Amateur boxing and risk of chronic traumatic brain injury: systematic review of observational studies

Mike Loosemore, lead sports physician,[1] Charles H Knowles, clinical senior lecturer and honorary consultant surgeon,[2] Greg P Whyte, professor of sport and exercise science[3]

[1]English Institute of Sport, London Region, Olympic Medical Institute, Northwick Park Hospital, Harrow HA1 3UJ

[2]Barts and the London NHS Trust and the Homerton University NHS Foundation Trust, Centre for Academic Surgery, Royal London Hospital, London E1 1BB

[3]Research Institute for Sport and Exercise Sciences, Liverpool John Moores University

Correspondence to: M Loosemore
mike.loosemore@eis2win.co.uk

ABSTRACT

Objective To evaluate the risk of chronic traumatic brain injury from amateur boxing.

Setting Secondary research performed by combination of sport physicians and clinical academics.

Design, data sources, and methods Systematic review of observational studies in which chronic traumatic brain injury was defined as any abnormality on clinical neurological examination, psychometric testing, neuroimaging studies, and electroencephalography. Studies were identified through database (1950 to date) and bibliographic searches without language restrictions. Two reviewers extracted study characteristics, quality, and data, with adherence to a protocol developed from a widely recommended method for systematic review of observational studies (MOOSE).

Results 36 papers had relevant extractable data (from a detailed evaluation of 93 studies of 943 identified from the initial search). Quality of evidence was generally poor. The best quality studies were those with a cohort design and those that used psychometric tests. These yielded the most negative results: only four of 17 (24%) better quality studies found any indication of chronic traumatic brain injury in a minority of boxers studied.

Conclusion There is no strong evidence to associate chronic traumatic brain injury with amateur boxing.

INTRODUCTION

In light of evidence of acute and chronic injuries associated with boxing, the British Medical Association (BMA) has passed a series of resolutions at its annual representative meetings calling for boxing to be made illegal.[1 2] The latest report from the BMA Board of Science Working Party on Boxing (now disbanded), published as a briefing paper, continues to campaign for a complete ban on boxing (amateur and professional), mainly because of the purported risk of cumulative brain injury (chronic traumatic brain injury).[2] Severe acute injuries in boxing (including those resulting in fatality), however, are relatively rare compared with other sports, even when professional and amateur boxing are grouped together.[3-5]

A series of important changes in rules and equipment aimed at improving the safety of boxing have been gradually introduced by boxing authorities since the early 20th century.[6 7] Whether such changes have improved safety remains contentious. The box shows changes relevant in amateur boxing. On the basis of published data available at the time, the BMA 2001 report acknowledged that the evidence for chronic traumatic brain injury in amateur boxing was "far less clear cut" than in professional boxing.[1] There have been several publications since this BMA report that have continued to examine the link between boxing, including the amateur sport, and chronic traumatic brain injury.[w1 w3 w4]

We carried out a systematic review to determine whether amateur boxing leads to chronic traumatic brain injury. We did not consider professional boxing, the incidence of acute injuries, or the moral or legal arguments regarding the sport. A problem with

Changes in rules and equipment in amateur boxing	
1906—	Requirement for a medical examination before the contest
1947—	Referees allowed in the ring
1950—	Boxing medicals and medical cards introduced with imposition of mandatory suspensions for certain injuries. Doctor must be present at ring side
1962—	Establishment of the Medical Commission of the Amateur Boxing Association (ABA)
1964—	Introduction of the "standing 8" count
1972—	First publication of *Medical Aspects of Amateur Boxing*
1984—	Head guards introduced for the Los Angeles Olympics
1992—	Computerised scoring system introduced at the Barcelona Olympics
1996—	Structure of the bouts changed from three rounds of three minutes to four rounds of two minutes
2000—	Introduction of the "outclassed" rule (Sydney Olympics): bout stopped automatically if one boxer leads the other by 20 points in any but the final round
2002—	Ringside physician regulations changed to include suitably trained paramedics present when the doctor is not trained or equipped for resuscitation (*Medical Aspects of Boxing*, 2002)
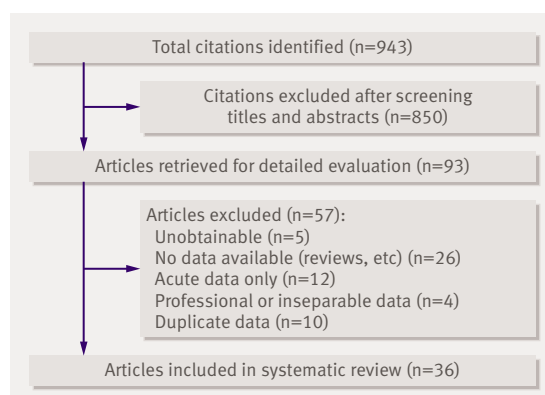
Study selection process for systematic review of chronic brain injury in amateur boxing

performing such a review is the absence of any clear definition of chronic traumatic brain injury. Historically, the first description of a link between boxing and cerebral dysfunction was that of Martland, who described "punch drunk" (although this was actually based on cases described to him by promoters).[8] This extreme form of injury, perhaps partially encompassed by the current term "chronic traumatic brain encephalopathy"[9] is rare. We clearly needed to consider much more subtle indicators that may be surrogate markers of chronic traumatic brain injury. In the absence of any ideal standards for this, we took the lowest thresholds—that is, any consistent change in the results of neurological examination, brain imaging, psychometric testing, electroencephalography, including a few other relevant studies for completion. We included studies of amateur boxers (including military and police), with the intervention (exposure) being participation in the sport and from which we could extract data.

METHODS

Though the quality and heterogeneity of available data meant that we could not undertake a meta-analysis, we have adhered as far as possible to the QUOROM statement for systematic reviews.[10] Because all included studies were observational in design, we also adhered to a protocol developed from a widely recommended method for systematic review/meta-analysis of observational studies (MOOSE).[11]

Search strategy

Two authors (ML (initial search) and CK (final arbitrator in selection)) carried out a comprehensive search of the literature using Medline and Premedline 1950 to December 2006, Embase, Evidence Based Medicine (EBM) reviews (including the Cochrane database of systematic reviews and the Cochrane central register of controlled trials), and the SPORTDiscus database. The only search term used was "boxing" because of the still manageable number of retrieved titles. In addition, MeSH terms were "("Boxing/adverse effects" OR "Boxing/injuries" OR "Boxing/mortality" OR "Boxing/physiology" OR "Boxing/psychology"[- MeSH]) * ("Boxing/adverse effects" OR "Boxing/injuries" OR "Boxing/mortality" OR "Boxing/physiology" OR "Boxing/psychology"). We hand searched and cross referenced the bibliographies of relevant papers and three books. Two authors were contacted, and one further reference was provided by a reviewer.

Selection

The figure outlines the study selection process. We included all studies from which we could extract data on outcomes, regardless of study design. We had no language restrictions, though papers were reviewed in detail only when the English title or abstract indicated the likelihood of relevant data. Abstracts and unpublished studies were not included. We also excluded papers with data from amateurs and professionals combined, unless we could separate the data, and those containing duplicate data from a prior publication by the same group.

Assessment of study quality

We assessed all manuscripts that met the selection criteria for quality. We defined quality as confidence that the study design, conduct, and analysis minimalised bias in the estimation of effect of the risk factor on the outcome measures. Quality assessment was based on published checklists produced to evaluate epidemiological studies that assess potential links between exposures to risk factors and harm.[11 12] This assessment in general reflected the level of evidence on the basis of the established hierarchy of observational studies.[12] Because the review included several types of observational study ranging from cohort to case series, we modified checklists to include six measures in total that best (although not universally) applied across study types: prospective study design, groups comparable on all important confounding factors, outcome assessed blind to exposure status, follow-up long enough for outcomes to occur (defined as over one year), relation between outcome and exposure appropriately measured, and appropriate statistical analyses used.

Data extraction and synthesis

ML extracted data, which were checked by CK. As far as possible, we obtained numerical data, though outcome measures were largely categorical in case series (proportions of participants with positive findings) or expressed as group differences in controlled studies. No quantitative data synthesis was performed. Exposure times were collected and expressed as median or mean number of bouts. Accepting that exposure to injury relates to quality, quantity, and length of bouts, we also included the type (level) of boxing where this was recorded. In cohort studies, exposure was presented as length of follow-up in years as well as number of bouts during the study period.

RESULTS

Literature identification, study design, and quality

We identified 943 citations on the basis of initial search terms, of which we selected 36 articles for the systematic review (from 93 retrieved for detailed evaluation, see figure).[w1-w36] Most exclusions were because there were no original data (n=26) or data were on acute injuries only (n=12) or were duplicate data (n=10). We excluded four studies because we could not separate data from amateur and professional boxers, including one often cited paper.[13] Five foreign case series from 1959-68 were irretrievable (although these would not necessarily have been included). Of the 36 selected, 16 evaluated findings from psychometric tests, 11 from brain imaging, 14 from electroencephalography, and 12 from neurological examination, with several including more than one

outcome measure (63 methods in all). We included four cohort studies, four controlled before and after studies, and 11 case-control studies, with the remainder (n=17) being case series (six of which were prospective—that is, before and after studies in which the cases acted as their own controls).

Overall quality was poor (median score 2/6, range 0-6) (table 1). Table 2 shows the characteristics of studies and table 3 the main results. All are tabulated by quality followed by time since publication—that is, most recent first (in some instances, some studies had different designs or quality and numbers of participants for different outcome measures so we then included the best quality in table 1). We have summarised results for the main outcome measures below in order of general quality.

Table 1 | Quality of included studies

Reference	Prospective	Groups comparable on confounding factors	Blinded outcome	Long enough follow-up	Exposure response measured	Appropriate statistics	Overall quality (max 6)
Porter[w1]	Yes	Yes	Yes	Yes	Yes	Yes	6
Porter[w2]	Yes	Yes	Yes	Yes	Yes	Yes	6
Zetterberg[w3]	Yes	Yes	No	No	Yes	Yes	4
Moriarty[w4]	Yes	Yes	No	No	Yes	Yes	4
Stewart[w5]	Yes	Na	No	Yes	Yes	Yes	4
Butler[w6]	Yes	No	No	Yes	Yes	Yes	4
Haglund[w7]	No	Yes	Yes	No	Yes	Yes	4
Brayne[w8]	Yes	Yes	No	No	Yes	Yes	4
Master[w9]	Yes	Yes	No	No	No	Yes	3
Heilbronner[w10]	Yes	No	No	No	Yes	Yes	3
Kemp[w11]	No	Yes	No	No	Yes	Yes	3
Murelius[w12]	No	Yes	No	No	Yes	Yes	3
Haglund[w13]	No	Yes	Yes	No	No	Yes	3
Haglund[w14]	No	Yes	No	No	Yes	Yes	3
Levin[w15]	Yes	Yes	No	No	No	Yes	3
Brooks[w16]	No	Yes	No	No	Yes	Yes	3
Thomassen[w17]	No	Yes	No	No	Yes	Yes	3
Holzgrafe[w18]	Yes	Na	No	No	No	Yes	2
Jedlinski[w19]	No	No	No	No	Yes	Yes	2
Rodriguez[w20]	No	NA	No	No	No	Yes	1
McLatchie[w21]	No	NA	No	No	Yes	No	1
Ross[w22]	No	NA	No	No	No	Yes	1
Jordan[w23]	No	NA	No	No	No	No	0
Legwold[w24]	No	NA	No	No	No	No	0
Jordan[w25]	No	NA	No	No	No	No	0
Casson[w26]	No	NA	No	No	No	No	0
Kaste[w27]	No	NA	No	No	No	No	0
Corsellis[w28]	No	No	No	No	No	No	0
Beaussart[w29]	No	NA	No	No	No	No	0
Szymusik[w30]	No	NA	No	No	No	No	0
Moriyasu[w31]	No	No	No	No	No	No	0
Nesarajah[w32]	No	No	No	No	No	No	0
Beaussart[w33]	No	No	No	No	No	No	0
Blonstein[w34]	No	NA	No	No	No	No	0
Pampus[w35]	No	NA	No	No	No	No	0
Blonstein[w36]	No	No	No	No	No	No	0

NA=not applicable.

Table 2 | Characteristics of included studies

Reference	Study design	Type of boxing, duration of follow-up, No of bouts (mean unless stated)	Outcome measures used	No of cases	No of controls	Selection of cases and controls	Methods used to control for confounding (when applicable)
Porter[w1]	Cohort	Club, 9 years, 80	Psychometric	20	20	Random	Age, geographical, sex, socioeconomic status
Porter[w2]	Cohort	Club, 2 years, 50	Psychometric	20	20	Random	Age, geographical, sex, socioeconomic status
Zetterberg[w3]	Controlled before-after	NS, 3 months, 1	Cerebrospinal fluid biochemistry	14	10	NS	Age, sex
Moriarty[w4]	Controlled before-after	Club, 7 days, 1-3	Psychometric	85	30	1 tournament	Age, sex, education
Stewart[w5]	Case series before-after	Club, 2 years, 0→11	Psychometric, EEG, Brain evoked potentials	369	0	Invitation	Before and after (that is, act as own controls)
Butler[w6]	Cohort	Club, 2 years, 4	Psychometric	86	78	Invitation	Age, sex
Haglund[w7]	Case-control	Club, NA, 28 (estimate)	CT, MRI	47	50	Random	Age
Brayne[w8]	Controlled before-after	NS, 2 hours, 1	Creatine kinase BB	16	16	Invitation	Age, sex
Master[w9]	Controlled before-after	Club, 1 bout, 1	Psychometric	38	28	Random	Age, sex, education, weight
Heilbronner[w10]	Case series before-after	NS, 5 min, 1 bout	Psychometric	28	0	Invitation	Before and after (that is, act as own controls)
Kemp[w11]	Case-control	Military, NA, 40 (median)	Psychometric, SPECT	34	34	Invitation	Age, sex
Murelius[w12]	Case-control	Club, NA, 28 (estimate)	Psychometric	50	50	Random	Age, education, sex
Haglund[w13]	Case-control	Club, NA, 28 (estimate)	Neurological, Psychometric, Pt MAO	50	50	Random	Age, education, sex
Haglund[w14]	Case-control	Club, NA, 28 (estimate)	EEG, brain evoked potentials	50	50	Random	Age, education, sex
Levin[w15]	Cohort	Club, 0.5 years, 2-7	Psychometric, MRI	2	13	Invitation	Age, sex, education, socioeconomic status
Brooks[w16]	Case-control	Club, NA, 26	Psychometric	29	19	Invitation	Age, sex, education, ethnicity
Thomassen[w17]	Case-control	Champions, NA, 76 (median)	Psychometric, EEG, neurological	53	53	Invitation	Age, sex, education, occupation,
Holzgrafe[w18]	Case-series before-after	Top class, 2 months, 1	MRI	13	0	Invitation	Before and after (that is, act as own controls)
Jedlinski[w19]	Case-control	>100 bouts, NA, 153	Psychometric, EEG, neurological	60	30	Invitation	Reported as "characterologic"
Rodriguez[w20]	Case series	NS, NA, NS	Regional cerebral blood flow	7	0	invitation	NA
McLatchie[w21]	Case series	Club, NA, 4-200	Psychometric, CT, EEG, neurological	20	0	Invitation	NA
Ross[w22]	Case series	Club, NA, 13-150	CT, EEG, neurological	13	0	Invitation	NA
Jordan[w23]	Case series	NS, NA, NS	MRI, CT	4	0	Selected*	NA
Legwold[w24]	Case series	Military, NA, 4	Neurological	7000	0	Compulsory	NA
Jordan[w25]	Case series	Knockouts, NS, 13	MRI, neurological	9	0	Selected	NA
Casson[w26]	Case series	Club, NA, 0-80	Psychometric, CT, EEG, neurological	5	0	Invitation	NA
Kaste[w27]	Case series	National, NA, 129	Psychometric, CT, EEG, neurological	8	0	Invitation	NA
Corsellis[w28]	Case series	NS (postmortem study), NA, NS	Histological	3	0	Selected†	NA
Beaussart[w29]	Case series before-after	NS, 1 bout, 1	EEG, neurological	123	0	Invitation	Before and after (that is, act as own controls)
Szymusik[w30]	Case series	Long career, NA, >100	EEG, neurological	60	0	Invitation	NA
Moriyasu[w31]	Case-control	NS, 1 bout, NS	EEG	10	300	NS	Non-boxing head injury patients
Nesarajah[w32]	Case-control	Mixed, NA, NS	EEG	50	75	Invitation	NS
Beaussart[w33]	Case series before-after	Club, 1 bout, 1	EEG	52	0	NS	Before and after (that is, act as own controls)
Blonstein[w34]	Case series	Knockouts, NA, NS	EEG	29	NA	Selected	NA
Pampus[w35]	Case series before-after	NS, NA, 1-4 bouts	EEG, neurological	207	0	Selected	Before and after (that is, act as own controls)
Blonstein[w36]	Case-control	Knockouts, 1 bout	EEG	24	24	Selected	Non-knockout boxers

EEG=electroencephalography; MRI=magnetic resonance imaging; CT=computed tomography; SPECT=single photon emission computed tomography; Pt MOA=platelet monoamine oxidase inhibitor; NA=not applicable; NS=not stated.
*Selected on basis of referral to clinic with neurological problems.
†Selected on basis of dying in psychiatric hospital and having reportedly boxed at some time in life.

Psychometric testing

Direct comparison between studies was confounded by the use of more than 20 different psychometric tests (up to 12 tests in a single study); however these tests give the highest quality evidence and were used in the four cohort studies[w1 w2 w6 w15] and in two controlled before and after studies.[w4 w9] The longer duration cohort studies found that, though there were differences from controls in baseline measurements in some psychometric tests (reflecting educational background), there was no longitudinal effect of boxing on psychometric testing, even at nine years.[w1] Indeed in three studies, boxers out-performed controls on some tests.[w1 w2 w6]

Controlled before and after studies observed the acute effects of a boxing bout on performance,[w4 w9] but the durations of altered results on psychometric assessment were not reported as boxers were not followed up long term. The positive findings in the smaller study[w9] were not replicated in the later, larger study, which had a longer exposure and found no overall differences,[w4] though a degree of association with exposure was present on subgroup analysis. One cohort study and two large well controlled series found an isolated abnormality of finger tapping in the non-dominant hand.[w12 w17] A further study with several positive findings used multivariate models to explore the effect of boxing on results of psychometric testing and introduced additional covariates to control for confounding factors.[w11] Although the case series had heterogeneous findings, a large well conducted, albeit uncontrolled, prospective study found no changes in results of psychometric tests from baseline over a two year period.[w5]

Neuroimaging

Imaging studies using contemporary techniques—computed tomography, magnetic resonance imaging, SPECT (technetium-99m hexamethylpropyleneamineoxime single photon emission computed tomography), and isotope studies of cerebral blood flow (Xe133 CBF)—have built on earlier work using pneumoencephalography in professional boxers.[14-16] Only one pneumoencephalographic study included an amateur boxer, who had the only normal results on encephalography.[14] Though these studies provided the next best evidence after psychometric testing, the overall quality was poor with no cohort studies except that of Butler et al,[w6] who reported in the methods that 67% of the boxers underwent computed tomography but commented no further on this in the results or discussion.

Most of the other studies had small numbers of participants (often reflecting a selected subgroup of the whole study group). Most found no consistent abnormalities, and results correlated poorly with findings from other tests when used. For example, Kemp et al, despite identifying abnormalities both on psychometric testing and SPECT, showed no correlation between these findings.[w11] The highest positive yield from a case series was in seven of 13 boxers who underwent computed tomography, though the exact abnormalities were not described.[w22] Other series found abnormalities in individual boxers who had competed in only seven and 14 bouts and were, at the time of study, aged 55 and 57, respectively.[w23 w26]

Electroencephalography and brain evoked potentials

In the 1940s to 1960s researchers extensively explored the potential of electroencephalography to indicate acute injury or chronic traumatic brain injury in amateur and professional boxers with variable results.[14 17-19] Numerous early studies (case series and before and after studies) showed changes in the electroencephalogram in about half of boxers studied,[w22 w24 w26 w27 w29 w31-33 w35] with more findings immediately after bouts,[w33 w35] although these findings were not followed up longitudinally. Two recent case series found abnormal results on electroencephalography in about half of amateur boxers studied, although results were inversely correlated with advancing age and experience (more findings in younger subjects and with fewer bouts).[w24 w27] A third found some abnormalities in three of 10 amateur boxers,[w22] though two were aged 14 and 16 and the other was aged 53 and all had normal results on psychometric testing, neurological examination, and computed tomography. While case-control studies from the 1960s observed more findings in boxers than controls,[w19 w32] these findings were in stark contrast to more recent case-control series and one prospective series that found no changes compared with controls[w5 w14 w17] or from baseline function,[w5] respectively.

Clinical neurological examination

There are several reports of clinical neurological abnormalities in small numbers of amateur boxers selected on the basis of evident symptoms or recorded acute neurological injury.[14 17 18] Nine case series that did not select, however, showed a wide variation in prevalence and severity[w18 w30] of findings (from none in 7000 boxers[w24] to 33 of 60[w19]). The widely cited study of McLatchie et al found that seven of 20 amateur boxers had abnormal results on neurological examination that correlated significantly ($P<0.05$) with increasing number of fights[w21] (although we consider that the statistical method used to detect this, Mann-Whitney U test, was not appropriate). Other studies found no correlation with exposure or other methods of testing when used.[w13 w17 w22] Of the three case-control series, two found that non-specific findings such as tremor, nystagmus, slurred speech, and fine movement abnormalities were similarly present in controls.[w13 w17] One large Polish study, however, found significant differences in the incidence of organic neurological dysfunction between high exposure group and controls or lower exposure groups.[w19]

Other outcomes

In 1973 Corsellis presented evidence of histological changes in the brains of 15 boxers, of whom three were

Table 3 | Results of included studies

Reference	Outcome measure	Measure of effect	Results in exposed group v controls (where applicable)	Result
Porter[w1]	Psychometric	Group comparison*	Better scores in 2/12 tests v controls	P<0.05
Porter[w2]	Psychometric	Group comparison*	Deterioration in finger tapping dominant hand (1/12 tests)	P<0.01
Zetterberg[w3]	CSF biomarkers	Group comparison*	Increase in 3/6 CSF biomarkers v controls and baseline (at rest)	P=0.04/0.001
Moriarty[w4]	Psychometric	Group comparison†	Improvement in 1/5 tests v controls and baseline	P<0.05
Stewart[w5]	Psychometric	Odds ratio, contingency analysis	No differences in contingency or odds of abnormality with exposure	Not significant
Stewart[w5]	EEG	Odds ratio, contingency analysis	No differences in contingency or odds of abnormality with exposure	Not significant
Stewart[w5]	Brain evoked potentials	Odds ratio, contingency analysis	No differences in contingency or odds of abnormality with exposure	Not significant
Butler[w6]	Psychometric	Group comparison*	Improvements in 10/12 tests from baseline	P<0.01-0.001
Haglund[w7]	MRI	Group comparison†, contingency analysis	Small numbers of abnormalities in boxers and controls	Not stated
Haglund[w7]	CT	Group comparison†, contingency analysis	CSP in 2/47 boxers v 4/50 controls, no group differences	Not stated
Brayne[w8]	Creatine kinase BB	Group comparison†, correlation	Significantly increased levels v controls and with exposure	P<0.01, P=0.05
Master[w9]	Psychometric	Group comparison*	Significant changes v controls in 5/8 tests used	P<0.001-0.047
Heilbronner[w10]	Psychometric	Multivariate analysis	Significant changes, both positive (motor) and negative (memory)	P<0.0001-0.004
Kemp[w11]	Psychometric	Group comparison†	Significant difference v controls in 4/5 tests	P<0.05
Kemp[w11]	SPECT	Contingency analysis	14/34 boxers v 5/34 controls abnormal	P<0.02
Murelius[w12]	Psychometric	Group comparison†	No significant difference except finger tapping (dominant hand).	P<0.001
Haglund[w13]	Platelet monoamine oxidase	Group comparison *	No difference between exposed group and controls	Not significant
Haglund[w13]	Neurological	Contingency analysis	1/47 boxers v 3/50 controls abnormal	Not significant
Haglund[w14]	EEG	Contingency analysis	No differences in contingencies of abnormalities	Not significant
Haglund[w14]	Brain evoked potentials	Group comparison†	No significant difference between exposed group and controls	Not significant
Levin[w15]	Psychometric	Multivariate analysis	Exposed group moved closer to control group results	P=0.10-0.89
Levin[w15]	MRI	NA	No abnormalities found in boxers (MRI not performed in controls)	NA
Brooks[w16]	Psychometric	Group comparison*	No evidence of neuropsychological abnormalities in boxers	Not significant
Thomassen[w17]	Psychometric	Multivariate analysis	No significant differences except finger tapping (dominant hand).	P<0.01
Thomassen[w17]	EEG	Multivariate analysis	No significant difference between exposed and control group	Not significant
Thomassen[w17]	Neurological	Contingency analysis	"Sparse discrete" findings in boxers and controls	Not significant
Holzgrafe[w18]	MRI	Contingency analysis	0/13 abnormal before and after exposure	Not significant
Jedlinski[w19]	Psychometric	Contingency analysis, correlation	11/60 abnormal v 0/30 controls, correlation with increasing bouts	Not stated, r=0.50
Jedlinski[w19]	EEG	Contingency analysis, correlation	24/60 abnormal v 2/30 controls, correlation with increasing bouts	Not stated, r=0.50
Jedlinski[w19]	Neurological	Contingency analysis, correlation	33/60 abnormal v 3/30 controls, correlation with increasing bouts	Not stated
Rodriguez[w20]	Regional cerebral blood flow	NA	No abnormalities	NA
McLatchie[w21]	Psychometric	Group comparison*	9/16 abnormal, significant differences v controls in 3/10 tests	P<0.05
McLatchie[w21]	CT	Correlation	1/20 abnormal in exposed group (dilated ventricles)	Not significant
McLatchie[w21]	EEG	Correlation	8/20 abnormal (various) correlating with increasing number of fights	P<0.05
McLatchie[w21]	Neurological	Correlation	7/20 abnormal correlating with increasing number of fights	P<0.05
Ross[w22]	CT	NA	7/13 abnormal (not specified)	NA
Ross[w22]	EEG	NA	4/8 abnormal	NA
Ross[w22]	Neurological	NA	1/8 abnormal	NA
Jordan[w23]	MRI	NA	1/4 abnormal (congenital or post-traumatic cyst of hippocampus)	NA
Jordan[w23]	CT	NA	1/4 abnormal (congenital or post-traumatic cyst of hippocampus)	NA
Legwold[w24]	Neurological	NA	68 concussions/7000 bouts, none resulting in neurological dysfunction	NA
Jordan[w25]	MRI	NA	0/9 abnormal	NA
Jordan[w25]	Neurological	NA	0/9 abnormal	NA
Casson[w26]	Psychometric	NA	2/5 abnormal as defined by "impairment index"	NA
Casson[w26]	CT	NA	1/5 abnormal (generalised cerebral atrophy)	NA
Casson[w26]	EEG	NA	1/4 abnormal	NA
Casson[w26]	Neurological	NA	1/5 abnormal (mild "organic mental syndrome," right Babinsky)	NA
Kaste[w27]	Psychometric	NA	0/8 abnormal	NA
Kaste[w27]	CT	NA	1/8 abnormal	NA
Kaste[w27]	EEG	NA	4/7 abnormal	NA
Kaste[w27]	Brain evoked potentials	NA	1/7 abnormal	NA
Kaste[w27]	Neurological	NA	0/8 abnormal	NA
Corsellis[w28]	Histological	NA	0/3 abnormal	NA

Beaussart[w29]	EEG	Contingency analysis	0/123 abnormal (before v after bout)	Not significant
Szymusik[w30]	Neurological	NA	6/60 abnormal ("boxer's encephalopathy")	NA
Moriyasu[w31]	EEG	NA	2/10 abnormal ("slightly slow patterns")	NA
Nesarajah[w32]	EEG	Not stated	30/50 abnormal v 6/75 controls	Not stated
Beaussart[w33]	EEG	Not stated	25/52 rhythm and slow posterior waves	Not stated
Blonstein[w34]	EEG	NA	0/29 abnormal	NA
Blonstein[w34]	Neurological	NA	0/29 abnormal	NA
Pampus[w35]	EEG	NA	11/26 abnormal after 3 bouts v 34/116 before any bouts	Not stated
Pampus[w35]	Neurological	NA	42/175 abnormal	NA
Blonstein[w36]	EEG	NA	4/24 abnormal after bout but returned to normal rapidly	NA

NA=not applicable; CSF=cerebrospinal fluid; CSP=cavum septum pellucidum; CT=computed tomography; EEG=electroencephalography; MRI=magnetic resonance imaging; SPECT=single photon emission computerised tomography.
*t tests (or equivalent non-parametric tests).
†Analysis of variance.

amateur.[w28] Aside from possible flaws of attribution in this study (such as alcohol, syphilis, and head injuries from other causes) in association with positive findings in professional boxers, the authors concluded that no changes specific to boxing were present in the amateurs. Two studies examined neurochemical changes in the blood[w8] and cerebrospinal fluid[w3] of boxers after competition compared with athletic or non-athletic controls, respectively, and found significantly higher concentrations in boxers. In the latter studies each boxer underwent two lumbar punctures.[w3] These increases were said to indicate disruption of the blood-brain barrier or acute neuronal and astroglial injury.

DISCUSSION

In this systematic review we found no evidence for a strong association between amateur boxing and chronic traumatic brain injury. In boxing the head might get hit repeatedly with resultant concussion, though less than in several more popular sports—such as rugby union and equestrian activities[3-5 19]—which may harm cerebral function. Whether clinically measurable long term brain injury occurs is a different and more important question. There is reasonable clinical,[8 14-16] radiological,[14 15 20] and histopathological[8 17 21 22 w28] evidence that this is the case in a proportion of professional boxers (10-20% in most studies), although most studies were performed at a time when safety standards were far less stringent than they are today.[7 9]

Amateur boxing is a different sport from professional boxing, including in its motivation to participate, rules, and equipment, but, most importantly, there is considerably greater exposure to injury in professionals (increased frequency and force of punches over a greater duration of career).[9] We looked at the data for chronic traumatic brain injury in amateur boxing alone. Although no formal synthesis was performed, the data can be described in summary. Overall, 15 of 36 studies (42%) included in the systematic review concluded that relevant abnormalities were present, at least in a proportion of boxers studied. When we expressed this as a function of all methods tested (see table 3) we attained a similar figure (28/63, 44%).

Limitations

It would clearly be impossible to perform a double blind randomised controlled trial for amateur boxing, though in general study design and conduct could have been greatly improved. Few studies were of sufficient quality to conclude anything other than a weak association when positive findings were reported, and none was sufficiently powered (no sample size calculations performed) to exclude a type II error when results were negative. Only two studies supplied confidence intervals for the main results. There was a definite tendency towards positive findings in studies of poorer quality and design. For instance, none of the four cohort studies[w1 w2 w6 w15] (quality 3-6) had positive results, with three actually showing improvements over the study period.[w1 w6 w15] This contrasts with the finding of abnormalities in over 50% of case series. With a cut-off of quality ≥3/6, only four of 17 (24%) studies and five of 26 (20%) methods of testing yielded abnormal results. The latter is in contrast to studies that scored ≤2 on quality, in which 62% (23/37) yielded positive results. Although perhaps not of importance, only two of 14 studies performed from 1990 onwards concluded that any measurable abnormality was present (and one of these was in a single boxer). The importance of using controls was illustrated by several case-control studies that showed that potentially severe abnormalities on clinical neurological examination[w13 w17] as well as neuroimaging[w7] were present equally in the control group.

Bias

Methods of selection were rarely adequately explained and occasionally performed on the basis of prior abnormal clinical or investigative findings.[w23] In terms of design, when controls were used these were poorly selected in terms of possible confounding factors. For instance, in one study that used psychometric tests, the controls (rugby and water polo players) were drawn from an undergraduate population, whereas many of the boxers had not completed their full time education.[w6] As no data on IQ had been gathered this factor could not be assessed, and it is acknowledged that education and vocabulary have a large weighting on results of neuropsychometric

> ## WHAT IS ALREADY KNOWN ON THIS TOPIC
>
> The safety of amateur boxing in terms of risk of chronic traumatic brain injury continues to be questioned
>
> No recent or systematic review has been performed to assess the evidence for this
>
> ## WHAT THIS STUDY ADDS
>
> A systematic review of observational studies indicates that, although the quality of evidence supporting or refuting the hypothesis was poor, the association between amateur boxing and chronic traumatic brain injury is not strong

testing. In respect of performance, remarkably in only two studies were observers blinded.[w1 w7 w12] Finally, though we did not carry out a formal analysis of publication bias, studies showing adverse effects might have been more likely to get published.

In studies that sought an association between exposure and outcome, few found an effect, raising the question of false attribution. Indeed, questions of specificity exist for almost all methods used. In psychometric testing, three well conducted studies found a single significant difference in the finger tapping test of the non-dominant hand.[w2 w12 w17] This finding has been replicated in other studies and seems to be worse with increased exposure to boxing. The association between finger tapping response and brain damage is difficult to assess in boxers, however, given the chronic damage to the fingers directly associated with repeated punches.[w1223] The observation in electroencephalography studies of an inverse association between exposure or age and positive findings[w21 w27] might similarly be explained by the recognised false positive rate of electroencephalography, particularly in the young.[24] The problems implicit in analysis are also illustrated by the revision of findings (from highly significant to zero) by a single group in two consecutive publications.[w29 w33] Imaging methods have similar inherent difficulties of interpretation with the relevance of some much championed findings, such as cavum septum pellucidum and ventricular abnormalities,[15 17 18 25] questioned by others.[26-28] This issue is well reviewed elsewhere,[26] and the relevance of many of these abnormalities remains dubious. In respect of blood concentrations of creatine kinase BB, increased levels have also been observed in oarsmen and marathon runners.[29] When, as in some series, participants in their 50s were described with clinical neurological abnormalities after a limited exposure (as few as seven bouts) some 30 years previously,[w24 w27] the sole attribution of these findings to boxing must surely be questioned.

Conversely, the current range of tests might lack sensitivity to detect subtle changes in neural structure or function. All these tests must be regarded as surrogate markers for the notional concept of chronic traumatic brain injury and clearly no conclusion can be reached on this without an ideal test for comparison or indeed a clear definition of what might constitute clinically relevant injury. Nevertheless, tests regarded as sensitive in general neurological practice have all been used. In particular, psychometric testing, regarded by some as the most sensitive,[w2123 30] provided the most conclusive negative results.[w1 w2 w4-6 w15] Similarly, it is generally accepted that magnetic resonance imaging is the best method of determining subtle parenchymal damage and degenerative change. In the six studies that used this, only one case series of four boxers concluded that relevant abnormality was present. This was a cyst in a single boxer, which was possibly congenital.[w23] No abnormalities were found in the single cohort study that used magnetic resonance imaging.[w15]

Finally, because of the short duration or "snapshot" design of nearly all studies (except that of longer follow-up cohort studies in which no detrimental effects were found[w1 w2 w5]), it is impossible to conclude whether or not longer exposure would have eventually led to chronic injury or whether such changes might present in much later life when further neuronal loss occurs with ageing. Implicit within this latter argument is the possibility that subclinical, sub-psychometric, and sub-radiological brain damage incurred as an amateur may contribute to that which becomes clinically evident in those who subsequently have a long professional boxing career. This was not, however, indicated by findings at nine year follow-up.[w1]

Conclusions

Amateur boxing is becoming an increasingly popular participation sport, especially within universities and for both sexes. The safety of boxing is an issue that stimulates emotive responses on both sides of the debate, and calls to ban the sport continue. This review neither seeks to endorse nor oppose the sport of amateur boxing. It is perhaps a question of personal philosophy whether it is incumbent on boxing to prove that it is safe, or on those who oppose it to prove that it is deleterious (although it might be argued that those wanting to alter the status quo have the responsibility to prove this). Nevertheless, on the basis of this systematic review, we conclude that the current evidence, such as it exists, for chronic traumatic brain injury as a consequence of amateur boxing is not strong.

1   British Medical Association. *The boxing debate*. London: Chameleon Press, 1993.
2   BMA Board of Science Working Party on Boxing. *Second report*. 2007. www.bma.org.uk/ap.nsf/Content/BoxingPU.

3 Finch C, Da Costa A, Stevenson M, Hamer P, Elliott B. Sport injury experiences from the Western Australian sports injury cohort study. *Aust N Z J Public Health* 2002;26:462-7.

4 Clark KS. Epidemiology of athletic head injury. *Clin Sports Med* 1998;17:1-12.

5 Zazyrn T, Cameron P, McCrory P. A prospective cohort study of injury in amateur and professional boxing. *Br J Sports Med* 2006;40:670-4.

6 Blonstein JL, Medical aspects of amateur boxing. *Proc R Soc Med* 1966;59:649-52.

7 Clausen H, McCrory P, Anderson V. The risk of chronic traumatic brain injury in professional boxing: change in exposure variables over the past century. *Br J Sports Med* 2005;39:661-4.

8 Martland HS. "Punch drunk." *JAMA* 1928;91:1103-7.

9 McCrory P, Zazryn T, Cameron P. The evidence for chronic traumatic encephalopathy in boxing. *Sports Med* 2007;37:467-76.

10 Moher D, Cook DJ, Eastwood S, Olkin I, Rennie D, Stroup DF, for the QUOROM Group. Improving the quality of reports of meta-analyses of randomised controlled trials: the QUOROM statement. *Lancet* 1999;354:1896-900.

11 Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. *JAMA* 2000;283:2008-12.

12 Khan K, ter Riet G, Popay J, Nixon J, Kleijnen J, eds. *Undertaking systematic reviews of research on effectiveness*. York: University of York, 2001. (CRD Report No 4.) www.york.ac.uk/inst/crd/report4.htm.

13 Cabanis EA, Perez G, Tamraz JC, Iba-Zizen MT, Roger B, Alfonzo JM, et al. Cephalic magnetic resonance imaging of boxers. Preliminary results. *Acta Radiol Suppl* 1986;369:365-6.

14 Mawsdley C, Ferguson FR. Neurological disease in boxers. *Lancet* 1963;ii:795-801.

15 Spillane JD. Five boxers. *BMJ* 1962;ii:1205-10.

16 Roberts AJ. *Brain damage in boxers*. London: Pitman Medical Scientific Publications, 1969.

17 Critchley M. Medical aspects of boxing, particularly from neurological standpoint. *BMJ* 1957;i:357-62.

18 Unterharnscheidt F, Sellier K. Boxing. Mechanics, pathomorphology and clinical picture of traumatic lesions of the CNS in boxers. *Fortschr Neurol Psychiatr Grenzgeb* 1971;39:109-51 (in German).

19 Toth C, McNeil S, Feasby T. Central nervous system injuries in sport and recreation: a systemic review. *Sports Med* 2005;35:685-718.

20 Jordan BD, Jahre C, Hauser WA, Zimmerman RD, Zarrelli M, Lipsitz EC, et al. CT of 338 active professional boxers. *Radiology* 1992;185:509-12.

21 Jordan BD. Chronic traumatic brain injury associated with boxing. *Semin Neurol* 2000;20:179-85.

22 Roberts GW, Allsop D, Bruton C. The occult aftermath of boxing. *J Neurol Neurosurg Psychiatry* 1990;53:373-8.

23 Butler RJ. Neuropsychological investigation of amateur boxers. *Br J Sports Med* 1994;4:28.

24 Gibbs FA, Gibbs EL. *Atlas of electroencephlopathy*, 2nd ed. Reading, MA: Addison-Wesley, 1958;1:324.

25 Bogdanoff B, Natter HM. Incidence of cavum septum pellucidum in adults: a sign of boxers encephalopathy. *Neurology* 1989;87:535-605.

26 Moseley IF. The neuroimaging evidence for chronic brain damage due to boxing. *Neuroradiology* 2000;42:1-8.

27 McCrory P. Carvum septum pellucidi—a reason to ban boxers? *Br J Sports Med* 2002;36:157-61.

28 Macpherson P, Teasdale E. CT demonstration of a 5th ventricle—a finding to KO boxers? *Neuroradiology* 1988;30:506-10.

29 Phillips J, Horner B, Ohman M, Horgan J. Increased brain-type creatine phosphokinase in marathon runners. *Lancet* 1982;i:1310.

30 Grindel SH, Lovell MR, Collins MW. The assessment of sports-related concussion: the evidence behind neuropsychological testing and management. *Clin J Sports Med* 2001;11:134-43.