the fornix (Crossman. A.R., 2000). In sagittal section the leaves are usually fused or contiguous. Separation of the leaves forming an intraseptal space anteriorly is known as a cavum septum pellucidum; posteriorly a similar space is referred to as cavum vergae.

A septal cavum was identified in 12 of 13 brains examined by Corsellis, cases 14 and 15 having died from intraventricular haemorrhage, could not be assessed. The width ranged from 1 mm to 8 mm with a mean of 5.17 mm. The importance of this finding is clear when it is compared to the frequency of such abnormalities in the brains of a non-boxing population. Schwidde (1952) found a cavum in 20% of an unselected series of 1,032. Corsellis *et al* examined the brains of 200 men and 300 women as controls. Twenty-five had come from general hospitals, and 475 had died in psychiatric hospitals. The authors acknowledged the select and biased nature of this 'control group', in whom cerebral degenerative conditions and the dementias of middle and old age were represented in large numbers. Cavum septum was present in 28.4% of this group. The mean width was 1.6 mm, compared to 5.17mm in the boxing group, but the striking feature was the presence fenestration, which was 3% compared to 77% in the boxing group.

In the non-boxing group, presence of a cavum septum appeared neither to be related to size of the lateral ventricles, nor frontal lobe atrophy (associated with conditions such as Picks disease, Huntington's chorea, Alzheimer's disease, and senile dementia).

Fenestration was closely related to enlargement of the lateral ventricles in the boxing group. The septi pellucidum in the boxers were very different from the non-boxers being on average three times wider and grossly fenestrated.

How boxing produces these changes is unclear. Payne (1968) suggested passive enlargement of the ventricles, though sudden pressure fluctuation within the cerebrospinal fluid was favoured by Mawdsley (1963). Corsellis *et al* postulated rotational shearing forces similar to those described by Strich. This mechanism requires rupture of the septum at its relatively thin attachments close to the corpus callosum. Subsequent ventricular dilatation may lead to further stretching of these leaflets, which comprise their medial wall. The consequence is further septal separation, with enlargement of fenestration due to mechanical stretching. Pittella and Gusmao (2005) examined 120 victims of fatal road traffic accidents, their work

suggesting that only high-intensity acceleration, sufficient to cause axonal and vascular damage, would lead to detachment of the leaves of the septum pellucidum. They suggested that the increased frequency seen in boxers implied that high intensity angular acceleration of the head over time, could cause greater deformation in midline structures.

All these theories require brain injury to have occurred with subsequent loss of nervous tissue, and they provide strong evidence in support of the damage caused to professional boxers reviewed in the series presented by Corsellis *et al* (1974)..

**ii) Cerebellar and cerebral scarring;**

The clinical picture of punch drunk syndrome suggests interruption of cerebellar pathways. Brandenburg and Hallervorden (1954) described loss and degeneration of Purkinje cells in a scattered pattern. Grahmann and Ule (1957) demonstrated localized folial atrophy. Corsellis *et al* (1973) used a grid system to count nucleolated Purkinje cells in a single sagittal section of cerebellum taken from each boxer, which were then compared to those obtained from a non-boxing population.

The mean Purkinje cell count in this non–boxing population did not vary significantly from one area to another. However, in boxers the cell count on the ventral aspect of the cerebellum was half to two thirds of that found on the normal dorsal aspect. This may be explained by the findings of Lindenberg and Freytag (1960) who studied the mechanism of cerebral contusion in acute head injury. Damage was in part thought to be due to the brain having been forced

*“...toward and into the only emergency exit of the skull, the foramen magnum, causing shearing strains in the medulla oblongata and the cerebellar tonsils”.*

A similar mechanism may account for the distribution of glial scarring in the same region in boxers.

In summary, cerebellar damage and selective loss of purkinje cells in boxers appears essentially different from any encountered in the various hereditary or other cerebellar atrophies that may be accompanied by dementia, supporting theories of a traumatic aetiology.

Cerebral scarring was demonstrated by Payne (1968) but not by Corsellis who found no scars in the grey or white matter, unless associated with vascular degeneration.

In most of the cases examined, up to and including the work of Corsellis *et al*, there was a trend towards reduced brain weight, enlargement of the lateral and third ventricles, with thinning of the corpus callosum. This indicated a material reduction in the volume of the cerebral hemispheres secondary to cell loss. This reduction of tissue in boxer's brains tended to be from the deep periventricular region more than the superficial cortex, demarcating it from the appearances of old age, and suggesting a different aetiology.

**iii) Degeneration of the substantia nigra;**

The most striking feature of Parkinsonism from a neuropathological perspective is the degeneration and loss of pigment cells in the substantia nigra. In the series described by Corsellis *et al* hospital records showed a Parkinsonian syndrome in four cases (3,4,6,9), corresponding with histopathological changes in all four. These subjects showed gross loss of nigral pigment, with almost complete absence in the most extreme cases. Seven of the remaining eleven cases also showed some degree of depigmentation.

The pattern of pigment loss was from the intermediate and lateral nuclear groups, the medial being spared. Theories as to the exact cause of this pattern were complicated by failure to stain plaques in this original work by Corsellis, a deficiency corrected in later work. (Roberts *et al.*, 1990)

Brandenburg and Hallervorden (1954) also described nigral depigmentation in their single case report, the patient having displayed “*indubitable Parkinsonism*”. Grahmann and Ule (1957) showed considerably more marked depigmentation in a patient with similar clinical affect. Thus it would appear that the Parkinsonian affect of punch drunk syndrome corresponds to specific nigral depigmentation.

**iv) Regional occurrence of Alzheimer’s neurofibrillary tangles.**

Neurofibrillary tangles are found in small numbers of neurons in many elderly people, but are virtually always accompanied by senile plaques. They are found in abundance in Alzheimer’s disease, but again plaques invariably accompany them. Distribution in Alzheimer’s disease commonly involves the anteromedial grey matter including the amagdaloid nucleus and hippocampus. Other rare neurological conditions associated with tangle formation, also have a specific topography in respect of tangle distribution. In the cohort of boxers examined, the tangles were spread diffusely throughout the cerebral cortex and brainstem, with intense deposition in the medial temporal grey matter. This is quite distinct from the pattern of distribution seen in any other condition, and suggests that chronic trauma predisposes to this specific pattern of distribution.

The initial staining techniques of Corsellis *et al* (1973) failed to demonstrate the presence of plaques associated with these tangles. Roberts (1990) using a different staining technique, confirmed plaques to be present in all cases, thereby linking the histopathological appearances of Alzheimer’s to those of dementia pugilistica.

The work by Corsellis *et al* was a clinical benchmark by which later studies were gauged. It clearly delineates the changes in the brains of a group of professional boxers, demonstrating pathologically widened and fenestrated cavum septi pellucidum, cerebellar scarring suggestive of trauma, loss of cerebral tissue distinct from patterns seen in old age, marked loss of pigment cells in the substantia nigra, and the presence of neurofibrillary tangles in a specific distribution.

To appreciate the relevance of this work to the whole of boxing, and in particular the sport as practiced today, it is important to understand the demographics of the study cohort, and in particular, specific confounding variables.

The group being studied is a highly select series of boxers, each of whom may have fought many hundreds of bouts between 1900 and 1940. Of the professionals, seven died in mental hospitals, two were formally diagnosed as demented, and two had anecdotal evidence of impaired mental function. Case 12 would appear to be an outlier, and the amateur subjects showed no neurological dysfunction that can be solely attributed to boxing.

Using the cases identification numbers from the original paper, four of the fifteen suffered brain injury outside the ring (1,2,4,13). Excessive alcohol consumption is documented in seven cases (1,3,4,5,7,9,10), though it must be noted that the topographical changes in the cerebellum of this series is very different to that seen in chronic alcoholics. Four cases (5,8,9,10) suffered hemiplegia as a result of cerebrovascular disease. The histopathological changes in the three amateurs are complicated by the many extraneous factors such that any conclusion must be guarded.

Many of these men died in institutional care, following which their brains became available for scientific study. They represent boxers with marked motor, cognitive and neuropsychiatric dysfunction, in the presence of specific brain damage as demonstrated by histopathological examination post mortem. They appear to be from an extreme limit of exposure to chronic head injury, and whilst they are not representative of all boxers, they provide valuable information on what happens to the brain if repetitive trauma is allowed to continue.

## **Neurofibrillary tangles in Alzheimer's disease, compared and contrasted with those found in Dementia Pugilistica.**

The clinical similarity of patients with Alzheimer's disease and dementia pugilistica is stated in many studies. A number specifically look at the microstructure and distribution of neurofibrillary tangles and senile plaques.

The parallel between Alzheimer's disease and dementia pugilistica was investigated at a histopathological level by Roberts, by demonstrating that antisera specifically staining the neurofibrillary tangles of Alzheimer's disease, also stained the tangles of eight cases of known dementia pugilistica (Roberts, 1988). The boxing specimens were from the original series described by Corsellis *et al* (1973), cases 2,3,4,5,7,10,11,12, which were compared to brain tissue from clinically and neuropathologically defined cases of Alzheimer's disease. The morphological similarity of the tangles suggested a common aetiology, but again the absence of plaques in the boxing cohort could not be explained.

The anomalous finding of neurofibrillary tangles in the apparent absence of any senile plaques was clarified by Roberts *et al.* (1990), using a refined histological staining technique, employing immunocytochemical methods, and an antibody raised to the  $\beta$  protein present in Alzheimer's disease plaques. All cases of dementia pugilistica with extensive tangle formation displayed presence of extensive  $\beta$ - protein immunoreactive deposits (plaques). Thus the single case described by Brandenburg and Hallervorden (1954) which displayed numerous plaques using the more dated techniques, raises a possible alternative hypothesis that this was a boxer with unrelated Alzheimer's disease, as opposed to dementia pugilistica.

Following an initial stimulus, it is postulated that a common pathogenic pathway leads to plaque and tangle formation in both Alzheimer's disease and dementia pugilistica. Trauma alone is implicated as a causative trigger in dementia pugilistica, whereas genetic, environmental factors, infection and trauma have all been suggested as relevant to Alzheimer's disease. The idea of disparate stimuli subsequently ending in a common pathway was developed in subsequent studies, which employed sophisticated staining techniques to look specifically at distribution and microstructure of plaques and tangles in an

attempt to clarify whether distinct clinical conditions as described in Alzheimer's disease and dementia pugilistica had equally distinct histopathological appearance.

Evidence of a common pathway is provided by the work of Dale *et al* (1991), which examined ubiquitin immunoreactivity in the brains of 16 ex-boxers, including 11 with dementia pugilistica. Ten of these had been described in the original work by Corsellis *et al* (cases 2,3,4,6,7,11,12,13,14,15). Ubiquitin is a protein thought to be involved in the ATP dependent non-lysosomal degradation of abnormal proteins. It is a protein consistently present in the inclusions associated with several neurodegenerative diseases, including Parkinson's, Motor-neurone, Pick's and Alzheimer's disease.

Ubiquitin positive staining pattern was present in all but one of the demented boxers; however, in the group of non-demented boxers, tangles, when present, showed no immunoreactivity to ubiquitin. The author concluded that ubiquitin is a component of a sub population of tangles in dementia pugilistica, suggesting a common genesis for the tangles in both Alzheimer's disease and dementia pugilistica.

Positive immunoreactivity to this protein did not, however, correlate with the degree of neuropathology, the number of years boxing, the number of fights or the professional/amateur status.

Tokuda *et al* (1991) added support to this observation in respect of tangle formation. They studied the brains of eight boxers; seven were once again drawn from the original cohort described by Corsellis *et al*. All cases showed a large number of tau-immunoreactive neurofibrillary tangles and also  $\beta$ -protein immunoreactive senile plaques in the cortex. This suggested a common aetiology and pathogenesis in plaque and tangle formation for both Alzheimer's and dementia pugilistica.

Hof *et al* (1992) examined the neurofibrillary tangles present in boxers. The study population comprised the brains of three professional boxers all of whom had fought over 600 fights in careers spanning 25 years; ante mortem presentation was in keeping with a diagnosis of dementia pugilistica.

The study demonstrated a differential distribution of neurofibrillary tangles in Alzheimer's disease and dementia pugilistica. In the former the tangles were concentrated in the deep layers of the neocortex (layers v, vi), in the latter they were selectively grouped in the superficial layers (ii, iii). This suggested that a more circumscribed population of cortical pyramidal neurons might be affected in dementia pugilistica than in Alzheimer's disease.

Further evidence for the pathophysiological differences between these histopathologically similar tangles was provided by Bouras *et al* (1997). This case series comprised two patients with dementia pugilistica, four cases of Alzheimer's disease and three controls. Microprobe mass analysis of aluminium and iron content in the hippocampus and inferior temporal cortex revealed a predominant accumulation of both metals within neurofibrillary tangles. Substantially higher levels of both aluminium and iron were found in dementia pugilistica compared to Alzheimer's disease. This suggests a possible association between neurofibrillary tangle formation and deposition of iron and aluminium, supporting theories of global dysregulation of transport of both metals in each condition.

A more detailed analysis of neurofibrillary damage was undertaken by McKenzie *et al* (1996). They looked at three types of cytoskeletal neurofibrillary lesion, neurofibrillary tangles, neurites and neuropil threads. By mapping the differential distribution of all three lesions, they were able to demonstrate strong parallels between Alzheimer's disease and dementia pugilistica. There was also a high degree of similarity in the pattern of neurofibrillary damage between Down's syndrome and Alzheimer's disease. The same basic pathological process appears to occur in all three disorders, though differences in biological and environmental trigger factors, such as trauma, may explain variations in the subsequent pattern of development of neurofibrillary lesions.

This was highlighted by a single case report of a 23 year old who died following a professional boxing contest (Geddes *et al.*, 1996). Medial temporal lobe structures were spared, but there were neurofibrillary tangles in all neocortical regions, with no other changes attributable to boxing. The preponderance of tangles at the anatomical sites where contusions are characteristically found suggests their formation may be related to impact trauma. These studies imply that the tangles in dementia pugilistica, whilst similar in many

respects to those in Alzheimer's disease, are quite distinct both in appearance and distribution. This suggests that disparate stimuli for each disease process leads to changes which may follow a common pathway, but subtle differences result in distinct and identifiable end points.

In summary it can be seen that histopathological evidence of chronic brain damage caused by boxing is limited to a small number of specimens. The clearly defined pathology is found within the professional group which may show evidence of large fenestrated cavum septi pellucidum, a distinctive pattern of cerebellar scarring, nigral depigmentation, reduction in periventricular mass and tangle and plaque formation that has many similarities to Alzheimer's disease. These marked histopathological changes appear to be the result of trauma. No statements can be made in respect of amateur boxing, due to lack of data.

Whilst it may be argued that these findings are not representative of contemporary boxing, they do represent an extreme point in terms of exposure. Current boxing practice is by definition part of that continuum and the challenge is to predict at what point to intervene and suspend boxing activity, before these changes occur.

Many young men and women take part in both amateur and professional boxing. Some will die at a young age due to illness or accident unrelated to their boxing career. This raises the possibility of increasing the available histopathological database to include brain specimens from those not at the extreme limit of exposure, as is the current case. It may then be possible to compare the pathological changes to a whole spectrum of clinical exposure to head injury from boxing. At present there is histopathological data to demonstrate what changes may occur if an individual continues to box. In the future similar studies may indicate levels of exposure beyond which damage might be expected to occur. This will allow the boxer to make an informed career choice.

**Table 4 Evidence table: Histopathology**

Author	Title	Year	Study Type	Amateur (A) Professional(P)	SIGN Grade
Stiller, J.W., Weinberger, D.	Boxing and Chronic Brain Damage	1985	Systematic review	A +P	2++
Roberts, A.H.	Brain Damage in Boxers	1969	Cohort	P	2+
Hof et al.	Differential distribution of neurofibrillary tangles in the cerebral cortex of dementia pugilistica and Alzheimer's disease cases	1992	Cohort	P	2 -
Tokuda et al.	Re-Examination of ex-boxers' brains using immunohistochemistry with antibodies to amyloid B-protein and tau protein	1991	Cohort	P	2-
Dale et al.	Neurofibrillary tangles in dementia pugilistica are ubiquitinated	1991	Cohort	P	2-
Roberts et al.	The occult aftermath of boxing	1990	Cohort	P	2-
Roberts, G.W.	Immunocytochemistry of neurofibrillary tangles in dementia pugilistica and Alzheimer's disease: Evidence for a common genesis	1988	Cohort	P	2-
Corsellis et al.	The aftermath of boxing	1973	Cohort	P	2-
Jellinger, K. and Seitelberger, F.	Protracted post traumatic encephalopathy Pathology, Pathogenesis and clinical implications	1970	Cohort	N/A	2-
Pittella, J.E., Gusmao, S.	Cleft cavum of the septum pellucidum in victims of fatal road traffic accidents: A distinct type of cavum associated with diffuse axonal injury	2005	Case series	N/A	3
Rabadi, M., Jordan, B.	Cumulative effect of repetitive concussion in sports	2001	Case series	A + P	3
Scully et al.	Presentation of case: Case records of the Massachusetts General Hospital	1999	Case report	P	3
Bouras et al.	A Laser Microprobe Mass Analysis of Brain Aluminum and Iron in Dementia pugilistica: Comparison with Alzheimer's Disease	1997	Case Series	P	3
McKenzie et al.	Comparative investigation of Neurofibrillary Damage in the Temporal lobe in Alzheimer's Disease, Downs Syndrome, and Dementia Pugilistica	1996	Case series	P	3
Geddes et al.	Neurofibrillary tangles, but not Alzheimer's-type pathology, in a young boxer	1996	Case Report	P	3
Unterharnscheidt, F.	A neurologists reflection on Boxing III. Vascular Injuries	1995	Case Series	A + P	3
Jordan et al.	Apolipoprotein E e4 and Fatal Cerebral Amyloid Angiopathy Associated with Dementia Pugilistica	1995	Case Report	P	3
Unterharnscheidt, F.	A neurologist's reflection on boxing. IV. Late and permanent brain damage	1995	Case Series	P	3
Friedman, J.	Progressive Parkinsonism in Boxers	1989	Case Report	P	3
McQuillen et al.	Trauma, Sport and Malignant Cerebral Edema	1988	Case Series	A	3
Mann et al.	Plaques and tangles and transmitter deficiencies in dementia	1982	Case Series	P	3
Harvey, P.K., Newsom Davis, J.	Traumatic encephalopathy in a Young Boxer	1974	Case Report	P	3
Blonstein, J.L.	Traumatic encephalopathy in a Young Boxer	1974	Case Report	P	3
Betti, O., Ottino, C.	Pugilistic encephalopathy	1969	Case Report	N/A	3
Payne, E.	Brains of boxers	1968	Case Series	P	3

**Table 4 Evidence table: Histopathology (cont'd)**

Author	Title	Year	Study Type	Amateur (A) Professional(P)	SIGN Grade
Tomlinson, B., Walton, J.	Superficial haemosiderosis of the central nervous system	1964	Case Report	N/A	3
Strich, S.	Shearing of nerve fibres as a cause of Brain damage due to head injury	1961	Case Series	N/A	3
Lindenberg, R.	The Mechanism of Cerebral Contusion	1960	Case Series	N/A	3
Grahmann,H., Ule, G.	Diagnosis of chronic cerebral symptoms in boxers (dementia pugilistica and traumatic encephalopathy of boxers)	1957	Case Report	P	3
Strich, S.	Diffuse Degeneration of the Cerebral White Matter in Severe Dementia following Head Injury	1956	Case Series	N/A	3
Brandenburg, W., Halleworden, J.	Dementia pugilistica mit anatomischem Befund	1954	Case Report	P	3
Schwidde, J.	Incidence of Cavum Septum Pellucidi and Cavum Vergae in 1,032 Human Brains	1952	Case Series	N/A	3
Kremer et al.	A Mid Brain syndrome following Head Injury	1946	Case Series	N/A	3
McCrory, P.	Boxing and the Brain. Revisiting chronic traumatic encephalopathy	2002	Expert Opinion	A + P	4
McCrory, P.	Cavum Septi Pellucidi - A reason to ban boxers ?	2002	Expert Opinion	P	4
Jordan, B.	Chronic Traumatic Brain Injury Associated with Boxing	2000	Expert Opinion	P	4
Erlanger et al.	Neuropsychology of Sports related Head Injury: Dementia Pugilistica to Post Concussion Syndrome	1999	Expert Opinion / Literature Review	A + P	4
Leach, R.	What Price Glory ?	1998	Expert Opinion	P	4
Bodensteiner, B., Schaefer, G.	Dementia Pugilistica and Cavum Septi Pellucidi: Born to Box ?	1997	Expert Opinion	A + P	4
Mendez, M.	The Neuropsychiatric aspects of Boxing	1995	Expert Opinion	A + P	4
Unterharnscheidt, F.	A neurologists reflection on boxing. II. Acute and chronic clinical findings secondary to central nervous system damage	1995	Expert Opinion	A + P	4
Stening, W.	Boxing	1992	Expert Opinion	A + P	4
Stern. M.	Head Trauma As A Risk Factor For Parkinson's disease	1991	Expert Opinion	P	4
Corsellis, J.	Boxing and the Brain	1989	Expert Opinion	P	4
Jordan, B.	Neurologic Aspects of Boxing	1987	Expert Opinion	A + P	4
Guterman, A., Smith, R.	Neurological Sequelae of Boxing	1987	Expert Opinion	A + P	4
Ryan, A.	Intracranial Injuries Resulting from Boxing: A Review (1918-1985)	1987	Expert Opinion	A + P	4
Charnas, L., Pyeritz, R.	Neurologic Injuries in Boxers	1986	Expert Opinion	A + P	4
Morrison, R.G.	Medical and Public health Aspects of Boxing	1986	Expert Opinion	A + P	4
Burns, R.	Boxing and the Brain	1986	Expert Opinion	A + P	4
Mortimer, J.	Epidemiology of Post-Traumatic Encephalopathy in Boxers	1985	Expert Opinion	A + P	4
Millar, A.	Boxing - time for fresh action	1984	Expert Opinion	A + P	4

**Table 4 Evidence table: Histopathology (cont'd)**

<b>Author</b>	<b>Title</b>	<b>Year</b>	<b>Study Type</b>	<b>Amateur (A) Professional(P)</b>	<b>SIGN Grade</b>
Lampert, P., Hardman, J.	Morphological Changes in Brains of Boxers	1984	Expert Opinion	A + P	4
Editorial	Boxing in the Army	1984	Expert Opinion	A	4
La Cava, G.	Prevention in Boxing	1983	Expert Opinion	A + P	4
Council on Scientific Affairs. A.M.A	Brain Injury in Boxing	1983	Expert Opinion	A + P	4
Editorial.Lancet.Vol. 1	Brain Damage in Sport	1976	Expert Opinion	P	4
Editorial. B.M.J. vol.4	Boxing and the Brain	1973	Expert Opinion	P	4
Elia, J.	Head Injuries in Boxing	1971	Expert Opinion	A + P	4
Unterharnscheidt, F.	About Boxing : Review of Historical and Medical Aspects	1970	Expert Opinion	A + P	4
La Cava, G.	Boxer's Encephalopathy	1963	Expert Opinion	P	4

**CHAPTER II**  
**ELECTROPHYSIOLOGY**

The physician Richard Caton (1875) first demonstrated the presence of electrical activity in the brain, though not until 1924 did the physiologist Berger produced an amplified graphical image, suggesting that his observations may provide a means whereby,

*"We may learn the physical basis of consciousness"* (Brazier, 1992)

The electroencephalogram (EEG) has three main clinical applications. Firstly the diagnosis and management of epilepsy, secondly indirect localisation of structural abnormalities such as tumour, though results are vague and provide no indication of underlying pathology. The third major use is in the investigation of specific neurological disorders such as encephalitis, which produce a characteristic EEG pattern. Metabolic disorders, altered consciousness, sleep and brain death are additional areas where EEG may provide supplementary information. EEG is often requested when patients with post-traumatic syndromes are being evaluated at a later stage, in the hope that it will provide a guide as to whether non-specific symptoms have an organic aetiology. Its use in this regard appears to have no rational basis (Aminoff, 1992). Despite such limitations EEG has been used widely in an attempt to understand chronic brain injury in boxing.

Busse and Silvermann (1952) presented the first evidence attempting to evaluate the worth of electroencephalography as a screening tool. In the preceding year the State of Colorado had required all professional boxers to undergo EEG prior to their being licensed, thereby providing a suitable cohort. The study concluded that 37.5% of boxer's tracings revealed disturbance of rhythm, well above that considered normal in contemporaneous studies. It was suggested that boxers who had been knocked out had more severe dysrhythmia, but no statistical analysis was cited, nor were there details of when tracings were taken in relation to the period of unconsciousness. No correlation was found between abnormality and length of ring career thus the authors were unable to demonstrate the value of EEG in predicting or screening for traumatic brain damage. Failure to compare any clinical findings in boxers with EEG deficiency also detracts from the value of this study.

The subsequent study by Kaplan and Browder (1954) addressed many of these failings. Their cohort comprised 1,043 professional boxers, whose boxing history was held by local

commissions. Fourteen hundred tracings were taken, including 40 taken within 10 minutes of losing a fight. Fights were observed at ringside by a physician, and additional cinematography was recorded in order to retrospectively assess degree of exposure to head trauma.

Ringside surveillance and subsequent analysis of slow motion films led to two main observations. Firstly boxing styles could be subdivided into “*sluggers*” and “*boxers*”. “*Sluggers*” relied on offensive tactics and brute strength to overpower an opponent, but in doing so they were observed to accept many blows to the head. The “*boxer*” was more agile, relying on both defensive and offensive skills to win, thereby avoiding excessive punishment to the head. These observations and descriptions are still valid today.

Secondly the authors noted that few blows in a single contest were truly effective blows to the head, which caused alteration in consciousness. The study only contains this statement with no statistical analysis or figures, and as such this is an anecdotal, though possibly relevant, observation.

Analysis of EEG recordings used a grading system that assigned each tracing to one of twelve basic categories. A number of tracings contained more than one category. Statistical analysis was performed using the chi-squared test after the tracings were subdivided into two groups, “*better organised tracings*” and “*less well organised tracings*”. No correlation was demonstrated between EEG recording and any one of the following parameters:

- Age;
- Number of fights;
- Style of fighter (“*slugger* vs “*boxer*”);
- Weight division;
- Fights won;
- Fights lost;
- Knockouts experienced.

The only demonstrable correlation was between disorganized EEG tracing and rating, poorly rated boxers having more disorganized tracings. A boxers rating is defined as his ability relevant to the best boxer for a given weight division. The authors concluded that there was no uniformly identifiable pattern in EEG seen in boxers that would lend itself to use as a diagnostic tool.

Blonstein and Clarke (1954) performed EEG readings on 48 amateur boxers. Twenty-four of this group had suffered a knockout within the preceding two weeks, the remainder being used as controls. The main finding was that four of the study group had abnormal tracings, which resolved within two months of injury.

This study lacked methodological description and statistical analysis, thus the conclusion that no correlation could be made between boxing history and EEG tracing remains only an observation.

Nesarajah *et al* (1961) reported results from a cohort of 50 amateur boxers, and 75 controls. The study group was found to have disordered electrical activity in 60% of readings, compared to 8% of controls. Poor methodology did not allow for any statistical significance to be attached to this figure.

Spillane (1962) examined a cohort of professional boxers referred to a regional neurological center for assessment of cerebral dysfunction developing in later life. Despite clear and reproducible neurological signs on clinical examination, only one of these boxers demonstrated an abnormal tracing, 80% being normal.

Mawdsley and Ferguson (1963) compared EEG findings and clinical affectation in a case series of ten professional boxers, all of whom demonstrated neurological signs and symptoms. Subjects in this group were exposed to a high number of bouts, ranging from 80 to over 1000, all commencing their boxing career in the early 1920's, before the inception of the BBB of C. Although only a small sample, they represent a cohort of neurologically impaired fighters, with high exposure to head trauma as witnessed by the number of fights.

Despite this, the authors were unable to demonstrate any correlation between clinical findings and EEG tracings.

The preceding studies mostly address the question of any cumulative damage that may manifest as EEG disturbance. A presentation in Paris (Beaussart and Beaussart-Boulenge, 1970a) briefly mentioned the findings in 123 amateur boxers, who were examined physically and by EEG before and within 10-15 minutes of a fight. The authors found no objective pathological change even when a fight ended in loss of consciousness. This concurred with observations from a previous study which compared EEG tracing with clinical findings in head trauma (Beaussart and Beaussart-Boulenge, 1970b). No correlation was found between EEG tracing and severity of original trauma. Whilst these two papers were published as abstracts for clinical meetings, and lack any methodological description, they do assent with previous studies.

Johnson (1969a,1969b) examined 17 boxers, 10 of whom had been previously cited (Mawdsley and Ferguson, 1963). Conflicting statements are made in the conclusion of two separate publications for the same study group. In the first paper (Johnson, 1969a) which looks specifically at the EEG in traumatic encephalopathy of boxers, the author states,

*“The correlation between the severity of the clinical syndrome and the degree of disorganization of the EEG is poor”*

In his subsequent paper (Johnson, 1969b) concludes,

*“The abnormal EEG recordings correlate with clinical and radiological evidence of brain damage”.*

Despite these paradoxical statements, the author makes a very important and valid observation that may explain the clinical picture,

*“The lesions responsible for encephalopathy are probably located in two main areas: neurological features in the upper brainstem, psychiatric features in the*

*Hippocampal-Fornical system... The scalp EEG reflects neural disorganization in the cerebral cortex in a syndrome that is largely sub-cortical"*

Jedlinski *et al* (1970) performed neurological, psychiatric and EEG examinations on a cohort of 60 amateur boxers who had fought 100-344 fights boxing over an average of eight years. Statistical analysis showed a positive correlation between neurological abnormalities and pathological EEG changes in the group of boxers with the longest careers, who had also had more fights. In this same series a positive correlation was also found between psychiatric and electroencephalographic abnormalities in this high exposure set. Overall 40% of EEG tracings were found to be abnormal, though there was no information relating to the timing of tracings, thus limiting the value of this series. The authors conclude in respect of the neurological, psychiatric and EEG abnormalities,

*"These changes are not yet pathological in the clinical meaning, but they should be regarded as prodromal symptoms and signs preceding the appearance of encephalopathy"*

In Robert's study of British professional boxers (1969) EEG tracings were performed on 168 subjects, with 98 police officers acting as controls. No differences were seen between boxers and controls. Although none of the observations reached clinical significance, it was noted that few abnormal EEG readings were found in cases of clinical encephalopathy. This group did however demonstrate a higher percentage of low voltage recordings. The author performed a literature search in which there were reports of 24 cases of presumed encephalopathy from whom EEG recordings had been taken. Fifteen of these records were found to be abnormal, but no statistical correlation could be established which demonstrated a constant EEG abnormality linked with a specific clinical syndrome such as cerebellar or extrapyramidal dysfunction.

Boxing protagonists may argue that the preceding studies pertain to a cohort of boxers from a different era, and as such results must be viewed with caution. The single case report of a boxer who began his career in 1962, raises the possibility that clinical encephalopathy may be seen in the modern era (Harvey and Davis, 1974). Although the subject displayed

pyramidal and extrapyramidal signs, in association with depression and paranoid mood swings, his EEG was normal.

The work of Thomassen *et al* (1979) provides more credible evidence to support the view that EEG is of little value in boxing. In this cohort study 53 former amateur champion boxers were compared to 53 matched controls. No relationship between abnormal findings and exposure to boxing could be demonstrated in neurological, neuropsychological or electroencephalographic parameters. In particular EEG abnormalities did not correlate with traumatic exposure to boxing. This study is ; however, flawed, by way of selection bias, as the subject group was comprised of previous champions. By inference, this group would embrace predominantly “*boxers*” rather than “*sluggers*”, using the vernacular of Kaplan And Browder (1954). This group was less liable to head trauma, and the results of Thomassen’s study are thus applicable to the more elite end of the spectrum of boxing skills.

In a study by Kaste *et al* (1982) the cohort investigated comprised 14 volunteers, eight amateurs and six professionals. Abnormalities were found in six of the thirteen in whom tracings were taken, but there is no statistical evaluation that would allow comparison of abnormal tracing with exposure data, professional status, or indeed any of the measured career parameters (age at debut, length of career, weight, number of fights, results of fights). The authors state that 46% of their group displayed abnormal readings, “*which may have been caused by brain injury*”. This poor methodology devalues the study.

The study by Ross *et al* (1983) had similar failings. The subjects volunteered after this study was advertised in a local newspaper. Such selection bias diminishes the findings, as many questions may be asked regarding the motives for any individual wanting to be medically scrutinised for signs of damage related to boxing. The subjects were both amateur and professional, with an age range from 14 to 74. There was a positive correlation between abnormal EEG and number of bouts fought, but no correlation between abnormal neurological signs and bouts fought. The authors state,

*“The EEG proved to be a better predictor of possible neurological abnormalities”*

concluding that the EEG should form part of a boxers regular examination. This statement appears in isolation and does not concur with the evidence as presented within the preceding paper.

Casson *et al* (1984) formulated a numerical representation of neuropsychometric dysfunction, the impairment index, which was a percentage of the abnormal neuropsychological tests on each boxer. In their study of 18 former and active boxers, both professional and amateur, 13 of 18 subjects had EEG performed. 53% were abnormal, and all of these subjects had an impairment index of greater than 50%. The true significance of this figure remains to be determined, as 15 of the total cohort of 18 subjects had impairment index of > 50 %. The authors state,

*"The subjects of this study were not selected at random and are not representative of all modern boxers"*

As such, any inferences from this study in respect of EEG and brain damage caused by boxing remains speculative.

Selection bias detracts from the findings of McLatchie *et al* (1987) who examined 20 amateur boxers who had replied to an invitation to take part in a study. 40% of those examined had abnormal tracings but there was no correlation between abnormal EEG and number of fights. The authors did observe a correlation between decreasing age and abnormal EEG, related to immaturity in the younger brains. They state in their discussion,

*"We must emphasise that it is not possible to conclude from our data that the abnormalities we have found are the result of boxing"*

Sabharwal *et al* (1987) add nothing to our understanding of EEG in boxing. Three of the four boxers in this series had abnormal EEG but the methodology does not allow any direct interpretation of this figure in terms of exposure to head trauma. What is more relevant is that all four subjects in this 1987 study showed clinical evidence of encephalopathy.

Haglund and Persson (1990) presented detailed reports in their retrospective neurophysiological study, which was part of a much wider investigation into Swedish amateur boxing. No “severe” EEG abnormality was found in either the study group of 50 boxers, or the control group of 25 footballers and 25 track and field athletes. However, minor differences did exist between study group and controls suggesting to the author the possibility of slight dysfunction in the boxing group. In keeping with other studies the EEG deviations did not correlate with number of bouts, number of lost fights, knockouts, or length of boxing career. It is interesting to note the disparity in presentation of results by Haglund in two separate publications. In the original work (Haglund and Persson, 1990) it is stated that there was a “*somewhat higher incidence of slight or moderate EEG deviations*” among boxers compared to controls. In a later publication (Haglund and Eriksson, 1993), it is stated,

*“There was a significantly higher incidence of slight or moderate encephalography deviations among the boxers”.*

In the low matched boxing group, one individual suffered from an undiagnosed immunological illness, with EEG changes and pathological findings on CAT and MRI. Exclusion of this individual removed the only demonstrable statistical difference between boxers and controls.

A four year prospective study of amateur boxers (Stewart *et al.*, 1994) involving 484 subjects showed odds ratio significantly less than one for electroencephalogram measures. This study, which focuses primarily on neuropsychometric assessment, is discussed in depth in another chapter.

A variety of other electrophysiological techniques are available, but their reported application in boxing has been limited.

Kaste *et al* (1982) state that latencies for brainstem evoked potential were within normal limits in all subjects studied, though this statement is meaningless in the context of flawed methodology and lack of controls.

Breton *et al* (1991) set out to examine possible cognitive impairment following blows to the head, using cognitive psychology and electrophysiology. Boxers' attention mechanisms and ability to orientate towards a significant stimulus were investigated using event related potentials, before and after a fight. This study failed to demonstrate any abnormalities of attention or detection processes. The authors suggest more studies involving greater numbers of boxers might allow more exact determination of possible cognitive impairment in boxers.

Haglund and Persson (1990), in addition to performing EEG, also measured brain electrical activity mapping (BEAM), brainstem auditory evoked potential (BAEP) and auditory evoked potential P 300 potential, (P300). As with EEG no neurophysiological variable was correlated to the number of bouts, number of lost fights or length of boxing career.

Stewart *et al* (1994) included brainstem evoked potentials as part of a battery of 29 tests administered to their cohort in a prospective study of central nervous system function in amateur boxers; however, the subsequent detailed statistical analysis does not allow the results of BEP studies to be isolated from other data.

In summary the evidence to support the use of electrophysiological studies in identifying chronic brain damage in boxing appears lacking. The histopathological data delineates the anatomical regions damaged by chronic exposure, which are remote from those areas that can be readily studied using electroencephalography and evoked potentials. None of the studies demonstrate a clear link between trauma secondary to boxing exposure and consistent and reproducible abnormalities in electrophysiological tests. This is true for both amateur and professional boxing and as such these tests are neither predictive for, nor diagnostic of, chronic traumatic brain damage. Despite this a number of governing bodies within professional boxing still require an EEG as part of a pre-fight medical screen.

**Table 5 Evidence table: Electrophysiology**

Author	Title	Year	Study Type	Amateur (A) Professional (P)	SIGN Grade
Stewart et al.	Prospective Study of Central Nervous System Function in Amateur Boxers	1994	Cohort	A	2 ++
Haglund, Y., Eriksson, E.	Does amateur boxing lead to chronic brain damage ? A review of some recent investigations	1993	Case control	A	2 ++
Stiller, J.	Boxing and Chronic Brain Damage	1985	Systematic Review	A + P	2 ++
Thomassen et al.	Neurological, electroencephalographic and neuropsychological examination of 53 former amateur boxers	1979	Case control	A	2 ++
Roberts, A. H.	Brain Damage in Boxers	1969	Cohort	P	2 +
Rodriguez et al.	Long term effects of boxing and Judo choking techniques on brain function	1998	Cohort	A + P	2 -
Casson et al.	Brain Damage in Modern Boxers	1984	Cohort	A + P	2 -
Ross et al.	Boxers - Computed Tomography, EEG, and Neurological Evaluation	1983	Cohort	A + P	2 -
Kaste et al.	Is Chronic Brain Damage in Boxing a Hazard of the Past	1982	Cohort	A + P	2 -
Jedlinski et al.	Punch Drunkenness	1970	Cohort	A	2 -
Jedlinski et al.	Chronic Post Traumatic Changes in the Central nervous System in Pugilists	1969	Cohort	A	2 -
Nesarajah et al.	Electroencephalographic changes in Ceylonese Boxers	1961	Cohort	A	2 -
Busse, E.W., Silverman, A.J.	Electroencephalographic changes in Professional Boxers	1952	Case series	P	2 -
Sabharwal, R.K.	Chronic Traumatic Encephalopathy in Boxers	1987	Case series	A	3
McLatchie et al.	Clinical neurological examination, Neuropsychology, electroencephalography and computed tomographic head scanning in active amateur boxers	1987	Cohort	A	3
Sironi, V.A., Ravagnati, L.	Brain Damage in Boxers	1983	Case series	P	3
Casson et al.	Neurological and CT evaluation of knocked out boxers	1982	Case series	P	3
Harvey, P., Newsom Davis, J.	Traumatic Encephalopathy in a young boxer	1974	case report	P	3
Johnson. J.	The EEG in the Traumatic Encephalopathy of Boxers	1969	Case series	P	3
Johnson, J.	Organic Psychosyndromes due to Boxing	1969	Case series	P	3
Beaussart, M.	"Experimental " study of cerebral concussion in 123 amateur boxers, by clinical examination and EEG before and immediately after fights	1970	Case series	A	3
Mawdsley, C., Ferguson, F.R.	Neurological Disease in Boxers	1963	Case Series	P	3
Spillane, J.	Five Boxers	1962	Case series	P	3
Blonstein, J.L., Clarke, E.	The Medical Aspects of Amateur Boxing	1954	Case series	A	3
Kaplan, H., Browder, J.	Observations on the Clinical and Brain Wave patterns of Professional Boxers	1954	Case series	P	3
Mendez, M.	The Neuropsychiatric Aspects of Boxing	1995	Expert Opinion	A + P	4
Unterharnscheidt, F.	A neurologists reflection on boxing. II. Acute and chronic clinical findings secondary to central nervous system damage	1995	Expert opinion	A + P	4

**Table 5 Evidence table: Electrophysiology (cont'd)**

<b>Author</b>	<b>Title</b>	<b>Year</b>	<b>Study Type</b>	<b>Amateur (A) Professional (P)</b>	<b>SIGN Grade</b>
Jordan, B.	Neurological Aspects of Boxing	1987	Expert Opinion	A + P	4
Guterman, A., Smith, R.W.	Neurological Sequelae of Boxing	1987	Expert Opinion	A + P	4
Ryan, A.	Intracranial Injuries resulting from Boxing : A review ( 1918-1985)	1987	Expert Opinion	A + P	4
Charnas, L., Pyeritz, R.	Neurologic Injuries in Boxers	1986	Expert Opinion	A + P	4
Morrison, R.G.	Medical and Public health Aspects of Boxing	1986	Expert Opinion	A + P	4
British Medical Association	Boxing. Report of the Board of Science and Education Working Party	1984	Expert Opinion	A + P	4
Millar , A.P.	Boxing - Time for fresh action	1984	Expert Opinion	A + P	4
Johnson et al.	Peak acceleration of the head experienced in boxing	1975	Expert Opinion	P	4
Blonstein, J.L.	Care of the Amateur Boxer	1977	Expert Opinion	A	4
Editorial. Aust/NJ Journal Psychiatry	Boxing	1971	Expert Opinion	A + P	4
Elia, J.C.	Head Injuries in Boxing	1971	Expert Opinion	A + P	4
Blonstein, J.L.	Medical aspects of Amateur Boxing	1966	Expert Opinion	A + P	4
La Cava, G.	Boxer's Encephalopathy	1966	Expert Opinion	P	4

## **CHAPTER III**

### **NEURORADIOLOGY**

Neuroradiological assessment of structural change suggestive of brain damage initially relied on indirect measurement of parenchymal volume using air encephalography. This technique also allowed inferences to be made on midline structures, such as the septum pellucidum, by observing movement of air across and through any deficits. The advent of computerised tomography allowed a more direct visualisation of brain structure, which has been superseded by magnetic resonance imaging.

The main limitation of neuroradiology is that it provides imaging of brain structure at a given point in time. Chronic brain injury due to boxing is thought to be a dynamic and evolving process and as such the challenge is to demonstrate any correlation that may exist between parenchymal change and exposure history. Serial radiological assessment may provide evidence of changes in evolution, contrasting markedly with the histopathological evidence, which can only ever show damage already having been done.

Critchley (1957) alludes to radiological evidence of frontal lobe atrophy and loss of white matter in boxers; however, the case series presented by Spillane (1962) appears to be the earliest record of pathological changes in boxers being demonstrated radiologically during life. Four of the five had a cavum septum pellucidum, in two cases enlargement of the lateral ventricles was also present.

The findings of Mawdsley and Ferguson (1963) concur with this original paper. Ten boxers were examined using air encephalography and 60 % were found to have a cavum septum pellucidum, with enlargement of the lateral ventricles. 30 % showed cerebral cortical atrophy, and in one case marked cerebellar cortical atrophy. The study group again comprises boxers who had presented with abnormal clinical neurology thought to be consequent upon their career in boxing. In conclusion the authors state,

*“In the absence of internal hydrocephalus, a cavum septum pellucidum is an uncommon finding, and its frequency in ex-boxers must be significant”*

The work of Johnson (1969b) augmented this study by adding another seven boxers to the group already described, confirming the presence of cavum septum pellucidum and cortical

atrophy. In a number of these cases, fenestration of the septum pellucidum is suggested by air collecting in the uppermost ventricle with the patient lying on their side.

The advent of computerised axial tomography (CAT) allowed a more detailed, and less invasive examination of the brain structures in vivo. The single case study by Harvey and Davis (1974) is the first description of mild ventricular dilatation demonstrated on CAT but of note is the fact that this study was augmented by lumbar air encephalography which showed a cavum septum pellucidum, not evident on the supposedly more advanced CAT.

The first case series to report CAT findings in boxers was that of Kaste *et al* (1982) though the findings are compromised by selection bias resulting from subjects having volunteered. The small study size, combining eight amateur and six professional boxers, also detracts from the power of the observation. Three of six professionals and one of eight amateurs had brain atrophy. This group of pathologically abnormal CAT scans also showed a cavum septum pellucidum in two of the three professionals and the same amateur with atrophy. There is no statistical analysis that allows comparison of exposure to head trauma (length of career, number of fights) with abnormal neuroradiological findings.

Criticism may be leveled at Casson *et al* (1982) in their case series of neurological and CAT evaluation of knocked out boxers. The study group comprised ten professional boxers, with ages ranging from 20 to 31 and total number of professional bouts ranging from 2 to 52. Nine of the subjects had been rendered unconscious for less than ten seconds, with post-traumatic amnesia lasting less than two minutes. Subject 4 was known to have a mild organic mental syndrome manifest by impairment of recent memory and recall, confusion and dyscalculia. This subject had a normal CAT scan and EEG. Neurological examination was normal in all others. Five of the remaining group had “*definitely abnormal CAT*”, three with mild generalized cerebral atrophy and two with central cerebral atrophy. The authors state,

*“Little or no correlation between neurological evaluation, EEG and CAT scan should also come as no surprise to clinicians”.*

This statement is made in the absence of any statistical analysis, and appears to be conjecture. The final conclusion also appears to be independent of any evidence contained within the published paper,

*“We submit that CAT findings of cerebral atrophy with or without a cavum septum pellucidum might predict the later development of clinical chronic encephalopathy in presently asymptomatic boxers”.*

Ross *et al* (1983) studied as their cohort volunteers with no control group for comparison. The study group contained 40 ex boxers, both amateur and professional, whose ages ranged from 14 to 74 years. Each scan was graded 0-4 on both sulcal and ventricular enlargement, 0 being normal, 4 most abnormal. Statistical analysis showed a significant relationship between the number of bouts fought and the composite CAT score ( $P=0.0229$ ). Assessing each score individually showed no correlation for sulcal enlargement alone ( $P=0.11$ ), but the number of bouts fought was significantly related to ventricular enlargement ( $P=0.027$ ). The study also showed correlation between EEG change and bouts fought, but not neurological deficit and bouts fought. Following publication of the paper by Ross *et al*, a number of letters critical of the methodology were published. Engleberg (1983) was critical of volunteer selection bias and small sample size limiting the validity of any conclusion. Ross replied,

*“The conclusions may or may not be applicable to boxers in general. We would like to point out, however, that our boxers had relatively few bouts, and we feel justified in assuming from our data that in those boxers having more bouts, worse CAT scores would have been found”.*

Such assumption lacks any scientific basis.

Casson *et al* (1982) performed cranial CAT. scans on 18 former and currently active amateur and professional boxers. The scans were evaluated by measuring the lateral ventricles using the criteria described by Huckman *et al* (1975), in addition to a qualitative

assessment of sulcal prominence. Presence or absence of a cavum septum pellucidum was also noted. The measurements enabled the authors to describe three types of atrophy:

- i) Generalised cerebral atrophy = both ventricles and sulci enlarged;
- ii) Central cerebral atrophy = isolated ventricular enlargement;
- iii) Cerebral cortical atrophy = isolated sulcal enlargement.

Eight of the eighteen subjects had abnormal CAT scans. Five had generalised cerebral atrophy, two displayed central cerebral atrophy and one had cerebral cortical atrophy. Three subjects had a cavum septum pellucidum. Of note is the fact that six of the eight fighters with more than 20 professional bouts had an abnormal CAT scan, yet only two of ten boxers with less than 20 professional fights had an abnormal CAT scan. The authors also devised an impairment index, which was a percentage of abnormal neuropsychological tests scores. Every subject with an abnormal CAT scan had an impairment index of greater than 0.5. The authors concluded that neuropsychological testing is a highly accurate means of detecting brain injury in fighters, with a high correlation with abnormal CAT scans and EEG. The authors state in the introduction,

*“The subjects of this study were not selected at random, nor are they representative of all modern boxers”.*

This is further witnessed by the fact that although the cohort were chosen to,

*“... eliminate those with known medical, neurological, psychiatric or substance abuse illnesses.”*

Five of the eighteen had evidence of organic mental syndrome with three showing disorientation, confusion and memory loss, one a horizontal nystagmus on lateral gaze, and one a positive Babinski sign. Any conclusions drawn from this study must therefore be viewed with caution, due to selection bias.

McLatchie *et al* (1987) examined an uncontrolled cohort of 20 amateur boxers who were subject to a battery of neurological, neuropsychological, EEG and CAT investigations. The CAT scans were normal in 19 out of 20. The abnormal scan showed a thickened skull vault with dilatation of the lateral and third ventricles, without any evidence of cortical atrophy. This finding could either represent central atrophy or a form of arrested hydrocephalus and as such its relationship to boxing remains uncertain. Although CAT scans were normal, seven had atypical neurology, eight an irregular EEG tracing and nine were deficient in neuropsychometric testing. The authors advised caution in drawing any direct conclusions from this study,

*“We must emphasise that it is not possible to conclude from our data that the abnormalities we have found are the result of boxing...our study group may be unrepresentative; it comprised only those who accepted the invitation to be examined and possibly they did so because they had complaints and were concerned”*

The advent of Magnetic Resonance Imaging (MRI) provided a more precise neuroradiological tool, with imaging of some areas superior to that previously obtained by CAT scanning alone (Gandy *et al.*, 1984) (Han *et al.*, 1984).

Levin *et al* (1987a) used MRI scanning as an adjunct to a controlled neurobehavioral study in 13 matched boxers. Only the boxers were subject to MRI with no controls. All scans were normal and the neuropsychometric analysis failed to demonstrate any statistical significance between the groups, leading the authors to conclude,

*“Our findings raise the possibility that young boxers may escape disabling brain injury, provided that their exposure in the ring is limited both in frequency an total duration”.*

They also add the following observation,

*“... caution is advised in drawing inferences from our data pending replication and follow-up study over a longer interval”.*

Jordan and Zimmerman (1988) reviewed the MRI and neurological findings in a group of nine elite amateur boxers, all of whom had been suspended secondary to a knockout or excessive head blows. MRI scans were performed between one week and three and a half months following the last bout. No abnormality was found on either MRI or neurological examination. The small sample size and selection bias does not allow any conclusion to be drawn from this study.

In a subsequent study Jordan and Zimmerman (1990) compared CAT and MRI findings in a group of 21 boxers. This group comprised a highly select cohort of both amateur and professional boxers who were referred for radiological imaging as they displayed abnormal neurology. Eleven had normal CAT and MRI, seven had abnormalities that were shown on both CAT and MRI. All abnormalities demonstrated on CAT were confirmed on MRI; however, a number of lesions including subdural haematoma, white matter changes and a focal contusion were more clearly visualized on MRI scan. This paper merely demonstrates the superiority of MRI over CAT and in doing so uses a cohort of boxers with defined neurological abnormalities. Such selection bias adds little to our understanding of the neuroradiology of boxing related brain injury.

Haglund and Bergstrand (1990) as part of the investigation commissioned by the Swedish government compared CAT and MRI findings in a case controlled retrospective study. The study group comprised amateur boxers classified as high match who had fought more than 30 bouts and low match with less than 10 bouts. The control group consisted of 25 track and field athletes and 25 football players. The aim of this arm of the study was to investigate whether morphological changes could be demonstrated in the brains of boxers. Ventricular size on CAT was assessed using the calculations described by Hanson *et al* (1975). Cortical sulcal width was assessed subjectively using a grading from normal to pathological. If present a cavum septum pellucidum was classified as small, intermediate or

large. The MRI scans were scrutinised mainly for anatomical alterations and changes in signal density of the brain parenchyma. No difference was found between the study and control group in any parameter measured. A cavum septum pellucidum was found more often in the control group than the study group of boxers (2/47 boxers, 4/50 controls). Although only 4% of the study group were found to have a cavum septum, the authors state,

*"The length of boxing career, number of fights lost and KO/RSC(H) correlated with the occurrence of a cavum septum pellucidum."*

*(KO = Knockout, RSC(H) = Referee Stops Contest due to excessive Head blows ).*

Jordan *et al* (1992) determined to assess the frequency of CAT abnormalities in a representative sample of active professional boxers. The study group comprised 338 men applying for issue or renewal of a boxing license in New York State, U.S.A., age range 17-46 years. Ventricular and sulcal size were compared to normal men of similar age range (20-30 years). An abnormal CAT scan was found in 7% of the boxers, which contrasts with the figures quoted in other studies that suggest a prevalence of 20-50%. The relatively high figures in these other studies may reflect the non-representative sample populations being observed. Jordan *et al* found no correlation with abnormal CAT scan and any of the following parameters: age, win/loss record, number of bouts, and abnormality of EEG. Cerebral atrophy and CSP were however correlated. In this study group 27% of boxers without a CSP had cerebral atrophy, compared to 44% and 67% of those subjects with small and large CSP respectively. 49% of boxers with a "borderline scan" had experienced a knockout (KO) or technical knockout (TKO), 68% with an "abnormal scan" had experienced KO/TKO. The cross sectional nature of this epidemiological cohort study determines that the directionality of the relationship between history of KO/TKO and abnormal CAT scan could not be confirmed. Whether central nervous system abnormalities reflected by an anomalous CAT scan finding predispose a boxer to KO/TKO, or whether KO/TKO results in brain injury manifest by CAT changes remains to be determined.

Holzgraefe *et al* (1992) attempted to determine a causal link between exposure to trauma and neuroradiological evidence of parenchymal damage to the brain in their prospective study of 13 amateur boxers. The hypothesis was that micro-haemorrhage was the cause of

encephalopathy in boxers and that this might be demonstrated on MRI scan. The subjects underwent MRI and neurological evaluation before and after each fight. Their average age was 24 and they had fought between 18 and 203 bouts. In addition to medical screening a subjective assessment of head punches received during each fight within the study period was noted. Five subjects demonstrated transient neurological dysfunction following their fights but with no demonstrable haematoma or structural change on MRI. The number of head punches did not correlate with the occurrence of neurological signs. The authors concluded,

*"Imaging methods cannot clarify the development of chronic encephalopathy."*

The significance of these findings is diminished by the small cohort size and it being limited to amateur boxers. A similar larger study in the professional field would be more beneficial as it is this group who appear to be more prone to chronic encephalopathy.

Detailed histopathological studies have demonstrated the presence of a cavum septum pellucidum in a significant number of the specimens examined (Corsellis *et al.*, 1973). Subsequent neuroradiological studies, from the earlier pneumoencephalograms through to CAT and MRI, also suggested that such pathological changes might be caused by trauma. Bogdanoff and Natter (1989) reviewed a cross-sectional group of 1,914 CAT scans. Fourteen demonstrated a CSP (0.73%). Of these nine were men and five women. Five of the men were boxers and thus it was concluded 55.6% of cavum septum pellucidi in adult men, were found in boxers. All nine men were referred, as there was a clinical indication, for CAT. The study group is therefore compromised by selection bias. The calculations and statistical analysis do not comment on how many of the remaining 1,906 patients scanned were boxers.

McCrory (2002) set out to evaluate the clinical evidence pertaining to cavum septum pellucidum in his review paper which encompassed all the major studies and papers available. Key points in conclusion are as follows:

- The new development or serial enlargement of a cavum septum on neuroimaging studies suggests, but does not confirm, the early development of dementia pugilistica, particularly if associated with other evidence of boxing related neuro-trauma. To date, insufficient prospective studies have been undertaken to substantiate this assertion;
- There is no convincing evidence to date that routine MRI or other neuroimaging techniques will detect early evidence of brain damage in boxers. Prospective studies using more sophisticated imaging techniques are required to answer this question.

A number of isolated studies have looked at additional ways of imaging the brain, in an attempt to link structure with function.

Kemp *et al* (1995) examined 41 boxers and 27 controls using both psychometric testing and technetium-99m hexamethyl-propyleneamineoxime single photon emission computerized tomography (Tc-99m HMPOA SPECT) cerebral perfusion scans. The control group comprised servicemen undergoing medical assistant training, introducing the possibility of selection bias, the inference being that they were more intelligent than the study group. The results showed significant differences between the two groups in both neuropsychometric test result and abnormalities of cerebral perfusion. The authors question whether these findings are reversible and suggest the need for further studies.

Proton magnetic resonance spectroscopy focused on the lentiform nucleus was performed on three ex-professional boxers who had developed a Parkinsonian syndrome (Davie *et al.*, 1995). Controls comprised six patients with idiopathic Parkinsonism and six normal subjects. The boxing group showed a reduction in absolute concentration of N-acetylaspartate compared to the other groups suggesting neuronal loss in the putamen and globus pallidus. The size of the study group diminishes its impact but it corroborates one hypothesis, that the extra pyramidal syndrome occurring in boxers may be distinct from idiopathic Parkinson's disease.

Magnetic resonance diffusion weighted imaging is sensitive to microscopic changes in Brownian motion of water molecules in brain tissue. The microstructure of the brain

imposes restriction on diffusion of water such that changes in the integrity of brain tissue may be inferred from increased diffusion (Zhang *et al.*, 2003). In this study 24 professional boxers and 14 controls were examined. The results suggested the presence of microstructural changes as witnessed by increased diffusion constant, even when routine magnetic resonance scan was normal. The authors suggest that measuring the average diffusion constant for the whole brain may be a useful index for monitoring the neurological well being of boxers.

Neuroradiology provides limited information in respect of chronic brain damage caused by boxing. The studies to date do not demonstrate any radiological abnormality attributable solely to amateur boxing. Neuroradiological evaluation of professional boxers is restricted due to the small sample size, selection bias, lack of controls and the cross sectional nature of many of the studies. The cohort examined by Jordan *et al* (1992) is the largest series, in which 7% of scans were found to be abnormal. The radiological findings did not; however, correlate with any measure of exposure to head trauma and the study itself was a cross sectional “*snapshot*” of brain imaging.

The true value of radiological imaging in evaluating chronic brain damage in boxing will only be provided by longitudinal studies where exposure variables are carefully documented and compared with any radiological deficit that is found to evolve on serial scanning over a period of time.

**Table 6 Evidence table: Neuroradiology**

Author	Title	Year	Study Type	Amateur (A) Professional (P)	SIGN Grade
Kemp et al.	Cerebral perfusion and neuropsychometric testing in military amateur boxers and controls	1984	Case control	A	2 ++
Haglund, Y., Eriksson, E.	Does amateur boxing lead to chronic brain damage ? A review of some recent investigations	1993	Case control	A	2 ++
Jordan et al.	CT of 338 active Professional Boxers	1992	Cohort	P	2 ++
Stilller, J.W., Weinberger, D.R.	Boxing and Chronic Brain Damage	1985	Systematic Review	A + P	2 ++
Zhang et al.	Increased Diffusion in the Brain of Professional Boxers: A Preclinical sign of Traumatic Brain Injury	2003	Cohort	P	2+
Davie et al.	Magnetic resonance spectroscopic study of Parkinsonism related to boxing	1995	Cohort	P	2+

**Table 6 Evidence table: Neuroradiology (cont'd)**

Author	Title	Year	Study Type	Amateur (A) Professional (P)	SIGN Grade
Haglund, Y., Bergstrand, G.	Does Swedish amateur boxing lead to chronic brain damage? 2. A retrospective study with CT and MRI	1990	Cohort	A	2+
Levin et al.	Neurobehavioural functioning and magnetic resonance findings in young boxers	1987	Case control	A + P	2 +
Jordan, B., Zimmerman, R.	Magnetic Resonance Imaging in Amateur Boxers	1988	Cohort	A	2 -
Ross et al.	Boxing injuries: Neurologic, Radiologic, and Neuropsychologic outcomes	1987	Cohort	A + P	2 -
Casson et al.	Brain Damage in Modern Boxers	1984	Cohort	A + P	2 -
Ross et al.	Boxers - Computed tomography, EEG and Neurologic Evaluation	1983	Cohort	A + P	2 -
Kaste et al.	Is Chronic Brain Damage in Boxing a Hazard of the Past?	1982	Cohort	A + P	2 -
Ross et al.	Acute Intracranial Boxing-Related Injuries in U.S. Marine Corps recruits : Report of Two Cases	1999	Case report	A	3
Chaudhuri et al.	Magnetic resonance spectroscopic study of Parkinsonism related to boxing	1995	Case series	P	3
Houston et al.	Use of Significance Image to Determine Patterns of Cortical Blood Flow Abnormality in pathological and at-Risk groups	1998	case series	A	3
Kemp et al.	Cerebral perfusion in amateur boxers. Is there evidence of brain damage ?	1991	Case series	A	3
Jordan, B., Zimmerman, R.	Computed Tomography and Magnetic Resonance Imaging Comparisons in Boxers	1990	Case series	A + P	3
Bogdanoff, B., Natter, H.	Incidence of cavum septum pellucidum in adults: A sign of boxer's encephalopathy	1989	Case series	A + P	3
MacPherson, P., Teasdale, E.	CT demonstration of a 5th ventricle - a finding to KO boxers ?	1988	Case series	P	3
Sabharwal et al.	Chronic Traumatic Encephalopathy in Boxers	1987	Case series	A	3
McLatchie et al.	Clinical neurological examination, neuropsychology, electroencephalograph and computed tomographic head scanning in active amateur boxers	1987	Cohort	A	3
Rodriguez et al.	Regional Cerebral Blood flow in Boxers	1983	Case series	A + P	3
Casson et al.	Neurological and CT evaluation of Knocked-out Boxers	1982	Case series	P	3
Cruikshank et al.	Two cases of acute intracranial haemorrhage in young amateur boxers	1980	Case report	A	3
Harvey, P.K., Newsom Davis, J.	Traumatic Encephalopathy in a Young Boxer	1974	Case report	P	3
Johnson, J.	Organic Psychosyndromes due to Boxing	1969	Case series	P	3
Mawdsley, C., Ferguson, F.	Neurological Diseases in Boxers	1963	Case series	P	3
Spillane, J.	Five Boxers	1962	Case series	P	3
McCrorry, P.	Cavum septi pellucidi - A reason to ban boxers?	2002	Expert Opinion	P	4
Moseley, I.F.	The neuroimaging evidence for chronic brain damage due to boxing	1999	Expert opinion	A + P	4

**Table 6 Evidence table: Neuroradiology (cont'd)**

<b>Author</b>	<b>Title</b>	<b>Year</b>	<b>Study Type</b>	<b>Amateur (A) Professional (P)</b>	<b>SIGN Grade</b>
Bodensteiner, J., Schaefer, G.	Dementia Pugilistica and Cavum Septi Pellucidi : Born to Box ?	1997	Expert Opinion	A + P	4
Unterharnscheidt, F.	A neurologists reflection on boxing. II. Acute and chronic clinical findings secondary to central nervous system damage	1995	Expert opinion	A + P	4
Marwick, C.	Protecting Boxers Who Won't Quit	1993	Expert Opinion	P	4
Guterman, A., Smith, R.	Neurological Sequelae of Boxing	1987	Expert Opinion	A + P	4
Ryan, A.	Intracranial injuries Resulting from Boxing A review ( 1918-1985 )	1987	Expert Opinion	A + P	4
Charnas, L., Pyeritz, E.	Neurologic Injuries in Boxers	1986	Expert Opinion	A + P	4
Morrison, R.G.	Medical and Public health Aspects of Boxing	1986	Expert Opinion	A + P	4
Han et al.	Head Trauma Evaluated by Magnetic Resonance and Computed Tomography	1984	Diagnostic Study	N/A	4
Gandy et al.	Cranial Nuclear Magnetic Resonance Imaging in Head Trauma	1984	Expert Opinion	A + P	4
British Medical Association	Boxing. Report of the Board of Science and Education Working Party	1984	Expert Opinion	A + P	4
Millar, A.	Boxing - time for fresh action	1984	Expert Opinion	P	4
Sironi, V., Ravagnati, L.	Brain Damage in Boxers	1983	Expert Opinion	P	4
Moore, M.	The Challenge of Boxing. Bringing Safety into the Ring	1980	Expert Opinion	P	4
La Cava, G.	Boxer's Encephalopathy	1963	Expert Opinion	P	4

## **CHAPTER IV**

### **NEUROLOGICAL / PHYSICAL EXAMINATION**

Appreciation of chronic brain damage caused by boxing requires that any recognised pattern of neurological deficit be linked to specific exposure to the presumed causative agent, head trauma.

The original observation by Martland (1928) is one of the earliest within the medical literature to use the term *“punch drunk”*, and it has been quoted widely since. The report is mainly an account of observations made by a third party who was not medically trained. The author states,

*“... we are placed in the position of accepting a series of objective symptoms described to us by laymen... A fight promoter whose ability to judge the physical condition of fighters is unquestionable has given me the names of twenty-three fighters whom he considers punch drunk ...”*

Demographic limitations allowed only five to be examined by the author who presented clinical findings in *“one case of advance Parkinsonian syndrome due to punch drunk”*. Although methodologically flawed, and anecdotal in the reporting of all but one of twenty three cases, the work of Martland is important, as it draws to the attention of the scientific community, the possible existence of neurological dysfunction in boxers. This would have allowed consideration of prospective monitoring of such individuals to establish a causal link between the putative agent, head trauma, and the clinical picture of neurological dysfunction. The need for such a prospective controlled study still exists to date.

Carrol (1936) based his anecdotal observational study on a two-year period during which he attempted to *“study the ‘punch-drunk’ in its natural habitat, the boxing world”*. His study involved mixing with, observing and examining boxers along with talking to managers and trainers. This allowed the development of a *“typical case”*. Carrol described the composite punch drunk as *“A slugger with distinct facial features...”* who displayed deterioration in attention, concentration and memory with mental and personality changes.

The case report by McAlpine and Page (1949) links a specific neurological presentation of mid brain syndrome, with a past history of boxing, though they state,

*“He had never received severe punishment until January 1948, when he was twice knocked out. Amnesia on each occasion did not exceed a few seconds”.*

The clinical features were dysarthria, tremor, and a mildly spastic gait with preserved intellect.

Critchley (1957) states:

*“My own neurological experience has comprised a series of 69 cases of chronic neurological diseases in boxers. Many of these – perhaps the great majority – should be looked upon as examples of punch drunkenness.”*

Description of 11 cases allowed illustration of observations pertaining to,

*“Characteristics of traumatic progressive encephalopathy in boxers.”*

The list was bereft of any accompanying scientific explanation, and included cases that displayed isolated convulsion, delinquency, gross delinquency and hysterical blindness. The signs and symptoms were cited as illustrative of the syndrome. These cases serve to illustrate the presence of clinical features that were thought by the author to be related to boxing. The lack of scientific objectivity and poor methodology relegate the value of this study to anecdotal observation.

Sercl and Jaros (1962) presented a case series comprising 1,582 boxers observed over a four year period encompassing 1,265 boxing matches. Although not clearly stated by inference the group appears to comprise only amateurs. Aged matched controls that had never boxed were used for comparison. The clinical examination was divided into three categories, extrapyramidal, vestibulocerebellar, and “other” which included *“intellectual changes, changes of character and changes of behaviour”* as sub categories. There is no description of the methodology used to determine the various degrees of abnormality measured merely a table enumerating findings in each group. Statistical evaluation using the chi-squared test allowed the authors to demonstrate that,

*“Pathologic clinical findings prevail in the boxers statistically significantly, as compared with the control group, with  $p < 0.001$ ”*

Examination of the results for each subset shows  $p < 0.001$  for extrapyramidal signs, and  $p < 0.025$  for “*other signs*”.

The authors concluded that 9% of their study group displayed signs suggestive of chronic boxers encephalopathy. There is no description of any selection process to exclude bias, confounding variables are not discussed, and more importantly there is no means whereby the reader is able to link abnormal neurology to exposure to trauma. The results for the study group merely list abnormal neurology with no methodological description as to how this was determined. This lack of objectivity and failure to show any causal link between exposure to head trauma and neurological dysfunction diminishes the validity of this study, and as such it stands as an observational narrative describing a group of boxers who have abnormal findings compared to a control group of their peers.

Spillane (1962) described five patients, all of whom were professional boxers who had fought 200-350 bouts. They had been referred to a regional neurological centre as they were found to display neurological signs as follows:

1. Dysarthria, spastic gait, extensor plantar reflexes, hyper-reflexia in the limbs, no evidence of impaired intellect
2. Dysarthria, dysphasia, ataxia, moderate right-sided weakness, right optic atrophy, sluggish pupillary responses on the left, absent pupillary response on the right
3. Confusion, disorientation, ataxia, positive Rombergs test, paroxysmal fine tremor in upper limbs.
4. Normal examination. Prone to violent behaviour.
5. Nystagmus on lateral gaze, dysarthria executive dysphasia, impaired memory and concentration. Known to be alcoholic.

All showed radiological evidence of parenchymal brain damage, with four showing cavum septum pellucidum. The paucity of histopathological data at this time did not allow any

conclusions to be drawn in respect of how brain damage may have resulted in the presenting physical signs, leading the author to conclude,

*“These cases illustrate the difficulties of aetiological diagnosis and emphasise the extent of our ignorance of the subject.”*

This cohort were not randomly selected as their inclusion in this study was due to their being referred for assessment as they displayed abnormal neurology.

La Cava (1963) refers to a personal study of 120 boxers, in whom the incidence of traumatic encephalopathy was found to be 20-25%, but there is no detail of the study. Of note is LaCava's description of diffuse cranial hyperostosis as a physical sign very frequently associated with traumatic encephalopathy. He suggests that thickening of the cranium is secondary to vasomotor disturbances of the diploic circulation consequent upon trauma. This statement stands in isolation without any scientific explanation, and merely represents a personal opinion.

The work by Roberts (1969) was the first study of chronic brain damage in a randomised cohort of boxers. The 224 subjects were chosen from a defined source population that comprised 16,781 professional boxers registered with the British Boxing Board of Control from 1929 to 1955. During this time the governing body of British Professional Boxing required that all professional boxers be registered and licenced on an annual basis thus the source population by definition contained all professional boxers. The author determined that 250 subjects would be a manageable number and represented 1.5% of the total source population. For each year of the study a number of boxers were chosen at random. These were then screened such that only those still resident in the United Kingdom, and who had held a professional licence for more than three years, were included in the study. If a boxer was ineligible on these two screening criteria the next randomly selected boxer was screened until such time as a representative sample of 1.5% of all boxers for that particular year had been recruited. Thus for 1938, 1217 boxers were licenced, consequently 18 were recruited, for 1954 only 235 boxers were licenced accordingly only 3 were recruited. Each figure represents a random selection of 1.5% of all eligible for that year. Of the 250

randomly chosen, 224 were included in the study. In this comprehensive publication, Roberts details findings in individual cases.

In summary he found 37 (17%) of the boxers had evidence of neurological dysfunction consistent with a diagnosis of *"Punch Drunk"* syndrome. Of these 24 (11%) had a *"mild condition"* and 13 (6%) were *"moderately or severely affected"*. Roberts was meticulous in his work, excluding a further 11 (5%) of subjects whose neurological dysfunction was adequately explained by a process other than a boxing injury. The neurological findings in the group of 37 boxers were divided by the author into two main motor syndromes, one predominantly cerebellar, the second predominantly extrapyramidal (mainly Parkinsonian). In addition there was often evidence of corticospinal tract dysfunction more often involving the left limbs. Roberts did not consider that isolated signs, such as a sense of disequilibrium, slurring of speech, subjective alcohol intolerance and pyramidal dysfunction, were enough to warrant a diagnosis of traumatic encephalopathy. Nevertheless the frequency of such phenomena was recorded. 187 of the subject group were deemed not to have traumatic encephalopathy. Of this group 23 (12%) reported disequilibrium, 14 (7%) were dysarthric and 24 (13%) reported subjective intolerance of alcohol. Of this subset (187 out of 224 = 83% of cohort), 75 had pyramidal signs, and/or disequilibrium, and/or dysarthria, and/or subjective alcohol intolerance. This was 40 % of a group considered to be normal. (33% of the total study group). There was a statistical trend for these signs and symptoms to occur more frequently among those with the greatest exposure to boxing. Although these subjects did not have a complete clinical picture allowing a formal diagnosis of traumatic encephalopathy, Roberts concluded,

*"There was indication that much minor clinical evidence of disturbed neurological function, demonstrable among those not diagnosed as having the syndrome of traumatic encephalopathy, was also related to their professional careers."*

There was within this study group a significant relationship between signs of traumatic encephalopathy and both length of career and number of bouts fought, this being clearly shown in the older subjects.

Johnson (1969b) examined 17 patients who had clinical features allowing a diagnosis of traumatic encephalopathy. Critchley (1957) had previously described 10 of this cohort in his publication. The neurological manifestations of encephalopathy were listed as pyramidal, extra pyramidal and cerebellar degeneration and epilepsy. These signs were listed in tabulated form with no description of objective methodology that might allow interpretation of how dysfunction was measured. The table recorded either “*positive syndrome*” or “*partial syndrome*”. The specific criteria for inclusion in this study of brain damage was that the subjects should have evidence of such process. The nature of this study does not allow extrapolation of results or conclusions to include all boxers. The study group comprised boxers who had fought 200-300 bouts in the 1920-30 era. The study does not allow for any attempt to be made to correlate head trauma and clinical findings.

Jedlinski *et al* (1970) studied 60 amateur boxers who had fought 100-344 bouts over careers spanning 5-17 years. The control group comprised 30 volunteers who wanted to take up boxing but had not fought. Study parameters encompassed neurological, psychiatric, and encephalographic assessment. 55% of the study groups were found to have abnormal neurology, graded from 0 to III as follows:

- 0 = negative result;
- 1 = functional disturbance;
- 11 = isolated low-grade signs of organic brain damage;
- 111 = more pronounced signs of organic brain damage or full clinical syndromes.

The abnormal group comprised 33 of the 60 examined (55%). Of these 33 the neurological abnormalities were absence or asymmetry of abdominal reflexes (18), dysarthria (7), slight ataxia of the cerebellar type (3), a slight deficiency of the mimic expression (5), evident asymmetry of the deep reflexes, paresis of the oculomotor nerve (1) and focal epilepsy (1). Assessment of the presence or absence of these signs lacks description, and a degree of subjectivity cannot be eliminated from the results. The figure of 55% abnormality in terms of positive neurology must be interpreted in the light of such methodological failings.

The histopathological study of Corsellis *et al* (1973) illustrated each of the pathological specimens with a descriptive narrative derived from anecdotal recollection of close relatives and friends, augmented by formal hospital records. These cases provide a fascinating outline of the behaviour, appearance and neurological deficits, both documented and perceived, in a group of men with proven pathological changes. Many of them displayed the triad of motor, cognitive and psychiatric dysfunction that allowed a diagnosis of traumatic encephalopathy or *punch drunk* syndrome to be made. Although some of the clinical details may be viewed as anecdotal there was no other means of collecting this data, and whilst flawed in some aspects of its methodology, the study is important in highlighting the reported clinical manifestations of this select cohort.

The single case report (Harvey and Davis, 1974) illustrates one boxer from the more recent past, who boxed from 1962-73, taking part in 75 amateur and 25 professional bouts. When examined in 1974 he was found to have bilateral ptosis, symmetrical extrapyramidal dysfunction characterised by a paucity of facial expression, poverty of movement, cogwheel rigidity in all four limbs and a typical extrapyramidal speech and gait. Tendon reflexes were brisk and the plantar response was extensor on the left. Overall the clinical picture was one of traumatic encephalopathy. Of note is the failure to document the exact level of trauma to this patient. Although the number of bouts is recorded, mention is also made of his sparring once a week over a five-year period with professionals, whilst the subject himself was still an amateur. This point was specifically highlighted in subsequent correspondence (Blonstein, 1974). The level of exposure to head trauma in this isolated case may have been significantly higher than for a boxer undertaking a purely amateur career.

Selection bias influences the study of Thomassen *et al* (1979) as the entire study group was former champion boxers, who by inference were more skilled and less likely to have received significant head trauma. Positive neurological signs were mild and isolated, including dysarthria, dysdiadokokinesia, nystagmus, single brisk tendon reflexes and Babinski sign. Such abnormalities were demonstrated in 36% of the boxers and 15% of the control group of football players. These differences did not reach statistical significance. No correlation could be demonstrated between occupational exposure and neurological

deficiency or indeed the two other parameters measured in this study (EEG and Neuropsychometric testing).

Similar selection bias placed limitations upon the work of Kaste *et al* (1982) as the subjects were all champion boxers who had volunteered and as such the cohort is unrepresentative and may again have included subjects less likely to have been exposed to a significant degree of head trauma. In addition this study lacked a control group. Six professional and eight amateur boxers took part. The only abnormal neurological findings were present in the oldest subject, a 53 year old professional, who displayed slight unsteadiness, slowness and apraxia. He had also been treated for mild hypertension and diabetes for two years. Specific details on this individual's exposure in terms of duration of boxing career were not included, precluding any attempts at correlating trauma to positive neurology. No other deficit was demonstrated in any other subject.

Recruiting subjects who had answered a newspaper advertisement immediately placed limitations on the validity of any conclusions drawn by Ross *et al* (1983). Of the 40 boxers enlisted for this study, 24 had a full neurological examination. There is no description of the methodology involved in assessing neurology, merely a list of abnormalities found which included memory loss, ataxia or tandem gait, diminished tendon reflexes and loss of pin prick sensation. The statistical analysis refers to either "*positive*" or "*negative*" neurology, with no further subjective description. The authors were unable to show any correlation between exposure and bouts fought, and in essence they based their conclusions on the extent of cerebral damage in boxers on the CT and EEG arms of their study.

The uncontrolled cross-sectional nature of the work by Casson *et al* (1984) results in some difficulty in terms of drawing relevant and meaningful conclusions. Their study group comprised 13 former professionals, two active professionals, and three active amateurs. The authors state,

*"The subjects of this study group were not selected at random, nor are they representative of all modern boxers".*

This is evident when reviewing the abnormal neurology demonstrated in five of the eighteen subjects. Three had an organic mental syndrome manifest by disorientation, confusion and loss of memory, and in one of these men a right Babinski sign was present. One subject had impairment of recent memory in isolation, and the fifth boxer had horizontal nystagmus and dysarthria. These findings must be viewed in light of the selection criteria sub section (5) that required “*No known history of neurological, psychiatric or serious medical illness*”.

It appears that these criteria may not have been fully applied during the selection process. One subject had in total seven amateur bouts in five years, recording four wins and three losses. He was never knocked out, nor did he complain of amnesia. He displayed an organic mental syndrome, with positive Babinski sign, mild generalized cerebral atrophy on CAT scan, and an abnormality on each of the neuropsychometric tests. These abnormalities appear not to be related to his limited boxing exposure.

Drew employed subtests of the Quick Neurological Screening Test (Benet, 2005b) to examine 19 active professional boxers, and 10 matched controls (Drew *et al.*, 1986). The subtests used consisted of rapidly reversing repetitive hand movements, finger to nose, thumb and finger circle, tandem walk and single foot stand. Failure on any of these screening tasks was deemed abnormal. There was very little overlap between subject and control group, with only one control making as many as two errors, whilst only three boxers had less than two errors (chi square = 11.97,  $p < 0.001$ ). Exposure was defined as the number of professional bouts and number of professional losses plus draws showed a high correlation with boxers test deficits. This study clearly demonstrates neurological dysfunction in a group of professional boxers competing in the modern era.

An element of selection bias is present in the work of McLatchie *et al* (1987). The source population for this controlled study of active amateur boxers comprised a list of active amateur boxers in Scotland. The boxers were extended a written explanation and invitation to attend the study. Other boxers volunteered having heard of the study from a source other than personal written invitation. The authors acknowledge these failings stating,

*“It is not possible to conclude from our data that the abnormalities we have found are the result of boxing.... In addition our study group may be unrepresentative; it comprised only those who accepted the invitation to be examined and possibly they did so because they had complaints and were concerned”.*

The control group was derived from patients with limb fractures attending the orthopaedic outpatients. 35% of the subjects had abnormal neurological examination, including extensor plantar reflex, dysdiadokokinesia, and slow pupillary reaction. Abnormal neurology in this group correlated significantly with increasing number of fights ( $p < 0.05$  Mann-Whitney test). In conclusion the authors comment:

*“The high number of abnormalities on clinical neurological examination is surprising. Signs uncovered by an experienced neurologist are always noteworthy, but caution must be applied to some of the minor neurological signs when they are searched for so intensely. None of the present subjects could be regarded as in any way physically disabled, rather the reverse”.*

Haglund *et al* (1990), addressed some of these deficiencies in their retrospective controlled study of amateur boxers. The study group was randomly selected from a pool of 1700 Swedish amateur boxers, 25 high matched boxers (> 30 bouts) and 25 low matched (<10 bouts) were recruited. The control group comprised 25 track and field athletes, and 25 footballers. There was a degree of selection bias in respect of recruiting the footballers, as they were chosen because they were considered *“typical headers of the football”*. The exact definition is not expounded but the inference is that these footballers were subject head trauma secondary to heading the ball. No significant differences were found between the groups in any of the physical or neurological examination.

Whilst the majority of studies involving physical examination have concentrated on assessment of neurological function, a small number have looked at laboratory assays and blood tests. The calcium binding protein S100 B is an important modulator of astrocytic proliferation and calcium flux following head injury. Levels were demonstrated to rise following both running and amateur boxing (Otto *et al.*, 2000) though the authors only

speculated on possible findings in professional boxing. The importance of S100B was highlighted in a subsequent study wherein it was shown that serum S100B was a sensitive biomarker for early prediction of the development of high intracranial pressure and fatal outcome following acute brain injury (Petzold *et al.*, 2002). The authors suggest monitoring of levels may allow early detection of patients at increased risk.

Preliminary findings in a single study showed a raised blood level of the isoenzyme creatine kinase BB (CK-BB) in a group of amateur boxers compared to a control group of cyclists (Brayne *et al.*, 1982). CK-BB is found in high concentration in the brain, and the inference from this study is that raised blood levels of this isoenzyme indicate disruption of the blood brain barrier.

The possibility of a blood test to screen for a genetic predisposition to chronic traumatic brain injury is raised by the work of Jordan (1997). Previous studies have identified apolipoprotein E (APOE) status as being determined by a susceptibility gene, expression of which leads to increased incidence of late onset familial and sporadic Alzheimer's disease. This polymorphic gene, which encodes a cholesterol carrier lipoprotein produced in the liver and brain (APOE), occurs in 3 common allelic forms, APOE  $\epsilon$ 2,  $\epsilon$ 3, and  $\epsilon$ 4. Six genotype combinations are therefore possible. Possession of the APOE  $\epsilon$ 4 increases the risk of Alzheimer's disease in a dose dependent fashion (Saunders *et al.*, 1994), whilst APOE  $\epsilon$ 2 is under represented in the Alzheimer's population (Chartier-Harlin *et al.*, 1994). Jordan examined 30 boxers who had volunteered, or been referred, raising the possibility of selection bias. The study suggests that possession of an APOE  $\epsilon$ 4 allele may be associated with increased severity of chronic neurological deficits in high exposure boxers as measured by number of bouts.

A number of studies contribute to our understanding of the physical and neurological signs associated with chronic brain damage in boxing. Whilst Martlands publication is mainly anecdotal it was of paramount importance in raising the awareness of a syndrome of chronic brain damage demonstrated by some professional boxers. Roberts found that 17% of a randomly selected cohort showed signs of neurological dysfunction manifest by cerebellar and extrapyramidal abnormalities. Overall 6% of the study group had clear neurological

signs in keeping with a diagnosis of traumatic encephalopathy. There was a significant relationship between encephalopathy and both length of career and number of bouts fought. This was demonstrated throughout all age groups, but was more prominent in the older ex-boxers.

Drew concurred with these findings in his study that showed neurological dysfunction in a group of professional boxers, being related to exposure in terms of number of losses and draws rather than total bouts fought. By definition a boxer who loses will have sustained more direct punches than the victor, and the accumulation of these blows over a career is reflected in this study.

A number of cohort and case control studies have failed to clearly demonstrate neurological dysfunction solely attributable to exposure to head trauma in amateur boxing.

**Table 7 Evidence table: Neurological/Physical examination**

Author	Title	Year	Study Type	Amateur (A) Professional (P)	SIGN Grade
McCrary <i>et al.</i>	A 16 year study of injuries to professional boxers in the state of Victoria, Australia	2003	Cohort	P	2 ++
Petzold <i>et al.</i>	Role of serum S100B as an early predictor of high intracranial pressure and mortality in brain injury: A pilot study	2002	Cohort	N/A	2 ++
Otto <i>et al.</i>	Boxing and Running Lead to a Rise in Serum Levels of S-100B Protein	2000	Case Control	A	2 ++
Haglund, Y., Eriksson, E.	Does amateur boxing lead to chronic brain damage	1993	Case control	A	2 ++
Haglund <i>et al.</i>	Does Swedish amateur boxing lead to chronic brain damage ? 1. A retrospective medical, neurological and personality trait study	1990	Case control	A	2 ++
Stiller, J., Weinberger, D.	Boxing and Chronic Brain Damage	1985	Systematic Review	A + P	2 ++
Brayne <i>et al.</i>	Blood Creatine Kinase Isoenzyme BB in Boxers	1982	Case Control	A	2 ++
Thomassen <i>et al.</i>	Neurological, electroencephalographic and neuropsychological examination of 53 former amateur boxers	1979	Case control	A	2 ++
Jordan <i>et al.</i>	Apolipoprotein E ε4 Associated with Chronic Traumatic Brain Injury in Boxing	1997	Cohort	P	2 +
Porter, M., O'Brien, M.	Incidence and Severity of Injury Resulting from Amateur Boxing in Ireland	1996	Cohort	A	2 +
Roberts. A.H.	Brain Damage in Boxers	1969	Cohort	P	2 +

**Table 7 Evidence table: Neurological/Physical examination (cont'd)**

Author	Title	Year	Study Type	Amateur (A) Professional (P)	SIGN Grade
Ross <i>et al.</i>	Boxing Injuries: Neurologic, Radiologic and Neuropsychologic Evaluation	1987	Cohort	A + P	2 -
Casson <i>et al.</i>	Brain Damage in Modern Boxers	1984	Cohort	A + P	2 -
Ross <i>et al.</i>	Boxers - Computed Tomography, EEG, and Neurologic Evaluation	1983	Cohort	A + P	2 -
Kaste <i>et al.</i>	Is Chronic Brain Damage in Boxing a Hazard of the Past	1982	Cohort	A + P	2 -
Jedlinski <i>et al.</i>	Punch Drunkenness	1970	Cohort	A	2 -
Jedlinski <i>et al.</i>	Chronic Post Traumatic Changes in the Central Nervous System in Pugilists	1969	Cohort	A	2 -
Sercl, M., Jaros, O.	The Mechanisms of Cerebral Concussion in Boxing and their Consequences	1962	Cohort	A	2 -
Smith <i>et al.</i>	Development of a boxing dynamometer and its punch force discrimination efficacy	2000	Diagnostic	A	3
Scully, R.E.	Presentation of Case: Case Records of the Massachusetts General Hospital	1999	Case report	P	3
Friedman, J.H.	Progressive Parkinsonism in Boxers	1989	Case report	P	3
McLatchie <i>et al.</i>	Clinical neurological examination, neuropsychology, electroencephalography and computed tomographic head scanning in active amateur boxers	1987	Cohort	A	3
Sabharwal <i>et al.</i>	Chronic Traumatic Encephalopathy in Boxers	1987	Case Series	A	3
Atha <i>et al.</i>	The Damaging Punch	1985	Diagnostic	P	3
Sironi, V., Ravagnati, L	Brain damage in Boxers	1983	Case series	P	3
Casson <i>et al.</i>	Neurological and CT evaluation of knocked-out boxers	1982	Case series	P	3
Lindsay <i>et al.</i>	Serious head injury in sport	1980	Case series	N/A	3
Harvey, P., Newsom Davis J.	Traumatic Encephalopathy in a Young Boxer	1974	Case report	P	3
Johnson, J.	Organic Psychosyndromes due to Boxing	1969	Case series	P	3
Govons, R.	Brain Concussion and Posture the Knockdown Blow of the Boxing Ring	1968	Case series	A	3
Mawdsley, C., Ferguson, F.R.	Neurological Disease in Boxers	1963	Case series	P	3
Spillane, J.D.	Five Boxers	1962	Case series	P	3
Martland, H.S.	Punch Drunk	1928	Case Report	P	3
Jordan, B.D.	Chronic Traumatic Brain Injury Associated with Boxing	2000	Expert Opinion Review	P	4
Unterharnscheidt, F.	A neurologists reflection on boxing. I. Impact mechanics in boxing and injuries other than central nervous system damage	1995	Expert opinion	A + P	4
Jordan, B.D.	Neurological Aspects of Boxing	1987	Expert opinion	A + P	4
Guterman, A., Smith, R.W.	Neurological Sequelae of Boxing	1987	Expert opinion	A + P	4
Charnas, L., Pyeritz, R.E.	Neurologic Injuries in Boxing	1986	Expert opinion	A + P	4
Morrison, R.G.	Medical and Public Health Aspects of Boxing	1986	Expert opinion	A + P	4
British Medical Association	Boxing. Report of the Board of Science and Education Working Party	1984	Expert opinion	A + P	4
Millar, A.P.	Boxing - Time for fresh action	1984	Expert opinion	P	4
Whiteson, A.L.	Injuries in professional boxing. Their treatment and prevention	1981	Expert opinion	P	4
Unterharnscheidt, F.	Injuries due to boxing and other sports	1975	Expert opinion	P	4

**Table 7 Evidence table: Neurological/Physical examination (cont'd)**

<b>Author</b>	<b>Title</b>	<b>Year</b>	<b>Study Type</b>	<b>Amateur (A) Professional (P)</b>	<b>SIGN Grade</b>
Unterharnscheidt, F.	Head Injury After Boxing	1972	Expert opinion	P	4
Blonstein, J.L.	Boxing Injuries	1969	Expert opinion	A	4
La Cava, G.	Boxer's Encephalopathy	1963	Expert opinion	P	4
Critchley, M.	Medical aspects of Boxing, particularly from a Neurological Standpoint	1957	Expert opinion	P	4
Carroll, E.J.	Punch Drunk	1936	Expert opinion	P	4

## **CHAPTER V**

### **NEUROPSYCHOMETRIC EVALUATION**

Clinical neuropsychology is an applied science concerned with the behavioural expression of brain dysfunction (Lezak, 2004a). In its simplest form it attempts to determine what makes people do what they do, and how. The early part of the 20th century provided a major stimulus to the development of clinical neuropsychology, precipitated by the urgent need for screening and diagnosis of brain injured and behaviorally disturbed servicemen during the First World War. Some of this early work attempted to link brain structure to function. Lesions usually affect contiguous areas of the brain and as such cognitive neuropsychology has generally hypothesized modularity of brain function, assuming that specific regions of the brain have specific dedicated functions (Lloyd, 2000).

With particular reference to boxing, the role and indeed challenge of neuropsychometric assessment is twofold. Firstly it may be used to establish a link between the clinical manifestations of boxer's brain damage and discrete structural regions that have been demonstrated deficient by other investigation such as histopathology, radiology, neurology, and electrophysiology. This essentially provides a connection between damage already done to a given structure and behavioural manifestations of that damage illustrated by abnormal function. The site and extent of injury may be shown on imaging, but the image alone will not identify the nature of any residual behavioural strengths and accompanying deficits. This requires neuropsychological assessment (Lezak, 2004a).

Secondly, and more importantly, neuropsychological testing may provide a dynamic assessment of brain executive activity, such that higher mental function may be monitored prospectively to determine any deterioration that may then be linked with exposure to head trauma. This may allow active observation of neuropsychological parameters during rather than after exposure, helping to determine the evolution of the clinical manifestations of brain damage attributed to boxing.

The earliest publications (Martland, 1928) (Carroll, 1936) allude to the presence of neuropsychiatric dysfunction in boxers. In the cohort they have studied, the detailed assessment of individuals is lacking, and the information is anecdotal narrative. Notwithstanding, they represent the earliest description of higher mental dysfunction in a

group of boxers, of such magnitude, the clinical features became apparent to non-medical observers.

Johnson (1969b) published the first formal description of neuropsychometric testing in boxers. The cohort consisted of 17 boxers referred for assessment as they were displaying symptoms thought to be related to their boxing career. Sixteen were ex-professional boxers with exposure amounting to 200-300 bouts and a mean age of 54. Deficiency in at least one neuropsychological test was demonstrated in 11 of the 16 examined in this way, but no clear criteria are provided regarding what constituted abnormality. Johnson used two main test batteries, the Wechsler adult intelligence scale and the Benton visual retention test.

The first is a comprehensive test of cognitive ability in adults (Benet, 2005e). It comprises a number of verbal and performance sub tests, including verbal comprehension, thought to be a temporal lobe function. The remaining components reflect overall intelligence. The Benton visual retention test assesses visual perception and memory, thought to be a function of the right medial temporal lobe (Benet, 2005d).

In his discussion, Johnson states that the clinical features of traumatic encephalopathy suggest damage in two main areas, the upper brainstem and Hippocampal–fornical region. Comparison is made with a single case report (Kramer, 1947) of traumatic mid brain syndrome, where the lesion was suggested to be at the level of the superior cerebellar peduncles. The similarity of this patients clinical presentation, to that seen in established boxers encephalopathy led Johnson to conclude that the common link was localised neuronal damage in the upper brainstem. The neuropsychometric tests used by Johnson were sensitive enough to detect dysfunction, but not specific enough to allow definitive statements about the anatomical site. There is thus some discrepancy between the clinical findings on neuropsychometric testing and the discussion of the presumed pathology.

The paper also included results of air encephalography, which showed perforation and rupture of the septum pellucidum in 10 cases, invariably associated with ventricular dilatation. Johnson demonstrates both neuropsychometric dysfunction and structural change. The fornix, being the inferior margin of the septum pellucidum, would appear to

provide some link as the fornico-hippocampal system is involved in recent memory, but the tests used are not specific enough to allow statements expressly linking anatomical abnormality and neuropsychometric dysfunction.

Roberts's study (1969) remains the only truly randomly selected study of chronic brain damage in ex professional boxers. Whilst selection criteria for subjects are excellent, the choice of neuropsychometric test is deficient by the author's own admission. Roberts states,

*"The major criteria in the choice of test of intellectual function were, therefore, that they should be brief and those least likely to irritate an ex-boxer who feared the implication that he was punch drunk"*

Any conclusions are thus limited, and it may be that the true extent of neuropsychometric dysfunction is underestimated due to the tests employed and the reasons for their utilization. Roberts administered the Ravens progressive matrices (Benet, 2005c), a test of non verbal intelligence that is sensitive to brain damage, and the Mill Hill vocabulary test which records a persons present recall of acquired information, and as such it is closely linked to the subjects acquired intellectual skills at that point in time. (Raven, 1997). One hundred and seventy-eight of the cohort were examined in this way.

Performance on the Ravens progressive matrices revealed a distribution equivalent to that expected in a random sample of the general population. The study group performed well below accepted normal values in the Mill Hill vocabulary test. Normative data was used for comparison, in the absence of a defined control group. The author suggested that the poor verbal function reflected primarily educational background. No consistent trend was found when psychometric data was compared to age and length of boxing career; however, there was some suggestion that low scores (25th percentile and below) were more frequently found in boxers with careers of greater than 10 years. It was suggested that there were a number of possibilities, including the postulate that constitutionally less intelligent individuals would box longer.

This study also included testing of memory by examining rote learning of a digit span and immediate and delayed recall of a pair of geometric designs. Length of boxing career was not related to impairment of memory as measured by these tests. Although objective evidence of reduced memory was absent, subjective complaints of poor memory tended to be more frequent in those boxers with longer careers.

Thomassen *et al* (1979) assessed neuropsychological function in 53 former amateur boxers, using the vocabulary subtest of the Wechsler adult intelligence scale, in addition to a psychological evaluation according to the methods of Luria, which allows assessment of both neurosensory and cognitive function (Lezak, 2004b). The control group which comprised football players, performed significantly better on the vocabulary test ( $p < 0.01$ ). However, it is noteworthy that both subjects and controls performed equal to or above the level of normal intelligence for the general population from which both groups were derived. Ten other subtests were administered in this study. Following statistical correction for differences in education, age, and vocabulary, only one test remained significantly different between the two groups. Motor dysfunction in the left hand. The overall conclusion was that no relationship could be demonstrated between abnormal findings in this study, and occupational exposure during the subjects boxing career.

Kaste (1982) used elements of the Wechsler Adult Intelligence Scale (Information, similarities, digit span, block design and object assembly), the Wechsler memory scale, the Wisconsin card-sorting test, the trail making test, the Benton visual retention test, and the Purdue pegboard test.

The Wisconsin card-sorting test was at this time thought to be a sensitive indicator of damage to the prefrontal cortex and this has been borne out in recent studies where this specific test has been utilised to assess dysfunction in the prefrontal cortex and basal ganglia by means of functional magnetic resonance imaging (Monchi, 2001).

Trail making test A requires the subject to connect in order the numbers 1-25 that are scattered randomly on a sheet of paper.

Trail making test B requires the subject to connect both numbers and letters in an alternating pattern (1-A-2-B-3-C-4 etc). It is generally believed that patients with right frontal lobe dysfunction perform poorly in A, and left frontal lobe lesions perform poorly in B (Alsworth, 1997).

The Purdue pegboard test is thought to be sensitive in predicting both the presence and laterality of cerebral lesions (Costa, 1963).

This study therefore employed a variety of neuropsychometric tests that were sensitive in their ability to screen for dysfunction, as well as in some cases being specific to given areas of the brain.

The mean intelligence quotient (IQ) of the boxers was higher than the Finnish average. Only two boxers showed marked deviation from normal standards. Of these two, one had abnormal neurological findings and the other displayed episodes of inappropriate and disinhibited behaviour. Full details of exposure history were absent from this study, compromising any conclusions that could be drawn.

Casson *et al* examined 18 former and still active amateur and professional boxers. Their study group comprised 13 former professionals, two active professionals, and three active amateurs. The authors state,

*“The subjects of this study group were not selected at random, nor are they representative of all modern boxers”.*

This is evident when reviewing the abnormal neurology demonstrated in five of the eighteen subjects. Three had an organic mental syndrome manifest by disorientation, confusion and loss of memory, and in one of these men a right Babinski sign was present. One subject had impairment of recent memory in isolation, and the fifth boxer had horizontal nystagmus and dysarthria. These findings must be viewed in light of the selection criteria stated by the author, sub section (5) that required *“no known history of neurological, psychiatric or serious medical illness”.*

One subject had in total seven amateur bouts in five years, recording four wins and three losses. He was never knocked out, nor did he complain of amnesia. He displayed an organic mental syndrome, with positive Babinski sign, mild generalized cerebral atrophy on CAT scan and an abnormality on each of the neuropsychometric tests. It cannot be stated with certainty that these abnormalities are related to boxing exposure.

A battery of neuropsychological tests was used, including the trail-making test, digit symbol test, Wechsler memory test (including both verbal and visual memory) and the Bender gestalt test. A full description of all the tests used appears absent.

The digit symbol test is a sub-test of Wechsler, which is sensitive to brain damage (Lezak, 2004c). The score is likely to be depressed even when damage is minimal; however, the results tend to be independent of the locus of the lesion, and as such it is of little use in predicting site or laterality of any traumatic deficit. The Bender visual motor gestalt test (Bender Gestalt) is the most frequently administered and thoroughly researched of all the drawing/copying tests (Fischer, 2004). Difficulties with this test are likely to appear with parietal lobe lesions (Black and Bernard, 1984).

This cross sectional study by Casson lacked a control group, comparing the subjects' results with established norms. All of the boxers had an abnormality on at least one of the neuropsychological tests. The author derived an impairment index for each boxer, consisting of the percentage of abnormal neuropsychological test scores. This impairment index correlated significantly with exposure as measured by the number of professional fights, suggesting a degree of accuracy and sensitivity of neuropsychological testing in detecting brain damage in this select group of boxers.

Drew *et al* (1986) examined 19 young active professional boxers, employing the Randt Memory test and the Halstead-Reitan Neuropsychological Test Battery. The Randt memory test allows for longitudinal assessment of mild and or moderate memory deficits (Fioravanti, 1985), measuring both acquisition of new material and delayed recall at a later time, thereby

allowing for determination of an overall memory index. Its use in a cross sectional study is open to question.

Halstead Reitan was developed to predict the presence of brain damage whilst offering a comprehensive view of a patients individual function (Benet, 2005a). In Drew's *et al* study the 19 subjects were drawn from an appropriate target population. The control group was basketball and baseball players matched for age, schooling and socioeconomic demographics. The active professional boxers were found to display a pattern of neuropsychological deficit consistent with the more severe punch-drunk syndrome as described in years past. 15 of the 19 boxers were in the impaired range on the Reitan Impairment index, compared to two out of ten in the control group. All subjects had boxed as amateurs, prior to embarking on a professional career. Statistical analysis comparing tests scores with amateur bouts, and amateur losses plus draws showed no correlation. There was a high correlation between professional bouts and professional losses plus draws with boxers test deficits. The total number of professional bouts alone appeared less indicative of actual exposure; the results suggesting the total number of losses plus draws was a better index of the injury received. This study adds weight to the argument that professional boxing causes brain damage, regardless of any modern rules or medical regulations.

The question of how much damage occurs as a result of exposure to amateur boxing alone was in part answered by the study of Brooks *et al* (1987). The study group comprised 29 amateur boxers, with 19 controls matched for age ethnicity and education. Eleven of these were prospective amateur boxers in training, who had neither fought nor sparred. Tests were selected on the premise that brain damage if present would be similar to that found in minor closed head injury. Therefore verbal memory, visuospatial memory and attention were assessed using subtests of the Wechsler scale, visual span, and the Rey-Osterrieth complex figure test. Information processing and motor function were gauged by means of the Paced Auditory Serial Addition Task (PASAT), and simple four choice reaction time. Intellectual abilities were examined using the Mill Hill Vocabulary Scale, and Ravens Progressive Matrices.

The Rey-Osterrieth Complex Figure Test requires the patient to copy a complex figure, thereby assessing perceptual organization and visual memory. Interpretation of the results may yield information on site and laterality of deficits with specific errors demonstrated by patients with frontal lobe lesions, distinct from those seen in parieto-occipital damage (Fischer, 2004).

PASAT was initially developed to monitor the recovery of patients who had sustained mild head injury (Gronwall, 1977). The patient is required to listen to a series of numbers, adding together the two most recent numbers in sequence. It is sensitive to cerebral dysfunction; in particular post concussion patients perform well below control levels, returning to normal after 60-90 days. More severe head injury results in significantly impaired performance, which does not improve. Patients with diffuse damage are more likely to perform poorly (Roman *et al.*, 1991), which may be explained by recent work which has mapped the areas of brain activated. During PASAT (Lockwood, 2004). positron emission tomography demonstrated activation of dispersed non-contiguous foci in the superior temporal gyri, bifrontal and biparietal sites, the anterior cingulate and bilateral cerebellar sites. The extent of sites activated accounts for the sensitivity of this test.

Brooks (1987) investigation of amateur boxers failed to demonstrate any evidence of significantly impaired performance for the study group. Within this boxing group different parameters, such as number of knockouts and length of career, were examined to determine their predictive potential in terms of cognitive performance. No feature was found to be a significant predictor of cognitive performance.

Levin *et al* (1987) conducted a prospective study to assess the neurobehavioral status of 13 young boxers, both amateur and professional. The study group was drawn from a source population comprising three local boxing clubs, resulting in the recruitment of eleven professionals and three amateurs. The control group consisted of matched athletes with similar medical and social histories, who volunteered following a media enrolment campaign. Five neuropsychological and intellectual domains were examined in all participants at the outset of this study, attention/information processing speed, memory, divergent thinking,

visuomotor speed, and reading of single words. Thereafter ten subjects in each group were assessed at six months.

Attention/Information processing speed was gauged by means of a revised PASAT, continuous performance test, and reaction time. The continuous performance test usually employs a recorded series of spoken letters, the subject being asked to indicate each time a given letter appears. Responses are scored for both omission and commission. The sensitivity of this test has been demonstrated in studies which have shown that 13 months after mild traumatic brain injury, patients made significantly more errors than controls (Cicerone, 1997).

Reaction time was evaluated using a computer response programme, research having demonstrated that even relatively mild head injury results in slowing of reaction time (MacFlynn, 1984).

Memory was appraised using the modified selective reminding procedure, thought sensitive to the initial impairment and recovery of long-term memory following mild head injury (Levin *et al.*, 1987b)

Short-term visual memory utilized the Benton visual retention test, and sub tests of the Wechsler Adult Intelligence Scale.

Divergent reasoning made use of the controlled word-association test, in which the subject must recall as many words as possible beginning with a given letter in one minute. Frontal lesions regardless of side tend to depress fluency scores, with left frontal lesions resulting in lower word production than right frontal lesions (Miceli *et al.*, 1981).

Visuomotor co-ordination, scanning and speed utilized the digit symbol test, Trail-making test, and Purdue pegboard test.

Statistical analysis in the study by Levin *et al* employed a 'between groups' design rather than a matched-pairs analysis, to mitigate against the significant disparity in reading ability between boxer and control found in this study. Baseline results disclosed more proficient verbal learning in the control group, though delayed recall and other measurements of memory did not differ. Reaction time was faster in the boxers.

Follow up at six months demonstrated improvement in the neuropsychological scores for both groups, as compared to baseline. In addition this six-month follow up showed neither

differences in scores between boxers and controls, nor in the magnitude of improvement from baseline for each group.

The authors advise caution in drawing any inferences from this study, pending replication and follow up study over a longer interval, recognising that such longitudinal investigation might disclose signs of delayed neurological disorder. This study is limited insofar as the exposure to head trauma during the six month study period is only between two and seven bouts, and exact level of exposure in sparring whilst mentioned remains indeterminate. Overall the guarded conclusion is that young boxers may escape disabling brain injury provided their exposure in the ring is limited in both frequency and duration. This statement can only be validated by a longer controlled prospective study.

McLatchie *et al* (1987) sought evidence of neurological dysfunction in a group of active amateur boxers. The boxers within the study group ranged in age from 18-49 years, with boxing exposure between 4-200 fights. Each of the group was subject to neurological, neuropsychological, electroencephalographic and neuroradiological assessment. The methodology describing the neuropsychometric tests state that three different control groups were used for comparison. Orthopaedic outpatients with limb fractures were controls for Inglis, Rey and Wechsler. A group of patients attending a local health centre were used for the computer-administered tests of visual memory. Staff and students of similar mean age were employed as controls for reaction time. Results of PASAT were not compared to controls. Detailed description of the neuropsychometric testing is lacking, with an explanation of any failing being represented in tabulated form. The choice of neuropsychometric test was determined by the presumption that boxing causes the same pattern of damage found in minor head injury, and as such the examination comprised digit span, word learning test of Inglis, Subtests of the Wechsler Memory Scale, the Rey figure test, PASAT and simple/four choice reaction time.

The paired associate word-learning test of Inglis, (1959) utilises recall of just three word pairs, this type of test being sensitive to the effects of lateralized lesions, in addition to eliciting the learning deficits found in Alzheimer's type dementia. Nine of the group

demonstrated abnormal neuropsychometry, but failure in consistency in terms of comparison to a control group compromise any conclusions that may be drawn.

Murelius and Haglund (1991) restrict their study to a retrospective neuropsychological analysis of amateur boxers, compared with a control group derived from matched athletes from football and athletics. The neuropsychometric tests comprised subsections of the Wechsler and Halstead Reitan batteries, examining sensory, cognitive, motor and memory tasks. There appears to be an overlap in the methodology wherein neuropsychometric and neurological function are assessed during the same examination. Detailed statistical analysis was employed to examine differences that may be due to educational background. In one test was there a significant difference between the groups; boxers who had taken part in a large number of bouts had a slightly inferior finger tapping performance. None of the boxers were considered to be intellectually impaired on the basis of test results. No significant correlation was found between number of knockouts, RSCH, or lost fights. It was also noted that a significant correlation existed between length of career in the soccer players and deficiencies in finger tapping bilaterally. The authors concluded that amateur boxing did not seem to lead to any serious signs of chronic brain damage.

Butler *et al* (1983) reviewed a strictly amateur cohort in a prospective study assessing neuropsychological function immediately pre and post bout, with a follow up within two years. Eighty-six amateur boxers were compared with a control group comprising 31 water polo and 47 rugby union players. The selection of tests was based on the findings of Kaste and Casson whose work suggested that short-term memory and speed of performance are the two most vulnerable areas; however, both of these studies possess methodological inconsistencies and as such their use a reference model allows the validity of Butlers work to be questioned, insofar as a broader neuropsychometric analysis may have revealed more abnormalities.

Tests comprised immediate/delayed visual recall, visual scanning, immediate/delayed word recall, speed of information processing, recall of design, PASAT and visual and word recognition. Detailed statistical analysis demonstrated no evidence of neuropsychological dysfunction due to amateur boxing either following a single bout, a series of bouts, or at

follow up within two years. A diverse range of parameters was examined yet failed to determine any correlation between exposure and cognitive function. Measures of exposure comprised number of previous contests, recovery from an earlier bout, number of head blows received during a bout and number of bouts between initial assessment and follow up (Range 46 - 712 days). The conclusion is that participation either in a single bout or a series of contests at amateur level does not cause subsequent neuropsychological damage.

This conclusion is supported by the work of Stewart *et al* (1994) who conducted a four year prospective study of 484 amateur boxers, 391 (81.2%) being followed up at two years. A clear definition of exposure was stated at the outset expressed in terms of the number of amateur bouts, sparring years and sparring with professional boxers. The last two of these parameters have not been addressed in many of the studies to date and it is important that they are quantified and included. The putative cause of brain damage is the repeated receipt of punches to the head therefore it is essential that all punches are included in any study not just punches accumulating during competitive bouts. The study examines change in neuropsychometric test result in relation to specific exposure. The choice of neuropsychological test was determined by analysis of previous publications indicating that the main areas damaged in boxing are the medial temporal and inferior frontal lobes, the cerebral white matter, the brainstem and cerebellum. This pattern of damage suggests that the following neuropsychological functions may be impaired: attention/concentration, reaction time, mental and motor speed, new learning (memory) coordination and balance, planning and sequencing abilities, and judgment. The test battery was designed to assess these functions. Rather than examine one function with a single test, the study looked at functional domains, each of which was examined by a number of different tests. The five cognitive functional domains were: attention/concentration, psychomotor speed, memory, visuoconstruction and mental control.

Statistical analysis involved calculation of individual z scores for each test, which were then combined to provide a single composite z score for each domain. The change score for each domain was derived as the difference between follow up and baseline composite z score. The exposure variables were defined as the number of bouts and sparring years up to the baseline examination and the number of bouts and sparring years during the two-year study period. This allowed for determination of any damage caused before, as well as

during, the study. A statistically significant association was found between change in memory function, perceptual/motor function and visuoconstructional abilities and the number of bouts up to baseline, which was defined as the point of inclusion in the prospective study. The pattern of associations for sparring up to baseline whilst similar to that found for bouts, was not statistically significant. The two-year study period demonstrated no statistically significant correlation between change in any functional domain, and exposure to either bouts or sparring.

The significant trends with past but not more recent bouts may possibly be due to a longer latency period before effects are manifest or a reflection of tighter safety controls in amateur boxing such that the observed associations may only be related to more severe trauma incurred during bouts prior to 1986. Increased numbers of bouts in the past appear to be associated with diminished performance in selected cognitive domains, though none of the changes observed were clinically significant.

Kemp *et al* (1995) confirmed this observation in a case control study of active military amateur boxers. Forty-one boxers were compared to 27 controls who were undergoing medical assistant training. Statistical correction allowed for any intellectual differences that may have been present as a result of education. Psychometric testing assessed reaction time, psychomotor learning, reasoning, perception/comparison, short-term memory and motor function. The boxing group had taken part in between 0 and 250 bouts the median being 40 bouts. As such the group was divided into low exposure (less than 40 bouts) and high exposure (more than 40 bouts).

Psychometric testing showed detrimental findings in the study group of boxers being more marked in those who had taken part in the most bouts. There was no difference in short-term memory between the groups; however, significant differences ( $p < 0.05$ ) were found in the remaining tests. The same two groups underwent perfusion imaging using Tc-99m HMPOA SPECT scanning, which showed significantly greater aberrations in perfusion pattern in the boxing group. The neuropsychometric test scores in the boxers with normal and abnormal perfusion scans were not significantly different. This would follow as the perfusion scan may examine areas of brain not directly activated in the processes required to complete the neuropsychometric battery. In conclusion the authors state,

*“This study has noted subtle impairment of two aspects of neurophysiology in those young men who receive recurrent head trauma from amateur boxing, the question remains... as to whether these findings are reversible or will have an effect on subsequent mental, physical or social well-being.”*

Porter undertook a nine year prospective study to test the hypothesis that there is an association between amateur boxing and chronic traumatic encephalopathy (Porter and Fricker, 1996, Porter, 2003). The study group comprised 20 randomly selected amateur boxers and 20 aged matched, socioeconomic controls. At nine year follow up, 19 of the boxers and 18 controls were still in the study (7.5% dropout). Each participant underwent a series of neuropsychometric tests at baseline, eighteen months, four years, seven years, and nine years. The choice of appropriate neuropsychological test was determined using the same rationale as employed by Stewart *et al* (1994), who matched areas of the brain known to be damaged by closed head injury, to tests of specific neuropsychometric function. Trail making tests A+B, digit symbol, digit span, paired-associate learning, Rey-Osterrieth A+B, finger tapping dominant/non-dominant and serial addition. Over the nine year study period tests were varied such that no subject ever repeated the same version of a given examination. The finger-tapping test used a modified version of indeterminate validity in which the subject used the fourth finger rather than the second, in an attempt to differentiate central from peripheral causes. Exposure data included age at debut, length of career, weight division, number of bouts, wins, losses, knockouts and RSCH stoppages. Sparring records were kept and recorded as *“minutes per month”*. Detailed statistical analysis demonstrated no evidence of decreased neuropsychological function in the study group. There was evidence of improved performance in the boxing group relative to the controls in Rey-Osterrieth A + B raising the possibility that the control group are subject to greater exposure to cerebral insult through participation in other sports such as Gaelic football. The authors acknowledge the small study size and possible existence of confounding factors but overall this comprehensive study demonstrates no evidence of traumatic encephalopathy in amateur boxing.

Neuropsychometric testing appears to provide a sensitive though non-specific means of identifying brain damage. Well-designed case control studies and examination of relevant cohorts suggest that there is no consistent evidence linking amateur boxing with the development of neuropsychometric dysfunction and a chronic brain syndrome. One study shows a link, albeit subtle, between exposure as measured by number of fights and neuropsychometric impairment.

A number of the studies on professional boxers display flawed methodology, including selection bias. In the case of Roberts, this may have underestimated the prevalence of dysfunction as the tests which were chosen were least likely to upset or offend the subject rather than those which would target dysfunction secondary to trauma. The neuropsychological deficiencies demonstrated by Drew *et al* (1986) concurred with the neurological impairment of this group of 19 professional boxers. There was again a high correlation between exposure, as measured by fights drawn and lost, and deficiency in test score. This study provides evidence for brain damage caused by boxing, which appears independent of any modern rules and regulations.

**Table 8 Evidence table: Neuropsychometry**

Author	Title	Year	Study Type	Amateur (A) Professional (P)	SIGN Grade
Porter, M.D.	A 9 year Controlled Prospective Neuropsychological Assessment of Amateur Boxing	2003	Case control	A	2 ++
Porter, M.D., Fricker, P.A.	Controlled Prospective Neuropsychological Assessment of Active Experienced Amateur Boxers	1996	Case control	A	2 ++
Kemp et al.	Cerebral perfusion and psychometric testing in military amateur boxers and controls	1995	Case control	A	2 ++
Stewart et al.	Prospective Study of Central Nervous System Function in Amateur Boxers in the United States	1994	Cohort	A	2 ++
Butler et al.	A prospective controlled investigation of the cognitive effects of amateur boxing	1993	Case control	A	2++
Haglund, Y., Eriksson, E.	Does amateur boxing lead to chronic brain damage ? A review of some recent investigations.	1993	Cohort study	A	2 ++

**Table 8 Evidence table: Neuropsychometry (cont'd)**

Author	Title	Year	Study Type	Amateur (A) Professional (P)	SIGN Grade
Murelius, O., Haglund, Y.	Does Swedish amateur boxing lead to chronic brain damage ? 4. A retrospective neuropsychological study	1991	Case Control	A	2++
Haglund et al.	Does Swedish amateur boxing lead to chronic brain damage ? 1.A retrospective medical, neurological and personality trait study	1990	Case control	A	2++
Brooks et al.	A neuropsychological study of active amateur boxers	1987	Cohort	A	2 ++
Drew et al.	Neuropsychological Deficits in Active Licensed Professional Boxers	1986	Cohort	P	2 ++
Stiller, J.W., Weinberger, D.	Boxing and Chronic Brain Damage	1985	Systematic Review	A + P	2 ++
Thomassen et al.	Neurological, electroencephalographic and neuropsychological examination of 53 former amateur boxers	1979	Case control	A	2++
Ravdin et al.	Assessment of Cognitive Recovery Following Sports Related Head Trauma in Boxers	2003	Cohort	P	2 +
Warden et al.	Persistent prolongation of simple reaction time in sports concussion	2001	Cohort	A	2 +
Jordan et al.	Apolipoprotein E e4 Associated With Chronic Traumatic Brain Injury in Boxing	1997	Cohort	P	2 +
Levin et al.	Neurobehavioral functioning and magnetic resonance imaging findings in young boxers	1987	Case control	A + P	2 +
Parkinson, D.	Concussion: Comparison of Humans and rats	1978	Cohort	N/A	2 +
Roberts, A.H.	Brain Damage in Boxers	1969	Cohort	P	2 +
Heilbronner et al.	Neuropsychological test performance in Amateur boxers	1991	Cohort	A	2 -
Ross et al.	Boxing Injuries: Neurologic, Radiologic and Neuropsychological Evaluation	1987	Cohort	A + P	2 -
Casson et al.	Brain Damage in Modern Boxers	1984	Cohort	A + P	2 -
Kaste et al.	Is Chronic Brain Damage In Boxing a Hazard of the Past?	1982	Cohort	A + P	2 -
Jedlinski et al.	Punch Drunkenness	1970	Cohort	A	2 -
Jedlinski et al.	Chronic Post Traumatic Changes in the Central Nervous System in Pugilists	1969	Cohort	A	2 -
Rabadi et al.	The Cumulative Effect of Repetitive Concussion in Sport	2001	Case series	A + P	3
Dax, E.C.	Preventing brain damage in boxers	1997	Case series	P	3
Byrne, A.	Neurological Injuries in Boxers: Lessons From One Family	1991	Case series	N/A	3
Sabharwal et al.	Chronic Traumatic Encephalopathy in Boxers	1987	Case series	A	3
McLatchie et al.	Clinical neurological examination, neuropsychology, electroencephalography and computed tomographic head scanning in active amateur boxers	1987	Cohort study	A	3
Harvey, P., Newsom Davis, J.	Traumatic Encephalopathy in a Young Boxer	1974	Case report	A + P	3
Blonstein, J.A.	Traumatic Encephalopathy in a Young Boxer	1974	Case report	A + P	3
Johnson, J.	Organic Psychosyndromes due to Boxing	1969	Case Series	P	3

**Table 8 Evidence table: Neuropsychometry (cont'd)**

Author	Title	Year	Study Type	Amateur (A) Professional (P)	SIGN Grade
Betti, O. O., Ottini, C.A.	Pugilistic Encephalopathy	1969	Case report	N/A	3
Mawdsley, C., Ferguson, F.R.	Neurological Disease in Boxers	1963	Case series	P	3
Jako, P.	Safety measures in amateur boxing	2002	Expert opinion	A	4
McCrory, P.	Boxing and the brain	2002	Expert opinion	A	4
Jordan, B.	Chronic Traumatic Brain Injury Associated with Boxing	2000	Expert opinion	P	4
Erlanger et al.	Neuropsychology of Sports-Related Head Injury: Dementia Pugilistica to Post Concussion Syndrome	1999	Expert opinion	A + P	4
Mendez, M.F.	The Neuropsychiatric Aspects of Boxing	1995	Expert opinion	A + P	4
Butler, R.J.	Neuropsychological investigation of amateur boxers	1994	Expert opinion	A	4
Odenheimer, G.L.	Acquired Cognitive disorders of the Elderly	1989	Expert opinion	N/A	4
Ryan, A.J.	Intracranial injuries resulting from Boxing: A review ( 1918-1985)	1987	Expert opinion	A + P	4
Jordan, B.	Neurologic Aspects of Boxing	1987	Expert opinion	A + P	4
Guterman, A.	Neurological Sequelae of boxing	1987	Expert opinion	A + P	4
Morrison, R.G.	Medical and Public Health Aspects of Boxing	1986	Expert opinion	A + P	4
Charnas, L., Pyeritz, R.	Neurologic Injuries in Boxers	1986	Expert opinion	A + P	4
Bowden, S.C., Walsh, K.W.	Boxing: Time for action	1985	Expert opinion	N/A	4
British Medical Association	Boxing. Report of the Board of Science and Education Working Party	1984	Expert opinion	A + P	4
Editorial: J R Army Med Corps	Boxing in the Army	1984	Expert opinion	A	4
Editorial: Lancet. Vol. 1	Brain Damage in Sport	1976	Expert opinion	P	4
Editorial: B.M.J.	Boxing and the Brain	1973	Expert opinion	P	4
Critchley, M.	Medical Aspects of Boxing, Particularly From A Neurological Standpoint	1957	Expert opinion	P	4

## **GENERAL DISCUSSION**

The evidence for the chronic brain damage associated with the sport of boxing can be subdivided into five main areas of clinical research.

The clinical data has been graded according to the SIGN protocol, and each relevant study has been scored. The scores for each individual area of clinical research can be used to give grades of recommendation, the grade being based on the strength of the clinical evidence presented rather than the importance of the topic under discussion. The cumulative data is summarised in table (9) and the individual grades are given for each subsection of the discussion.

**Table 9 SIGN Grading: Summary table for research fields.**

Clinical Research Field	SIGN GRADE							
	1++	1+	1-	2++	2+	2-	3	4
<b>Histopathology</b>	0	0	0	1	1	7	25	28
<b>Electrophysiology</b>	0	0	0	4	1	8	12	15
<b>Neuroradiology</b>	0	0	0	4	5	5	16	7
<b>Physical/Neurological</b>	0	0	0	8	3	7	15	15
<b>Neuropsychology</b>	0	0	0	12	6	6	10	18

**i) Histopathology: Grade D**

The data available in respect of histopathological changes is extremely limited. Corsellis *et al* (1973) provides the only comprehensive study with subsequent works having re-examined many of the original cohort using more complex staining techniques. Conclusions are only pertinent to this group or those boxers with similar demographics. The study group represents a cohort of men who had profound neurological and psychological impairment, such that many ended their days subject to institutionalised care. Thereafter their brains became available for examination, providing a biased sample unrepresentative of all boxers and particularly those in contemporary competition. These specimens are from a group at the limits of exposure to head trauma within their sport. They fought over 50-100 years ago during a time when many of the modern rules and constraints were not in place. Whilst contemporary professional boxing forms part of a continuum in terms of exposure to head trauma, the relevance of these histopathological studies to present day boxing remains questionable. In professional Boxing there is evidence to show that the exposure in terms of duration and number of fights has decreased significantly since the 1930's. During this time

the average duration of a professional boxers career has dropped from nineteen to five years with mean number of career bouts reduced from 336 to 13 (Clausen *et al.*, 2005).

Professional boxers may show evidence of large fenestrated cavum septi pellucidum, a distinctive pattern of cerebellar scarring, nigral depigmentation, reduction in periventricular mass and tangle and plaque formation that has many similarities to Alzheimer's disease. The similarities in appearance and distribution of both plaque and tangle are matched only by the subtle differences. Such differences include laminar distribution, iron and aluminium content and ubiquitin immunoreactivity. It has been postulated that differential triggers may lead to a common pathway with subtle variation leading to distinct end points in terms of appearance and distribution. The challenge must be to predict to whom and when these changes will take place and correlate their evolution to changes in brain function. This can only ever be achieved by examining a much broader range of histopathology derived from boxers with a whole spectrum of ante mortem clinical exposure to head trauma

An additional challenge for medicine is whether to use established histopathological changes in Alzheimer's disease to help understand brain damage caused by boxing or whether to proactively investigate the evolution of Alzheimer's type neuropathology using the sport of professional boxing to provide a dynamic cohort of prospective neurohistopathology, leading to a greater understanding of a far more prevalent disease.

#### **ii) Electrophysiology: Grade D**

The electroencephalogram has been the primary electrophysiological tool used for assessment of brain function in respect of boxing. The significance of electrophysiological studies in identifying and monitoring brain injury in boxing is concisely summarized in the statements made by Charnas and Pyeritz (1986),

*"The EEG samples electrical activity at the brains cortical surface, an area less severely involved in chronic complications. Evoked potentials are primarily adjuncts to the neurologic examination to detect disease in sensory pathways of vision hearing and sensation. None of those pathways is reported to be abnormal in the*

*chronic brain syndrome of boxers. Thus the information provided by electrophysiological studies is either redundant or not clearly useful”.*

This concurs with the concluding remarks made by Johnson,

*“The lesions responsible for encephalopathy are probably located in two main areas: neurological features in the upper brainstem, psychiatric features in the Hippocampal-Fornical system... The scalp EEG reflects neural disorganization in the cerebral cortex in a syndrome that is largely sub-cortical...”*

It is apparent that electrophysiological investigations have neither a predictive nor a diagnostic role in determining chronic brain damage in professional and amateur boxing.

### **iii) Neuroradiology: Grade C**

The majority of neuroradiological studies are cross sectional examining scans at a specific point in time. Clarification of any directionality regarding the association between radiological changes and brain damage requires a longitudinal investigation of such changes with documentation of boxing exposure in parallel. The role of neuroradiological imaging in predicting, detecting and monitoring the chronic changes attributable to boxing appears limited (Moseley, 2000). Early studies examined boxers who had fought on a far more frequent basis with greater exposure to head trauma. Later more sophisticated techniques have largely failed to demonstrate systematic evidence of brain damage that can be attributed to boxing alone. The main problem encountered to date is that studies have looked at a cross sectional “*snapshot*” of data in an attempt to comment on a process that is thought to be dynamic. Longitudinal studies where a boxer is used as his own control for comparison at a future date are required.

These studies must be in parallel with a comprehensive and detailed exposure history that encompasses both active fights and training sessions involving sparring. More sophisticated neuro-imaging techniques involving the use of both magnetic resonance spectroscopy and HMPAO SPECT may have a vital role in determining dynamic brain function but more studies are needed.

There exists at present a vast amount of data that has yet to be analyzed. Over ten years ago the British Boxing Board of Control introduced a requirement for annual computerised tomography. The CAT brain scans were superseded in the late 1990's by annual MRI brain scans with a requirement for a magnetic resonance angiogram at the granting of the initial licence. On average 600 professional boxing licenses are granted or renewed each year under the jurisdiction of the Board of Control which keeps a meticulous record of each boxer's career in terms of total fights, wins, losses and stoppages. It would be possible to compare exposure variables as documented by career record to serial scans performed on each boxer. The database held by the British Boxing Board of Control is in excess of 6,000 scans. Whilst it would be more favourable to conduct such studies in a prospective manner this data exists and may provide important information in terms of the evolution of neuroradiological changes in parallel with exposure to head trauma in professional boxing.

#### **iv) Physical/Neurological: Grade C**

As with many of the previous investigative techniques, physical and neurological examination provide a cross sectional assessment of function at a given point in time. Selection bias has affected the validity of many studies. The case series reported by Spillane is a select cohort. All five had boxed and all displayed neurological or behavioural dysfunction that had resulted in referral to a specialist neurological centre. The value of these findings would have been greatly augmented if the subjects had been followed through their boxing career allowing comparison to a baseline. Each boxer would have acted as his own control against which any changes could be compared. Deterioration in neurological function could then be compared to data on exposure that would have been collected in parallel. Similar failings pertain to the work of Johnson (1969a, 1969b) and Corsellis *et al* (1973).

Selection bias detracts from the conclusions of a number of other neurological studies. Thomassen *et al* (1979) examined a select group of champions. It may be argued that skilled boxers, who are less likely to be struck to the head, could only achieve such status. This study may thus underestimate the frequency of neurological dysfunction by examining a select elite group. This work also raises a question regarding fine motor dysfunction in the left hand. Casual observation might suggest a reason for this finding. The majority of

boxers adopt an orthodox style, using the left hand as a lead. It might be postulated that over a period of time peripheral trauma might result in deficiencies in motor function in this hand. The converse might also be proposed which presumes that if most lead punches are thrown with the left hand the right side of the head is more likely to be struck, with an increased possibility of trauma to the right motor cortex governing the left hand. Further studies are required to evaluate this theory.

Motivation to seek inclusion in a study conducted by Kaste (1982) could have been self-awareness of symptoms such that the cohort comprised an increased number of symptomatic subjects. The source group comprising champion boxers, less likely to have suffered head trauma, may however have mitigated potential skewing of results.

In his general review Jordan (1987) alludes to a need for prospective evaluation and data collection and in a later publication, (Jordan, 2000), it is concluded that large scale epidemiological surveys of well defined boxing populations to assess the frequency of chronic traumatic brain injury are essentially non-existent. Many of the neurological studies to date are cross-sectional analyses of a select group at a given point in time. Many combine both amateur and professional subjects and fail to use objective ratings or strict definitional criteria for abnormality.

The evidence, whilst limited, suggests amateur boxers show no evidence of neurological deficit that can be attributed to their chosen sport. Professional boxers with prolonged exposure may demonstrate neurological impairment manifest by incoordination, dysarthria, Parkinsonism, gait disturbance and pyramidal signs. Measures of prolonged exposure include number of professional fights including number of losses and draws, which may equate with number of head blows received. Neurological studies provide only a diagnostic statement of damage having occurred and provide no predictive value that would determine which boxers are at risk. For this to occur, dynamic evaluation using prospective controlled trials would be required.

The use of genetic markers such as APOE  $\epsilon$  4 may allow the boxing authorities to advise certain individuals of a possible increased risk to their health but more studies may be

required to quantify such a threat. Biomarkers such as S100B rise after brain injury and levels may be used as a prognostic guide. The value of such a test in boxing remains debatable as such levels only bear witness to damage having been done.

#### **v) Neuropsychometry: Grade B**

Methodological failings impose constraint on conclusions in respect of neuropsychometric testing, in a number of studies. Selection bias and lack of a suitable control group impact on any conclusions that may be drawn from the work of Johnson (1969a, 1969b) in his study of professional boxers.

The comprehensive study by Roberts (1969) lacks suitable controls and a biased selection of specific neuropsychometric tests may have underestimated the prevalence of dysfunction and as such this work provides little additional information in respect of neurological dysfunction in professional boxers.

Similar criticism may be leveled at Kaste (1982) whose work is flawed, as all subjects were either amateur or professional champion boxers who had volunteered. The study lacks any description of what was deemed abnormal during assessment and there was no control group. The only definitive finding was that 12 of the 14 subjects took longer in the trail-making test than the average performance time for "*normal subjects*". This finding may be significant but any such import is lost as the study does not state which trail making test was used, nor is there any means whereby the abnormality can be compared to exposure in terms of length of career and number of fights. Kastes study adds nothing to our understanding of neuropsychometric dysfunction caused by boxing.

The choice of subject in McLatchie's *et al* (1987) work was compromised by selection bias as the cohort was derived from those who responded to a written invitation to take part, as well as some who volunteered. The authors acknowledge this failing, accepting that the group may not be representative, and as such any abnormalities cannot be attributed solely to boxing. Interpretation of results is compromised by both the selection bias of the original study group and the variable nature of the controls.

One study on amateur military boxers (Kemp *et al.*, 1995) demonstrates significant dysfunction in 80% of neuropsychometric tests used, which correlated with exposure to head trauma as measured by number of fights. The deficiencies were described as “*subtle*” and there is no suggestion of overt manifestation of a chronic brain syndrome.

Stewart *et al* (1994) examined 484 amateur boxers in a two-year prospective study. Whilst no deficiencies were found in any subject during the study period there was a significant statistical association between number of bouts prior to inclusion in the study, and deficiencies in memory, perceptual/motor and visuoconstructional ability. The authors highlight the fact that whilst these differences are statistically significant they are not clinically significant, implying that no subject displayed any overt signs. These findings concur with those of many others linking deficiency in a given parameter to exposure to head trauma, as measured by length of career and number of fights

It would appear that neuropsychometric testing is a sensitive, though non-specific, means of identifying brain damage. The results when used in the evaluation of brain dysfunction in boxers have; however, been inconsistent. This has been in part due to the limited number of studies and their methodological failings, which is mainly manifest by selection bias. This bias is seen in the choice of subject, choice of specific neuropsychometric test and the choice of control. Overall the evidence to date shows that amateur boxers appear to escape neuropsychological dysfunction and do not develop a chronic brain syndrome as a result of boxing.

Drew (1986) published the only study demonstrating neuropsychometric dysfunction in a cohort of modern boxers wherein deficiencies are correlated to trauma, as witnessed by number of losses and draws in professional fights.

There is a need for long term, prospective, well designed and suitably controlled studies to be carried out particularly in professional boxing. This will allow definitive statements to be made in terms of the neuropsychometric deficiencies that may be caused.

## **CONCLUSION**

The development of a chronic brain syndrome as a result of boxing appears to be related to exposure to head trauma, measured in terms of length of career, number of bouts, and number of draws and losses.

Amateur and professional boxing are two distinct sports, the rules and regulations of which are markedly different. The maximum length of a senior amateur bout is 12 minutes of boxing, contrasting with 36 minutes in the professional code. Amateur boxing has a number of requirements within the system of scoring that reduce the potential for excessive head blows by terminating or suspending a bout at the discretion of the referee. Such provision is absent within professional boxing.

Histopathological studies have examined a small group of professional boxers, demonstrating a distinct pattern of damage to the septum pellucidum, cerebrum, cerebellum, substantia nigra, with the regional occurrence of neurofibrillary tangles. This group is derived from boxers at the limits of exposure in terms of length of career and number of bouts. Contemporary professional boxing is part of a continuum of exposure, which a recent study has suggested is unlikely to reach the levels seen in the histopathological cohorts of 50-100 years ago. There is no conclusive evidence of any such pattern of damage being solely attributable to amateur boxing.

Electrophysiological investigations have no part to play in diagnostic or prognostic evaluation of chronic brain damage in either amateur or professional boxing.

Neuroradiological studies have been unable to demonstrate a direct correlation between exposure variables and cerebral atrophy. In professional cohorts the development or enlargement of a cavum septum pellucidum, particularly if it becomes fenestrated, is suggestive of neurotrauma. The majority of radiological studies have been cross sectional, providing limited information mainly in respect of professional boxers. There is a need for prospective studies that monitor exposure variable alongside neuroradiological changes. There is no evidence of neuroradiological change as a result of participation in amateur boxing.

The most comprehensive neurological study to date investigated 224 professional boxers, boxing between 1929 and 1955. There was evidence of neurological abnormality in 17%, manifest by cerebellar or extrapyramidal dysfunction. The conclusions of many other studies on professional boxers have been compromised by poor methodology and selection bias. There is no compelling evidence of neurological impairment wholly attributable to amateur boxing.

Neuropsychometric testing provides a sensitive though non-specific means of monitoring brain function. Well-designed case control and cohort studies have largely examined amateur boxers, demonstrating no consistent evidence of chronic brain damage or neuropsychometric dysfunction in this group. Roberts's study (1969) may have underestimated the prevalence of such impairment in professional boxers due to biased selection of screening tests. The study by Drew (1986) demonstrates impairment in modern professional boxers, which correlates to exposure as measured by the number of bouts lost and drawn.

The use of genetic testing to screen for potentially vulnerable individuals remains unclear.

## **RECOMMENDATIONS**

- i. Post mortem specimens from patients who have boxed in the modern era should be obtained in order to expand the database in respect of histopathological evidence.
- ii. Governing bodies within professional boxing should be advised that the use of electroencephalography (EEG) as a means of screening is of little value.
- iii. Prospective neuroradiological studies should be undertaken using MRI scans of the brain in parallel with a meticulous exposure history to head trauma, including bouts and sparring.
- iv. Further assessment is required regarding the role of genetic testing, using APOE  $\epsilon$ 4 as a marker for predisposition to detrimental effects of brain injury in boxing.
- v. The use of neuropsychometric testing in amateur and professional boxing should be encouraged. This may provide a dynamic assessment of cognitive function, allowing intervention by way of suspending from activity any boxer who falls below a certain pre-determined level on serial examination.
- vi. There is a need for uniformity of regulation throughout professional boxing, such that risk and exposure variables are constant worldwide.
- vii. The cumulative nature of neurotrauma in boxing requires that particular attention be paid to the amount of exposure during sparring. This should be documented, accurately, along with results of neuropsychometric tests. Results may then allow specific advice to be given in terms of risk.
- viii. Meticulous scrutiny of professional career records may allow regulations to be drawn up that will protect by exclusion a boxer who is persistently losing. Exposure as measured by draws and losses is correlated to neuropsychometric dysfunction.
- ix. Reducing the number of rounds in professional boxing will reduce the overall exposure to head trauma.

- x. The use in professional boxing of a standing eight count may allow the referee to intervene to protect a boxer. At present no such provision exists.
  
- xi. The British and American Medical Associations have called for an outright ban on amateur and professional boxing. The clear difference in the risk involved in each code requires that this position be re-appraised in light of the evidence presented in this thesis.

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