Chronic traumatic encephalopathy in sport: a systematic review

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ABSTRACT

Objective To provide a critical review of chronic traumatic encephalopathy (CTE) by considering the range of clinical presentations, neuropathology and the strength of evidence for CTE as a distinct syndrome.

Data sources Seven electronic databases were searched using a combination of MeSH terms and key words to identify relevant articles.

Review methods Specific inclusion and exclusion criteria were used to select studies for review. Data extracted where present included study population, exposure/outcome measures, clinical data, neurological examination findings, cognitive assessment, investigation results and neuropathology results.

Results The data from 158 published case studies were reviewed. Critical differences between the older descriptions of CTE (the 'classic' syndrome) and the recent descriptions (the 'modern' syndrome) exist in the age of onset, natural history, clinical features, pathological findings and diagnostic criteria, which suggests that modern CTE is a different syndrome. The methodology of the current studies does not allow determination of aetiology or risk factors.

Conclusions The clinicopathological differences between the 'classic' CTE syndrome and the 'modern' syndrome suggest that the new syndrome needs a different nomenclature. Further research is required to clearly define the clinical phenotype of the modern CTE syndrome and establish the underlying aetiology. Future research needs to address these issues through large-scale, prospective clinicopathological studies.

INTRODUCTION

Tremendous media attention surrounding sport-related concussion has been directed towards the potential for long-term problems in athletes with high exposure to head contact (ie, both concussive and subconcussive impacts) during a career in contact sport.[1–7] This attention has been fuelled by the publication of autopsy case studies of retired professional athletes[8–11] and research reporting increased mortality rate due to neurodegenerative diseases in former professional athletes.[12] There is also evidence from retrospective surveys[8–11] supporting an association between long-term cognitive, psychiatric[13] and neurobehavioural problems and participation in sport.

In recent years, chronic traumatic encephalopathy (CTE) has been redefined from the original condition resembling Alzheimer's disease (AD) in professional boxers to a new condition observed in athletes, military personnel and civilians that shares many features with known psychiatric disorders and other forms of dementia. At present, the lack of operational criteria to confirm either a clinical or pathological diagnosis of CTE presents a considerable limitation to understanding this condition.[14]

A number of recent reviews have been published examining a diverse range of aspects associated with CTE.[14–19] The purpose of this paper was to systematically review the evidence for CTE in sportsmen and sportswomen and to consider the important differences between the original description of CTE and the modern description of CTE.

METHODS

Articles were retrieved via online database searching, hand-searching reference lists and cited reference searches. Articles were limited to those printed in English language journals between 1850 and April 2013. The online databases searched were MEDLINE, CINAHL, EMBASE, Mosby's Index, PsycEXTRA, PsycINFO and Scopus. Key words, MeSH terms and combinations of these were used. Key words included CTE, dementia pugilistica, punch drunk syndrome, traumatic encephalopathy, CTE, repetitive head injury, sports concussion, multiple concussions, chronic concussions, subconcussive blow and sports-related traumatic brain injury. This search yielded 158 published case studies for review. Detailed information relating to demographic characteristics, athletic participation, concussion history, age of onset, clinical features, cognitive findings and neuropathological features is provided in online supplementary tables S1 and S2. The search methodology and hits are described in figure 1 using the PRISMA style.[20]

'CLASSIC' CTE IN PROFESSIONAL BOXERS

In 1928, Dr Harrison Martland, a medical examiner, presented 23 unverified cases believed to be experiencing a 'punch-drunk' state that had been described to him by a boxing promoter. He personally examined five but only described the clinical details of one in the article: a 38-year-old man who fought professionally for 7 years, having started his career at the age of 16. The boxer had sustained two knockouts (one for a duration of 1 hour). Clinical examination, 20 years after the onset of the patient's symptoms, revealed that the boxer had tremor, gait ataxia and pyramidal tract dysfunction, but possessed normal intelligence. Martland's diagnosis was 'paralysis agitans' (Parkinson's disease (PD)) in this case.[21]

The incidence of classic CTE has proven difficult to establish, mostly due to a lack of high-quality prospective studies. Roberts[22] studied 250 retired boxers from a cohort of 16 781 UK boxers, registered between 1929 and 1955, and reported that lesions of the nervous system were present in 37 cases (17% of total). It is important to note that

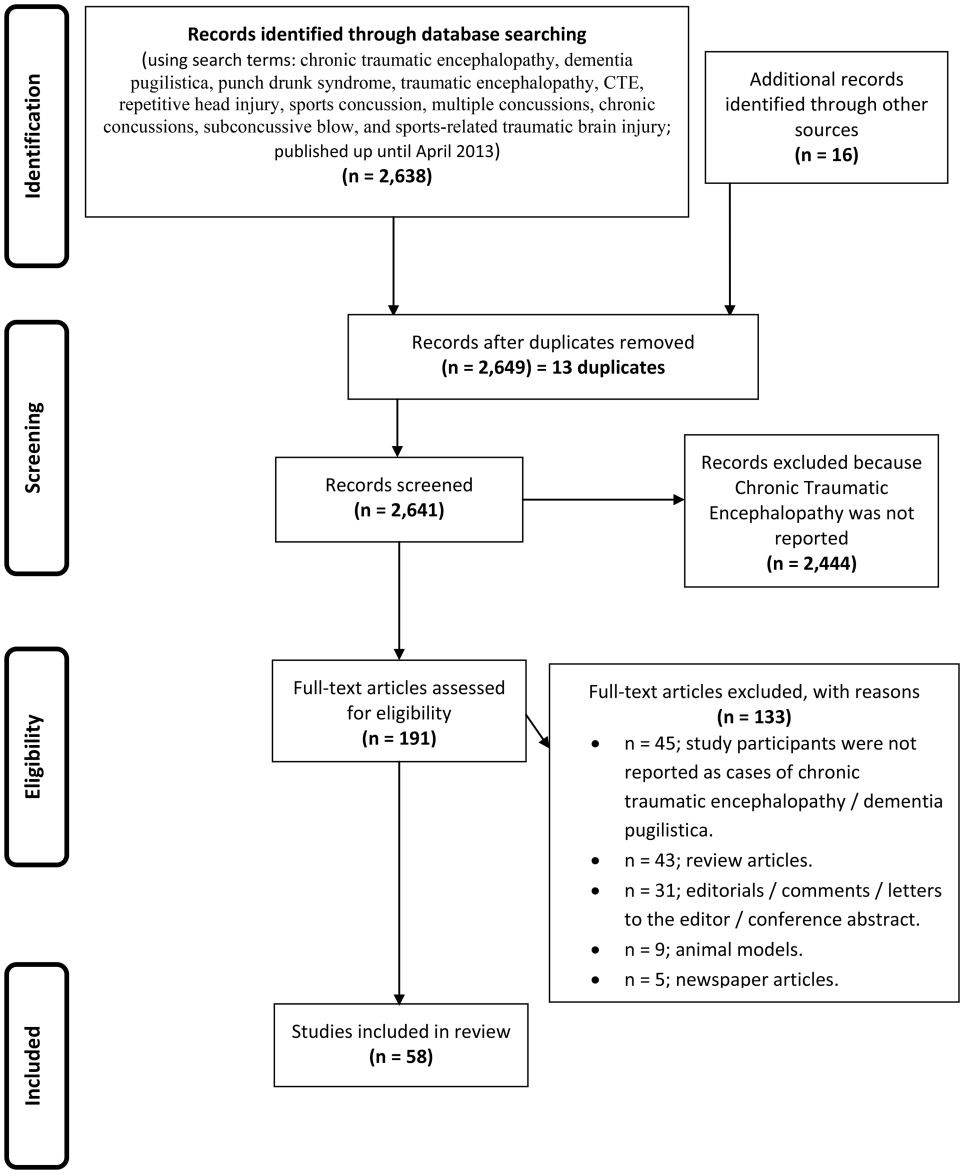

Figure 1 PRISMA flow diagram.

the oldest boxers in this cohort fought in the late 1800s, in an era where bare-knuckle championships were still conducted and there was little medical supervision or weight matching of boxers. Of the 37 cases reported by Roberts, the author provided details on only 11 (see online supplementary table S1). A careful review of the clinical details in professional boxers led McCrory *et al*[23] to question the certainty of the 'CTE' diagnosis in most cases. In part, this lack of certainty reflects the relatively crude investigational technology available in the 1960s (eg, pneumoencephalograms as the only available brain imaging modality) at the time Roberts studied these retired boxers. The rates cannot be generalised to accurately reflect the prevalence levels in modern-day boxing because the current day boxers experience reduced exposure to repetitive head trauma and increased medical monitoring preparticipation.[24]

After reviewing the published cases, McCrory[25] noted that cognitive deterioration was typically detected 10–20 years postretirement. Interestingly, the early descriptions noted that the physical signs and problems, but not the cognitive deficits, progressed postretirement. These retired athletes seemed to have one of two clinical syndromes. The first, present in about 70% of the cases, was characterised by dysarthria, pyramidal dysfunction and cognitive deficits and was not progressive. The second clinical syndrome (which was progressive) was characterised by dysarthria and pyramidal dysfunction, but with intact cognitive abilities (approximately 30% of cases).[22 26 27]

An obvious challenge in attributing all the clinical features of these syndromes solely to a career in boxing is that some retired athletes have comorbidities that can contribute to neuropsychiatric problems, such as alcohol dependence, drug abuse, apolipoprotein E genotype[28] and various medical problems. As such, clinical and autopsy cases need to be examined carefully.[29]

The neuropathology of classic CTE has been described in detail and includes (1) cavum septum pellucidum with septal fenestration; (2) cerebellar scarring involving Purkinje cell loss and thinning of the granular layer; (3) degeneration of the substantia nigra and locus coeruleus and (4) diffuse neurofibrillary tangles (NFTs) involving the medial temporal region,

uncus, amygdala, hippocampus, parahippocampal gyrus and fusiform gyrus along with the more lateral temporal, insular and frontal cortices.[30]

The neuropathological burden appears to correlate with the level of boxing exposure as measured by the duration of career and the number of bouts[30] (see online supplementary table S2). Roberts *et al*[27] re-examined 14/15 brains originally described by Corsellis *et al*,[30] as well as six additional boxers' brains using immunocytochemistry, and 19/20 cases also demonstrated widespread diffuse β-amyloid deposits and τ. Schmidt *et al*[31] found that the τ positive NFTs observed in two boxers with pathological evidence of CTE were identical in both isoform ratio and phosphorylation state to those observed in AD. These two cases continue to be the only examples of classic CTE where detailed biochemical analysis has been conducted.[14]

Classic CTE does not appear to advance in a predictable and sequential series of stages,[32 33] and progression of physical symptoms is only present in approximately one-third of cases.[22] The extent to which age-related changes, psychiatric or mental-health illness, alcohol/drug use or coexisting dementing illnesses contribute to this process is largely unaccounted for in the published literature. The case descriptions contain extensive histories of psychiatric illnesses, severe substance abuse and other medical or neurological problems that might contribute to or confound the neuropathological findings. In addition, the potential genetic risk in those former athletes with a family history of neurodegenerative disease and the extent to which this contributes to the clinical and pathological profiles also require further investigation.[23]

'MODERN' CTE

Four independent research groups have reported case studies of retired athletes believed to have CTE.[11 34–36] The original publications[37 38] introduced changes in the clinical features and the neuropathology as compared with the classic entity described by Roberts *et al*[27] and Corsellis *et al*[30] in their boxing patients. One research group defined CTE as the "chronic cognitive and neuropsychiatric symptoms of chronic neurodegeneration following a single episode of severe traumatic brain injury or (more commonly) repeated episodes of mild traumatic brain injury."[39] This subtle definitional shift makes it unclear as to whether we are now dealing with a new condition (modern CTE vs classic CTE), a variant of a single disease or another unrelated pathology (eg, frontotemporal dementia (FTD)).

The 'modern' form of CTE, since 2005, encompasses a broad spectrum of clinical symptoms and pathological findings in former athletes.[24 40] When compared with the classical CTE entity, there are differences in exposure rates, clinical presentation, cognitive and neurobehavioural features, diagnostic criteria, age of symptom onset, disease progression and putative neuropathological characteristics (see table 1). The incidence of modern CTE is unknown; it has been estimated at less than 4% of professional American football players, based on the numbers of cases obtained in a given period versus the number of athletes who died during the same period. If all of these professional athletes at risk were to be used as the exposure, then the incidence rate would be less than 0.01%.

The initial case of modern CTE was reported by Omalu *et al* in 2005, with two additional cases reported in 2006 and 2010, and further cases reported in 2011 (for review, see Refs. 9, 35, 37 and 45). Of the 17 cases reported by Omalu *et al*[35], 11 (approximately 65%) were identified as having neuropathology consistent with a diagnosis of CTE. Hazrati *et al*[34] examined the brains of six former Canadian Football League players who presented with neurological decline and three (50%) demonstrated neuropathological changes consistent with CTE; however, these cases also had vascular disease, AD and cancer comorbidities. The other three cases were diagnosed with AD, ALS and Parkinson's disease.[34] McKee *et al*[11] also reported on two retired boxers.[8] In their recent large neuropathological case series involving 85 patients, consisting of athletes (n=64, including 33 former NFL players) and military veterans (n=21), 80% showed at least some evidence of the neuropathology reported to characterise CTE (see Discussion section below).

Signs and symptoms

Although the modern CTE description describes gait disorders, speech slowing and extrapyramidal signs, neuropsychiatric and behavioural symptoms reportedly predominate early and are prominent throughout the course of the condition.[22 46 47] These neuropsychiatric symptoms include mood disorder (mainly depression), paranoia, agitation, social withdrawal, poor judgement and aggression. Cognitive impairment tends to emerge later[33 46] and typically includes impairment across the domains of orientation, memory, language, attention, information processing speed and executive functioning.[47] Less characteristic of classic CTE, cognitive impairment in modern CTE reportedly progresses over time.[8 11] Disease staging and disease phenotypes of modern CTE (table 2) have now been proposed based on the level of neuropathological evidence of disease on autopsy rather than clinical presentation.[11 35]

It may be that the description of the modern CTE symptomatology is confounded by the retrospective nature of the data collection and the heavily biased case selection. Consequently, the reported clinical observations (ie, suicidality, emotional lability, aggression and disinhibition) are likely to be skewed by selection bias.[14]

In a recent review article, Jordan[17] proposed clinical criteria for the diagnosis of CTE which classified clinical features into four categories in line with other neurological diseases: definite, probable, possible and improbable CTE. He recommended that, in light of the lack of currently available biomarkers to observe the natural history of CTE, characterisation of preclinical and prodromal CTE (similar to the preclinical phases that have been documented in AD) is premature.[17]

IS THERE A PRECLINICAL CTE STATE?

Although no longitudinal studies have been performed describing the clinical phenotype or the progression of neuropathology, there is evidence from retrospective surveys supporting an association between participation in elite sport and long-term cognitive, psychiatric and neurobehavioural problems.[8–11 48 49] In many cases, the causes for these outcomes are multifactorial and numerous methodological confounds exist. However, there is some neurophysiological and radiological evidence suggesting that persistent or prolonged disturbance of the brain function may occur following concussive injury.[44 50–54] Preliminary data in a small positron emission tomography imaging study suggest that subcortical and amygdala τ deposition was detected in vivo in five retired American football players who exhibited mood and cognitive symptoms.[55] It is possible that a subgroup of athletes exhibit persistent clinical or physiological dysfunction with associated neuropathology.

Neuropathology

Of the 61 pure athlete (with only a background in sport) cases reported by McKee *et al*,[11] 15 (or 25%) demonstrated no pathological features of CTE (cases: 19–32, 34), 4 (approximately 7%) also fulfilled criteria for an AD diagnosis (cases: 87,

Table 1 Features of classic versus modern CTE

Characteristic	Classic CTE	Modern CTE
Number of reported cases	Approximately 250 (11 detailed)[27] Approximately 15[30] Approximately 10[41] Approximately 6[42] Approximately 3[43]	85 (17 not considered CTE pathology)[8 11] 17 (6 not considered CTE pathology)[35]
Age of onset	Late 50s—early 60s[22]	Staging of the disease[11] Stage I: 22.2 years (SD=5.6 years) Stage II: 39.0 years (9.3 years) Stage III: 44.3 years (10.7 years) Stage IV: 57.2 years (15.4 years) Early 40s[35]
Age at death range (mean)	57–91 years[30]	14–98 years (mean: 54.1 years±23.3 years)[11] 18–52 years (mean: 41 years)[35]
Exposure	60–700+ bouts and/or 7–25 years' boxing[27] >50% of sample had 300+ bouts and/or 15 years' boxing. A number of cases also fought in an unknown number of booth contests[30]	5 and 24 years as a professional boxer; unreported number of bouts & 48 professional bouts, respectively[8]; otherwise unreported career lengths/exposure; primarily American football, hockey, and military exposure[11]; No data on the career lengths/exposure; level of play—high school, collegiate and NFL football; professional boxing; wrestling; MMA[35]
Progression	30% progress—physical symptoms may progress	Yes, mean 18.6 years[8]; Yes; noted in first three cases, but no progression reported in other cases[35]
Clinical features	Dysarthria, movement difficulties (slowing and 'unsteady on feet'), tremor, later onset of memory problems, alcohol sensitivity	Neuropsychiatric and behavioural symptoms prominent. Cognitive deficits and dementia with progression
Genotype risk	ApoE 4[28]	No ApoE 4 genotype risk[11]
Diagnosis	Clinically: clinical assessment and limited radiological evaluation[27 30]	Neuropathologically confirmed on autopsy
Classic neuropathology	Septal fenestration, cerebellar scarring (inferior surface of the lateral lobes), degeneration of the substantia nigra and locus coeruleus, diffuse neurofibrillary tangle inclusion (medial temporal region, uncus, amygdala, hippocampus, parahippocampal gyrus, fusiform gyrus, lateral temporal, insular and frontal cortices). NFTs spread diffusely through the cerebral cortex and brainstem, with vast concentrations in the medial temporal grey, uncus, corticomedial part of the amygdala nucleus, hippocampus, parahippocampal nucleus, fusiform gyrus, lateral temporal area, insula and frontal cortex, with an absence of senile plaques[30]	
Modern neuropathology	Contingent upon stage of disease: Stage I: mild lateral ventricular enlargement, focal epicentres of perivascular p-τ NFTs and astrocytic tangles (prominent in the sulcal depths and superior in the dorsolateral frontal cortices), rare isolated NFTs in the superficial laminae; low density NFTs in the locus coeruleus (2/7 cases); TDP-43 in the frontal subcortical white matter and fornix (4/7 cases) Stage II: mild enlargement of the frontal horn of the lateral ventricles or third ventricle (6/11 cases), a small cavum septum (4/11 cases), the third ventricle was enlarged and slightly concave (3/11 cases), pallor of the locus coeruleus and substantia nigra (3/11 cases), severe gliosis and atrophy of one mamillary body (1/11 cases), p-τ pathology commonly in the superior, dorsolateral, lateral, inferior, and subcallosal frontal; anterior, inferior, and lateral temporal; inferior parietal; insular and septal cortices. NFTs in the superficial layers of the cortex, moderate density in tge locus coeruleus, nucleus basalis of Meynert, and amygdala, low densities p-τ NFTs in the hypothalamus, CA1 hippocampus, entorhinal cortex, thalamus, substantia nigra, dorsal and medial raphe nuclei of the midbrain, distorted axonal varicosities in the frontal and temporal cortices and white matter tracts, TDP-43 present (11/14 cases), found in the cerebral subcortical white matter, brainstem or medial temporal lobe (8/14 cases), severe TDP-43 (3/14 cases) Stage III: mild cerebral atrophy with dilation of the lateral and third ventricles, septal abnormalities (5/12 cases), ranging from the cavum septum, septal perforation or absence, moderate depigmentation of the locus coeruleus (7/12 cases), mild depigmentation of the substantia nigra (6/12 cases), atrophy of the mamillary bodies, thalamus, sharply convex contour of the medial thalamus, thinning of the hypothalamic floor and thinning of the corpus callosum, NFTs widespread throughout the superior frontal, dorsolateral frontal, inferior orbital, septal, insular, temporal pole, superior middle and inferior temporal, and inferior parietal cortices, extensive NFTs in the hippocampus, entorhinal cortex, amygdala, nucleus basalis of Meynert and the locus coeruleus, frequent NFTs in the olfactory bulbs, hypothalamus, mamillary bodies, substantia nigra and dorsal and dorsal motor nucleus of the vagus, dentate nucleus of the cerebellum and spinal cord, severe axonal loss and distortion in the frontal and temporal cortices, TDP-43 in the cerebral cortex, medial temporal lobe or brainstem of most cases, more widespread in three cases Stage IV: atrophy of the cerebral cortex and white matter, marked in the medial temporal lobe, thalamus, hypothalamus and mamillary bodies, ventricle enlargement, sharp concave contour of the third ventricle, cavum septum pellucidum, septal perforations or absence, pallor of the locus coeruleus and substantia nigra, striking neuronal loss in the cortex, hippocampal sclerosis affecting the CA1 and subiculum and astrocytic p-τ, p-τ abnormalities throughout the cerebrum, diencephalon, basal ganglia, brainstem and spinal cord, dense TDP-43 in the cerebral cortex, medial temporal lobe, diencephalon, basal ganglia, brainstem and, less frequently, the spinal cord	

CTE, chronic traumatic encephalopathy; NFTs, neurofibrillary tangles; p-τ, phosphorylated τ protein.

89, 91, 92), 4 (approximately 7%) possessed Lewy bodies (cases: 92, 95, 96, 97), 3 (or approximately 5%) demonstrated FTD pathology (cases: 100, 102, 103) and 3 (approximately 5%) showed evidence of PD (cases: 91, 100, 101). Of these 'pure athlete' cases, only 15 (approximately 25%; cases: 36, 39, 41, 43, 45, 50, 52, 58, 60, 63, 64, 67, 68, 72, 77) had 'pure CTE pathology' (defined as having any clinical symptoms and pure pathology (with TPD-43+ as a minimum), and the absence of any other neurodegenerative disease and/or no other non-CTE neuropathology). However, within these 15 'pure athlete, pure CTE' cases, there was not always a consistent association between pathology and clinical presentation (eg, cases 43 and 68 were initially considered to be asymptomatic and only subsequently reported to have neurobehavioural features; and case 36's only symptom was a headache).

When both athlete and military cases were considered, CTE was the sole diagnosis in 43 cases (or approximately 70%), with a greater proportion of these 'pure CTE' cases represented in stages III and IV disease, where a more florid pathology has been reported.[11] The pathophysiological hallmark of these cases

Table 2 Histopathological classification of modern CTE

BU CSTE criteria—four stages of disease[11]	Omalu *et al*—four phenotypes[35]
Stage 1 Normal brain weight. Focal epicentres of perivascular p-τ and NFTs and astrocytic tangles involving the sulcal depths and typically affecting the superior and dorsolateral frontal cortices	Phenotype I Sparse to frequent NFTs and neuritic threads in the cerebral cortex and brainstem but without involvement of the subcortical nuclei (basal ganglia) and cerebellum. No diffuse amyloid plaques in the cerebral cortex
Stage 2 Normal brain weight. Multiple epicentres at the depths of the sulci with localised spread from epicentres to the superficial layers of the adjacent cortex. No NFTs or p-τ involvement in the medial temporal lobe	Phenotype II Sparse to frequent NFTs and neuritic threads in the cerebral cortex and brainstem with or without such pathology in the subcortical nuclei (basal ganglia) and cerebellum. Diffuse amyloid plaques in the cerebral cortex
Stage 3 Mild reduction in brain weight. Mild cerebral atrophy with dilation of the lateral and third ventricles. Septal abnormalities. Moderate depigmentation of the locus coeruleus and mild depigmentation of the substantia nigra. Atrophy of the mamillary bodies and thalamus. Widespread p-τ pathology in the frontal, insula, temporal and parietal lobes. NF pathology in the amygdala, hippocampus and entorhinal cortex	Phenotype III Brainstem predominant: moderate to frequent NFTs and neuritic threads in the brainstem nuclei, absent or sparse NFTs and neuritic threads in the cerebral cortex, subcortical nuclei (basal ganglia) and cerebellum. No amyloid plaques in the cerebral cortex
Stage 4 Marked reduction in brain weight with atrophy of the cerebral cortex. Marked atrophy of the medial temporal lobe, thalamus, hypothalamus and mamillary bodies. Severe p-τ pathology affecting most regions of the cerebral cortex and the medial temporal lobe, sparing the calcarine cortex. Severe p-τ pathology in the diencephalon, basal ganglia, brainstem and spinal cord. Marked axonal loss of subcortical WM tracts	Phenotype IV Absent or sparse NFTs and neuritic threads in the cerebral cortex, brainstem, and subcortical nuclei (basal ganglia). No cerebellar involvement. No diffuse amyloid plaques in the cerebral cortex

CTE, chronic traumatic encephalopathy; LC, locus coeruleus; NF, neurofibrillary; NFTs, neurofibrillary tangles; p-τ, phosphorylated τ; SNr, substantia nigra; WM, white matter.

is the presence of regionally specific τ-immunoreactive NFTs, astrocytic tangles and neuropil neurites observed in both the cortical and subcortical regions.[8 11]

The reported neuropathological characteristics of both entities (classic and modern CTE) share a number of common features such as fenestrated septum pellucidum, cerebral atrophy, NFT inclusion (although found in greater amounts in modern CTE), β amyloid deposition (found in greater amounts in classic CTE), reduced pigmentation of the substantia nigra and locus coeruleus and enlarged ventricles. Modern CTE in the latter stages also includes frontotemporal lobe atrophy with extensive τ pathology and TDP43+ distributed throughout the neocortex, medial temporal lobe, diencephalon, brainstem and spinal cord (see online supplementary table S2). A comparison of TDP-43 pathology with the classic CTE cases is not possible because detailed TDP-43 studies have not been performed on the classic CTE cases. Gavett *et al*[56] reviewed 51 cases that included both classic and modern CTE patients and noted that diffuse amyloid plaques were found in 47%, neuritic amyloid plaques in 27% and amyloid angiopathy in 6%. Similar findings were noted by McKee *et al*.[11]

Although many similarities in neuropathological findings have been reported by the two primary research groups studying CTE, there are also some differences. McKee *et al*[8 11] reported a marked accumulation of τ-immunoreactive astrocytes as a hallmark feature, but this was not observed in the cases examined by Omalu *et al*.[35] Omalu *et al*[35] reported a lobar cortical distribution but not a prominent periventricular topographic distribution, whereas McKee *et al*[8] noted that the initial pathological changes were perivascular and at the base of the sulci and in the later stages were primarily affecting the frontotemporal regions. Both groups have attempted to provide a pathological classification of modern CTE. McKee and colleagues have classified CTE into four stages, while Omalu and colleagues have described four phenotypes of CTE (see table 2).

BRAIN PATHOLOGY IN NORMAL AGEING

Longitudinal aging studies provide unique and important information relating to clinical features, neuropathology and the relation between clinical features and neuropathology. For example, during the Honolulu-Asia Aging Study,[57] follow-up clinical and neuropsychological evaluations have been conducted with 3508 men who were free of dementia at the study onset and a total of 593 brain autopsies have been completed to date (for review see Ref. 58).

Postmortem brain examinations demonstrate diverse pathology. For example, in older adults clinically diagnosed as 'pure AD', fewer than 50% of these people had the typical pathological features of AD. Moreover, neuropathological abnormalities are found in approximately 40% of neuropsychologically normal patients.[58–60] Similar differences between the clinical presentation (ie, living diagnosis) and postmortem neuropathology have also been reported in other aging study samples.[57 61 62] For example, the Nun Study is a longitudinal study of aging and AD in 678 Catholic sisters. The participants were aged 75–102 years at the beginning of the study in 1991.[63 64] Interestingly, results from this study have revealed that a substantial proportion of the nuns who demonstrated mild (58%) and moderate (32%) stages of AD neuropathology did not show evidence of memory impairment. Even in the nuns with the most severe expression of AD neuropathology, a small percentage (8%) did not demonstrate memory impairment.[63] Further, the Framingham Heart Study, which has recruited three generations of families in a longitudinal study, reported 75% sensitivity (27/36 patients with pathologically verified AD were clinically diagnosed with AD) and 92.9% specificity (52/56 patients without AD were correctly identified as not having AD).[65]

In a recent study of former NFL players,[12] the mortality rate from neurodegenerative disease was three times greater than that of the general population. However, the sample size in this study was small with only two cases of AD and six ALS cases in the total sample of 334 cases. Although this is an intriguing observation, the study lacked power to be definitive.

It is clear from these aging studies that neuropathological abnormalities are not necessarily correlated with clinical features and may be seen in cognitively normal older adults. Therefore, assumptions regarding causal relationships between neuropathology and clinical presentation should proceed

cautiously, with careful consideration for methodological limitations, moderating variables and possible alternative explanations (see online supplementary table S2 in the article by Nelson *et al*[66]). Clinicopathological correlations will be more reliable after using matched control observations and adequately sized series.[14]

DISCUSSION

We identified 158 autopsy cases in the literature that have been examined for CTE. There are important differences in the modern version of CTE, described in recent autopsy cases, and the classic description of 'dementia pugilistica' that create confusion in the understanding of these conditions. There are critical differences in age of onset, progression, clinical features, pathological findings and diagnostic criteria that suggest we might be dealing with two or more conditions. Of the 85 autopsies that have been performed in athletes over the past 10 years, 20% had 'pure' neuropathology consistent with CTE, 52% had CTE plus other neuropathology, 5% had neuropathology but no CTE and 24% had no neuropathology (see table 3).

Although the clinical phenotype is not yet clarified, CTE is characterised by distinct neuropathological findings.[8 11 35 56] The distribution of τ-immunoreactive astrocytes distinguishes the modern CTE entity, with preferential involvement of the superficial cortical layers occurring on a background of relative scarcity of β-amyloid plaques, which is more characteristic of the classical CTE entity. The unique characteristic of modern CTE appears to be the location of the neuropathology, in the grey matter and perivascular space at the depth of sulci, moreso than the specific proteins or lesion types. These findings however, need to be independently verified.

In light of the currently available evidence, a conservative operational definition for the modern CTE disease process is provided below.

1. A presenting clinical profile that includes (but is not limited to) cognitive (eg, attention and memory) and mental health problems.
2. Neuropathology that includes only the neurofibrillary phosphorylated-τ and TDP-43+ observed in the characteristically described regional pattern, in the absence of other neuropathology such as amyloid and α-synuclein.
3. The absence of any other disease or disorder that may conceivably explain the clinical or pathological findings.

In elderly patients, it is important to appreciate that neuropathological comorbidity is very common, and this can influence the clinical features. In AD, more than two-thirds of patients demonstrate neuropathological comorbidities including cerebrovascular diseases, synucleinopathies, tauopathies, frontotemporal lobar degeneration and TDP-43—related diseases (see Ref. 66, p. 373). These findings have the potential to skew correlations between neuropathological findings and clinical or cognitive features. In the recent publication of CTE cases, 80% demonstrated CTE; of those cases 63% were pathologically diagnosed with 'pure CTE' and the remaining 37% possessed pathological comorbidity.[11]

Table 3 Modern CTE neuropathology in athletes

	McKee	Omalu	Hazrati	NIH	Total	Per cent
Number of autopsy cases	61	17	6	1	85	–
Pure CTE neuropathology	15	2	0	0	17	20.0
CTE + other neuropathology	31	9	3	1	44	51.8
Neuropathology but no CTE	0	1	3	0	4	4.7
No neuropathology	15	5	0	0	20	23.5

CTE, chronic traumatic encephalopathy; CTE+, CTE and other neuropathology; NIH, National Institutes of Health.

At present, a diagnosis of CTE can only be made postmortem. The spectrum of neuropathology in cognitively intact older adults and older adults with neurological problems is often diverse, not unitary, which adds methodological complexity to clincopathological correlational studies. In the various case series presented to date, 20–50% of those with clinical features did not show the neuropathology of CTE, and 5% of those with the neuropathology did not show clinical features.

Furthermore, the clinical phenotype of modern CTE is unclear. The reported clinical features are tremendously broad, ranging from an isolated symptom of headache to severe neuropsychiatric illness and dementia. The clinical features overlap with a number of known psychiatric conditions and neurodegenerative diseases. The recent characterisation of CTE[39] does not adequately consider plausible differential diagnoses, mediating variables, moderating variables or multifactorial neuropathological processes.

At present, there are no published epidemiological, cross-sectional or prospective studies relating to CTE. The classical entity[22] was estimated to occur in approximately 17% of the exposed populations (this may be an overestimate given the diagnostic uncertainty) and it has been suggested that modern CTE occurs in fewer than 5% of professional American football players[67]—although the actual prevalence is unknown.

The strongly presented causal assumptions in the literature relating to concussive and subconcussive brain impact exposure derived from the case studies are scientifically premature, especially given the absence of cross-sectional, epidemiological, prospective or longitudinal studies on the topic. The recently published case series[11] adds considerably to the knowledge base relating to the neuropathology of CTE. In view of the relatively limited number of cases examined, together with the potential case-selection bias in autopsy-based studies, in addition to the limitations associated with verifying clinicopathological correlation, further research is required in order to better delineate this putative disease process.

It is important to conduct systematic research in the area to address specific unanswered questions. First, it is not known whether similar, or even identical, neuropathological findings are observed in other samples that share clinical characteristics with CTE such as patients with drug or steroid abuse, alcohol abuse histories, chronic psychiatric problems, cardiovascular/cerebrovascular disease or other health conditions. Second, the extent to which the reported underlying neuropathology contributes to the reported clinical features (eg, cognitive deficits, psychiatric features) is uncertain. Third, the potential existence of a genetic contribution to the observed neuropathology has not been determined. Fourth, possible mediator or moderator variables for the association between the neuropathology and the clinical features have not been identified. Finally, we do not have a methodology for identifying individuals who are at future risk or who might currently have CTE. Psychiatric problems and cognitive impairment usually have multifactorial, not unitary causation—this will require further attention in future studies. The important next step in the process of potentially answering some of the unresolved issues associated with CTE is to conduct large-scale, prospective, longitudinal, clinicopathological studies.

What are the new findings?

- The definition of chronic traumatic encephalopathy (CTE) has changed from the original 'classic' description seen in boxers.
- The clinical phenotype of CTE is unknown and cannot be diagnosed in vivo.
- A large scale prospective, longitudinal clinicopathological study is required to answer some of the currently unresolved issues associated with CTE.

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Contributors All authors were involved in the design, analysis and writing of the manuscript and each author had the right of veto over the publication.

Competing interests AG has a clinical practice in neuropsychology involving individuals who have sustained sports-related concussion (including current and former athletes). He has received travel funding from the Australian Football League (AFL) to present at a Concussion in Football Conference in 2013. Previous grant funding includes the NSW Sporting Injuries Committee, the Brain Foundation and the Hunter Medical Research Institute, supported by Jennie Thomas. GI, PhD has been reimbursed by the government, professional scientific bodies and commercial organisations for discussing or presenting research relating to mild TBI and sport-related concussion at meetings, scientific conferences, and symposiums. He has a clinical and consulting practice in forensic neuropsychology involving individuals who have sustained mild TBIs (including professional athletes). He has received research funding from several test publishing companies, including ImPACT Applications, Inc, CNS Vital Signs and Psychological Assessment Resources (PAR, Inc). He is a coinvestigator, collaborator or consultant on grants relating to mild TBI funded by several organisations, including, but not limited to, the Canadian Institute of Health Research, Alcohol Beverage Medical Research Council, Rehabilitation Research and Development (RR&D) Service of the US Department of Veterans Affairs, Vancouver Coastal Health Research Institute and Roche Diagnostics Canada. PMC currently receives financial research support from the National Health and Medical Research Council, the University of Melbourne, Victorian Department of Planning and Community Development, Sport and Recreation Division and the Eastern Health Network. Previous competitive grant funding includes the Australian Research Council, International Rugby Board, the University of Melbourne, the University of Otago (NZ), National Hockey League (USA), VicHealth, Australian Football League Research Foundation, Royal Australasian College of Surgeons and the Australian Sports Commission. He has a clinical and consulting practice in neurology and sports medicine involving individuals who have sustained concussion and TBI. He has received travel funding from the Medical Commission of the International Olympic Committee (IOC), the International Football Federation (FIFA), the American Academy of Neurology and the Jockey Club (UK). He receives book royalties from McGraw-Hill and from 2001–2008 was employed by the British Medical Journal Publishing Group. He has conducted clinical drug trials on anti migraine (Glaxo-Welcome; Janssen-Cliag; Novartis; Parke-Davis; Schering) and antispasticity drugs (Ipsen) through the Eastern Health Clinical Trials Unit in Melbourne. This drug trial work has not involved any financial payment to PMC directly. He received consultancy fees in 2010 from Axon Sports (USA) for the development of educational material (which was not renewed) and has received support since 2001 from CogState Inc for research costs and the development of educational material. He is a cofounder and shareholder in two biomedical companies (involved in eHealth and Compression garment technologies) but does not hold any individual shares in any company related to concussion or brain injury assessment or technology.

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Table 1. Cases of reported chronic traumatic encephalopathy exposure, clinical descriptions, and cognitive findings.

Case No.	Source [Reference]	Sport / Activity	Age	Exposure				Age and Symptom Onset Clinical Description / Symptoms Reported Cognitive Findings	Pathology Reported[§]
				Age Started	Years of Participation	Level of Play	Number of Concussion(s) & Concussion Severity		
1	Case 1 [Roberts 1969]	Boxing	60	15	13 (200 bouts)	P, B	Number: 0 Severity: N/A	Age and Onset: 29yrs Clinical Features: Slurred speech, left arm tremor, limping left leg, paranoid delusion, Parkinsonian resting tremor (L), slowed movements, markedly akinetic, euphoric. Cognitive Findings: Lacks insight, poor memory, demented (slowed thinking, inability to register).	No
2	Case 2 [Roberts 1969]	Boxing	50	12	10 (80 bouts)	P, B	Number: 0, 3 TKOs Severity: N/A	Age and Onset: 22yrs Clinical Features: Slurred speech, unsteady on feet, increasingly insensitive to alcohol, 10yrs post progressively worsening tremor, outbursts of uncontrollable temper, emotionally labile, Parkinsonian tremor. Cognitive Findings: Not conducted	No
3	Case 3 [Roberts 1969]	Boxing	58	14	15 (300+ bouts)	P	Number: 1 Severity: NR	Age and Onset: 30yrs Clinical Features: Speech abnormalities (past 10+ yrs), mild degree of ataxia, slow movement, terminal intention tremor. Cognitive Findings: Mentation was extremely slow, cerebellar dysarthria.	No
4	Case 4 [Roberts 1969]	Boxing	48	9	13 (300 bouts)	P, B	Number: 0, 7'al TKOs Severity: N/A	Age and Onset: NR Clinical Features: Alcohol intolerance, slurred speech, expressionless face, inconstant rhythmic Parkinsonian tremor in right arm. Cognitive Findings: Intact	No
5	Case 5 [Roberts 1969]	Boxing	53	15	10 (96 bouts)	P	Number: 2, 7'al TKOs Severity: NR	Age and Onset: Neurology report aged 33 years; slurred speech, headaches, memory difficulty, & depression. Diagnosed with punch drunk & discharged from military service. Clinical Features: Chronic alcoholic, apathetic, slurred speech, mentation slow. Cognitive Findings: Not conducted	No
6	Case 6 [Roberts 1969]	Boxing	57	17	10 (110 bouts)	P, B, SP	Number: 4 Severity: NR	Age and Onset: 27yrs Clinical Features: Dribbled & slurred speech, unsteady gait, mining accident exacerbated his problems; increasingly irritable & liable to outbursts of anger, paranoid delusion, euphoric. Cognitive Findings: Demented, disoriented to time & place, mentation markedly slow.	No
7	Case 7 [Roberts 1969]	Boxing	57	12	9 (150 bouts)	P, B	Number: 0 Severity: N/A	Age: NR Clinical Features: Slurred speech, mild truncal ataxia and unsteady gait, drag left foot. mTBI exacerbated his difficulties. Cognitive Findings: Intact	No
8	Case 8 [Roberts 1969]	Boxing	45	17	13 (137 bouts)	P	3 NR	Age: NR Clinical Features: Slurring dysarthria, expressionless face, forgetful, mild euphoria, slow movements. Cognitive Findings: Intact	No
9	Case 9 [Roberts 1969]	Boxing	58	19	NR (250+ bouts)	P	3 NR	Age and Onset: "Many years" Clinical Features: Slurred speech, dibbled, unsteady on feet and falls, poor memory. Cognitive Findings: Intact	No
10	Case 10 [Roberts 1969]	Boxing	35	11	NR (70 bouts)	P, B	1 NR	Age and Onset: N/A Clinical Features: N/A Cognitive Findings: Intact	No
11	Case 11 [Roberts 1969]	Boxing	39	17	7 (60 bouts)	P, B, SP	3 NR	Age and Onset: Licence not renewed at 24yrs Clinical Features: Dysarthric, very slow cerebration. Cognitive Findings: Poor memory	No
12	Case 1 in McKee et al 2009 [Brandenburg & Hallervorden	Boxing	51	17	11	Unknown	Unknown Unknown	Age and Onset: 38yrs; memory & speech Clinical Features: Personality/behaviour change - agitation'; 'Movement abnormalities: Parkinsonism, slowed speech' Cognitive Findings: Retrospective reports: memory loss, dementia	Yes

Case No.	Source [Reference]	Sport / Activity	Age	Exposure				Age and Symptom Onset Clinical Description / Symptoms Reported Cognitive Findings	Pathology Reported[§]
				Age Started	Years of Participation	Level of Play	Number of Concussion(s) & Concussion Severity		
	1954] *								
13	Case 2 in McKee et al 2009 [Grahmann & Ule 1957] *	Boxing	48	15	14	Unknown	Unknown Unknown	Age and Onset: 36yrs; euphoria & dementia Clinical Features: Personality/behaviour change - dysphoria; 'Movement abnormalities: Parkinsonism, slowing, ataxia.' Cognitive Findings: Retrospective reports: memory loss, dementia	Yes
14	Case 3 in McKee et al 2009 [Neubuerger et al 1959]	Boxing	53	14	23 (150 bouts)	P, B	Number: KO'd 30 times Severity: NR	Age and Onset: 46yrs; tense, tremulous, suspicious, and irritable, with some “delusory phenomena”. Clinical Features: Four years after initial presentation, he returned complaining of persistent bilateral frontal and temporal headaches. From the age of 50 to 53, he was observed frequently, continuing to complain of headaches, occasional blackout spells, and tremulousness. Intermittent fine, rapid tremor of the head and neck, which occasionally spread to the arms, particularly the right. A slight increase in tone was noted in the right arm, along with some decrease in ability to perform rapid alternating movements. The electroencephalogram showed intermittent bursts of 4- to 5-second slow waves, with or without sharp waves, apparently originating in the left temporal area. Cognitive Findings: Simple tests of mental function showed inability to recall five digits forward, to subtract 7 from 100 serially, to perform any but the simplest calculations, and to recall presidents and dates of world wars. Psychological tests revealed loss of immediate recall and of the ability to learn new tasks. The full-scale intelligence performance was 84.	Yes
15	Case 4 in McKee et al 2009 [Neubuerger et al 1959]	Boxing	58	18	7 (10 bouts)	P	Number: NR Severity: NR	Age and Onset: 48yrs Clinical Features: He retired age 24yrs because of a "paralysed left side," but tried an unsuccessful comeback one year later. In the year following a cholecystectomy he became forgetful, confused, irritable, and moody. At this time the Mayo Clinic, documented that he was an affable, alert, restless patient, disoriented as to time and place, able to perform only the simplest calculations, and unable to find his way about Rochester unescorted. He showed an ataxic gait, decreased speed of motion in the left hand, increased tendon reflexes, and extensor plantar reflexes on the left. The impression was "psychotic reaction—the result of organic brain disease—most likely in the nature of a traumatic encephalopathy (punch drunk)". He deteriorated progressively, several hospitalizations were necessary because of confusion, hyperactivity, loquaciousness, and "nervous breakdown." He died of progressive pulmonary insufficiency, having required oxygen continuously for the last few months of his life. Cognitive Findings: NR	Yes
16	Case 5 in McKee et al 2009 [Courville 1962]	Boxing	49	Unknown	4	P	Number: NR Severity: NR	Age and Onset: Age NR, Clinical Features: Confusion, memory difficulty, & "erratic behaviour. Cognitive Findings: NR	Yes
17	Case 6 in McKee et al 2009 [Mawdsley & Ferguson 1963], Case 1	Boxing	54	14	19 (250 bouts)	P	Number: KO'd 4 times Severity: He was badly beaten on several occasions, and after one bout had a period of amnesia lasting 12 hours.	Age and Onset: 30yrs slurred speech, difficulty sleeping at night, and increasing lethargy and drowsiness during the day. Clinical Features: Shortly after retirement unsteady gait and clumsy with his hands, fastening laces and buttons and writing became difficult. His speech and gait slowly deteriorated. In his youth he had been aggressive, and throughout his boxing career was a heavy drinker. He is still prone to outbursts of rage and violence but drinks little alcohol, because small amounts aggravate his ataxia. At 34yrs he was discharged from the Army on psychiatric grounds. Between the ages of 37 and 44 he was admitted to mental hospitals on three occasions after episodes of violence. His speech was slurred; his gait was ataxic. The CSF was normal. EEG was within normal limits. Lumbar air-encephalography showed generalised dilatation of the ventricular system. Cognitive Findings: Progressive deterioration in his memory over the past 20yrs. Clinical and psychometric evidence of dementia with a distinct defect of retentive memory. Falling off in his social habits, and slovenliness of his dress.	No

Case No.	Source [Reference]	Sport / Activity	Age	Exposure				Age and Symptom Onset Clinical Description / Symptoms Reported Cognitive Findings	Pathology Reported[§]
				Age Started	Years of Participation	Level of Play	Number of Concussion(s) & Concussion Severity		
18	Case 7 in McKee et al 2009 [Mawdsley & Ferguson 1963], Case 2	Boxing	58	16	21 (500bouts) then >1000 booth fights	P, B	Number: Never KO'd but received many beatings with fights stopped due to helpless state. Severity: NR	Age and Onset: Retired aged 36yrs because his legs were becoming unsteady. Clinical Features: Unsteadiness of gait slowly worsened following onset. At 38yrs onset of slurred speech, with an onset of hand tremor 2 years later. His speech was dysarthric and monotonous, his gait distinctly ataxic. His facial expression was fixed, and he showed a constant, coarse tremor of the arms and hands which was more obvious on the right. Tone was increased in his arms and legs. Finger movements were clumsy. Plantar responses were flexor. Clinical exam: CSF was normal; EEG was abnormal; cavum septi pellucidi; the two leaves were widely separated and faintly defined. Cognitive Findings: A gross defect of retentive memory which was confirmed on psychometric testing.	No
19	Case 3: Mawdsley & Ferguson 1963	Boxing	69	16	13 (100 bouts - lost 40)	P, SP	Number: 4 Severity: NR	Age and Onset: 50yrs: memory deterioration Clinical Features: Severe memory issues for recent events. He became increasingly depressed and irritable, and was apt to fall asleep during the day and to have occipital, throbbing headaches almost daily. Speech and gait were normal. Cognitive Findings: Clinical testing showed grossly defective memory, which was confirmed by psychometry.	No
20	Case 4: Mawdsley & Ferguson 1963	Boxing	57	15	10 (204 bouts) then >1000 fights in booths	P, B, SP	Number: Not KO'd, though several TKOs Severity: NR	Age and Onset: NR Clinical Features: Retired aged 24yrs due to a grand-mal convulsion. Continued suffering fits at intervals of a few days; their frequency gradually decreased, but continued at a rate of one major attack each month. Occasional paranoid hallucinatory states which were accompanied by clouding of consciousness and usually followed a series of grand-mal fits. Fine nystagmus on lateral deviation of the eyes and severe impairment of fine hand movements. The CSF contain 50mg of protein per 100 ml. EEG beyond normal limits. The lateral ventricles were greatly dilated. Cognitive Findings: In the past 3 years his wife noticed deterioration in his memory. A gross defect of retentive memory was apparent clinically, and psychometric testing showed evidence of intellectual deterioration.	No
21	Case 5: Mawdsley & Ferguson 1963	Boxing	55	15	7 (100 bouts) then booths & sparring partner until 30yrs age	P, B, SP	Number: KO'd once but regularly beaten Severity: NR	Age and Onset: 30yrs: right hand tremor Clinical Features: Tremor slowly increased in amplitude, and his writing steadily deteriorated. At 35yrs his gait became unsteady and his speech became slurred. These symptoms have progressed. He then began to show defects of memory and developed paranoid delusions requiring psychiatric hospitalisation on two occasions. He was grossly dysarthric; his gait was spastic and ataxic - a constant "pill-rolling" tremor of both hands at rest and gross intention tremor on purposive movements of the right arm. CSF was normal. The EEG showed slight abnormalities. Air encephalography demonstrated dilated lateral ventricles, cerebral sulci were widened and excess of air in the subarachnoid space overlying the cerebral hemispheres. There was a cavum septi pellucidi with two clearly defined leaves, well separated. Cognitive Findings: There was clinical and psychometric evidence of dementia and gross memory defect.	No
22	Case 6: Mawdsley & Ferguson 1963	Boxing	55	12	19 (90 + 320 bouts)	P	Number: 12 Severity: 12 times protracted amnesia post-fight	Age and Onset: 33yrs: left arm and hand became weak and unsteady. Clinical Features: At age 50yrs his wife noticed slurring of his speech and unsteadiness of his gait. His writing slowly deteriorated. During the past 4 years, on seven occasions he lost consciousness for 30 to 45 minutes. Facial expression was "fixed" and Parkinsonian, and his speech was dysarthric. He had an ataxic gait. There was sustained nystagmus on lateral deviation of the eyes and restriction of upward gaze. Tone was increased in the left arm and leg. Fine movements of the left hand were clumsy, and there was gross intention tremor on purposive movements of the left arm. CSF was normal. EEG showed slight abnormalities. Lumbar air-encephalography showed slight dilatation of the lateral ventricles. The cerebral sulci were coarse and wide, and there was an excess of air over the cerebral hemispheres. There was a cavum septi pellucidi; the two leaves were clearly seen and were not widely separated. Cognitive Findings: Clinical and psychometric evidence of intellectual impairment and memory	No

Case No.	Source [Reference]	Sport / Activity	Age	Exposure				Age and Symptom Onset Clinical Description / Symptoms Reported Cognitive Findings	Pathology Reported[§]
				Age Started	Years of Participation	Level of Play	Number of Concussion(s) & Concussion Severity		
								defect.	
23	Case 7: Mawdsley & Ferguson 1963	Boxing	63	16	Claimed to have boxed 'nightly' for 10 yrs	NR	Number: NR Severity: NR	Age and Onset: 38yrs: staggered gait. In his early 50s he noticed gait unsteadiness and heaviness of his legs, and found he was unable to run or to walk quickly. Clinical Features: At 50yrs he had a single episode of LOC for a few minutes; unsteadiness of gait and speech difficulty slowly worsened. His speech was dysarthric, his gait was grossly ataxic, and he was unable to walk without support. Upward gaze was restricted. He had nystagmus on full lateral deviation of the eyes, slower and coarser in amplitude on looking to the right. There was intention tremor of the right hand. Air-encephalography suggested advanced cerebellar atrophy. Cognitive Findings: In the past 10 years, deterioration in his memory was observed, otherwise no further reported cognitive findings beyond suggestion of dementia.	No
24	Case 8: Mawdsley & Ferguson 1963	Boxing	59	14	22 (600 bouts)	P	Number: 5 Severity: On one occasion - LOC 60mins; On several occasions he was dazed for hours after being beaten.	Age and Onset: NR Clinical Features: His only complaint was of poor eyesight. He denied any other disability and it was impossible to obtain a detailed history from him. He had always been a heavy beer drinker and was involved in many brawls and had convictions for assault. Because of his violent behaviour he was admitted to a mental hospital when he was 40. His wife left him 3 years ago because of his drunkenness and violence. Constantly chattering or singing, he was impervious to discipline. His facial expression was fixed. His speech was slow and dysarthric. He walked with an ataxic gait on a broad base, taking short, shuffling steps. There was rigidity of all four limbs, and a coarse tremor of the hands. Fine movements of the fingers were impaired, and there was slight intention tremor in both hands. CSF contained 70 mg of protein per 100 ml. The EEG was abnormal. Air-encephalography - the lateral ventricles showed considerable symmetrical dilatation of the lateral ventricles. There was a cavum septi pellucidi, the leaves being faintly defined and well separated. Cognitive Findings: There was gross impairment of intellect and memory.	No
25	Case 9: Mawdsley & Ferguson 1963	Boxing	33	14	13 (80 bouts)	A	Number: No KO's reported Severity: One of his fights was stopped when he was concussed and this bout was followed by a period of amnesia lasting 6 hours.	Age and Onset: 19yrs; speech becoming slurred, memory deterioration & untidy handwriting. Clinical Features: From 19yrs experienced persistent speech & memory difficulties. He reduced his frequency of boxing - only occasionally did he fight in the following 5 years before he ceased completely. At this time he began to experience almost constant occipital, throbbing headaches, which latterly occurred at weekly intervals. His only neurological abnormality was slight but definite slurring dysarthria. CSF contained 55 mg of protein per 100 ml. Cognitive Findings: None reported	No
26	Case 10: Mawdsley & Ferguson 1963	Boxing	51	14	22 (300 bouts)	P	Number: No KO's reported Severity: NR	Age and Onset: 35yrs retired experiencing a set, expressionless face and slurring of his speech, and was noticeably clumsy in the use of his hands. His wife noticed a progressive mental impairment. Clinical Features: Pronounced slurring dysarthria and an expressionless Parkinsonian-like face. During the last 10 years of his life he spent most of the day sitting apathetically at home. He became slovenly in his dress and habits, he took no interest in his family's welfare. Cognitive Findings: Deteriorating memory reported but not formally assessed	Yes
27	Case 8 in McKee et al 2009 [Constantinidis & Tissot 1967] *	Boxing	58	16	7	Unknown	Number: Unknown Severity: Unknown	Age and Onset: 25yrs; cognitive decline & hemiparesis. Clinical Features: Personality/behaviour change - dysphoria, irritability, confusion, paranoia, aggression/violence, poor insight/judgement'; epilepsy; 'Movement Abnormalities: Parkinsonism, decreased facial movement, gait problems, ataxia.' Cognitive Findings: Retrospective reports: memory loss, dementia.	Yes
28	Case 9 in McKee et al 2009 [Payne 1968]	Boxing	?	12	12	P, SP	Number: Unknown Severity: Unknown	Age and Onset: 30yrs Clinical Features: At 30yrs admitted to psychiatric institution and diagnosed with 'manic-depressive psychosis'. He spent many year thereafter institutionalised. Cognitive Findings: NR	Yes

Case No.	Source [Reference]	Sport / Activity	Age	Exposure				Age and Symptom Onset Clinical Description / Symptoms Reported Cognitive Findings	Pathology Reported[§]
				Age Started	Years of Participation	Level of Play	Number of Concussion(s) & Concussion Severity		
29	Case 10 in McKee et al 2009 [Payne 1968]	Boxing	46	15	20 (300 bouts)	P, B	Number: 1 KO but 'had taken many beatings' Severity: NR	Age and Onset: 33yrs: headache and noise sensitivity. Clinical Features: At 43yrs he had a left ventricular failure due to malignant hypertension, at which time examination detected slurring of speech and an unsteady gait; his dysarthria and ataxia became progressively more severe; he became violent and paranoid. He was emotionally labile; 1mth prior to his death medical examination noted additional diagnosis of papilloedema and left CNIII palsy. EEG at this time demonstrated a possible right parietal lesion. Cognitive Findings: NR	Yes
30	Case 11 in McKee et al 2009 [Payne 1968]	Boxing	46	19	13 (200 bouts)	P	Number: 50 Severity: NR	Age and Onset: 31yrs: headache, poor concentration, insomnia, enuresis, & depression. Clinical Features: He drank heavily, many convictions for drunkenness & several for larceny, marriage breakdown, could not maintain employment. During his many hospitalisations he threatened and abused medical staff. Aged 39yrs first noticed slurring of his speech, and mild impairment of coordination of his left arm. EEG showed diffuse abnormality and air encephalogram demonstrated evidence of brain atrophy. Cognitive Findings: Not formally assessed; however, in his final year of life his memory was poor, he was sometime confused and vague.	Yes
31	Case 12 in McKee et al 2009 [Payne 1968]	Boxing	45	16	14 (300 P bouts) & several yrs at A level	A, P	Number: NR Severity: Unknown	Age and Onset: 40yrs Clinical Features: Alcoholic, prone to violence. He had slurred speech & shuffling gait. EEG demonstrated slight theta activity in left temporal area. He unsuccessfully attempted extended period of alcohol abstinence; complained of headaches, depression, poor concentration, insomnia & enuresis, slurred speech, nystagmus, coordination problems. CSF was 60mgm%. Cognitive Findings: NR	Yes
32	Case 13 in McKee et al 2009 [Payne 1968]	Boxing	44	15	Approx. 14 (initially B every night) (200 P bouts)	P, B	Number: NR Severity: NR	Age and Onset: 28yrs retired but no report of symptoms. Clinical Features: Vaguely described as occasionally unsteady on his feet and experiencing slurred speech. Slightly enlarged ventricles, cavum septi pellucidi with small fenestrations, slight cerebral atheroma. Cognitive Findings: NR	Yes
33	Case 14 in McKee et al 2009 [Payne 1968]	Boxing	28	12	12 (28 bouts (17-11 Win-Loss record)	P	Number: NR Severity: NR	Age and Onset: NR Clinical Features: Prematurely ended his career due to imprisonment. Died four years later of a stab wound to the heart. Cognitive Findings: NR	Yes
34	Case 15 in McKee et al 2009 [Corsellis et al 1973]	Boxing	63	11	14 (400 bouts)	P	Number: NR Severity: NR	Age and Onset: NR Clinical Features: He changed completely, drank & gambled heavily, marriage breakdown, socially isolated, violent outbursts, became vagrant, speech slurred, right-sided ptosis. Cognitive Findings: NR	Yes
35	Case 16 in McKee et al 2009 [Corsellis et al 1973]	Boxing	77	Boyhood'	Retired in early 30s (700+ bouts)	P, B	Number: NR Severity: NR	Age and Onset: NR Clinical Features: By 50yrs old he staggered slightly, slow and slurred speech, next 10 yrs he became child-like, right upper limb tremor, markedly ataxic, nystagmus in right. Cerebral atrophy & punch-drunk syndrome were diagnosed. Cognitive Findings: NR	Yes
36	Case 17 in McKee et al 2009 [Corsellis et al 1973]	Boxing	62	16	13 (300+ bouts)	P	Number: NR Severity: NR	Age and Onset: NR Clinical Features: By retirement he had already become muddled and by 36yrs he often fell backwards, paranoid, at age 44yrs early Parkinsonism was suggested, at 50 yrs slurred speech was evident and the term 'punch-drunk' was mentioned, at 56yrs extrapyramidal tremor of upper limbs and ataxia of lower limbs. By early 60s, hospital notes suggested 'diffuse degenerative brain disease affecting extrapyramidal & pyramidal systems as well as causing mental impairment'. Cognitive Findings: NR	Yes

Case No.	Source [Reference]	Sport / Activity	Age	Exposure				Age and Symptom Onset Clinical Description / Symptoms Reported Cognitive Findings	Pathology Reported[§]
				Age Started	Years of Participation	Level of Play	Number of Concussion(s) & Concussion Severity		
37	Case 18 in McKee et al 2009 [Corsellis et al 1973]	Boxing	69	15	25 (600 bouts)	P	Number: ? Severity: NR	Age and Onset: NR Clinical Features: In his mid-30s he became unsteady on his feet by age 40 he had a shuffling gait and a marked tremor in his hands. At 57yrs he attended hospital and was found to have a spastic gait and slurred speech. Punch-drunk syndrome was diagnosed. Cognitive Findings: By 64yrs he was disoriented to time and place and did not recognise his relatives.	Yes
38	Case 19 in McKee et al 2009 [Corsellis et al 1973]	Boxing	61	As a child	18yrs	P, B	Number: ? Severity: NR	Age and Onset: NR Clinical Features: This patient was described as a "deaf mute". He sometimes boxed in a trance, drunk excessively in his 20s and by the end of his career at the age of 30 he could no longer manage his personal affairs. He became neuritic around 35yrs and was placed in a home. At age 60yrs he developed a right facial weakness and right homonymous hemianopia. Cognitive Findings: NR	Yes
39	Case 20 in McKee et al 2009 [Corsellis et al 1973]	Boxing	83	13	25 (500 bouts)	P, B	Number: "Occasionally" Severity: NR	Age and Onset: NR Clinical Features: He was fit until age 32yrs when his legs began to give way. Post-retirement he had two failed marriages. By age 65yrs he was placed in a nursing home and later a psychiatric facility, where it was noted he possessed paranoid delusions, dysarthria, ataxia - with slowed shuffling gait and had Parkinsonian signs with left leg weakness. Cognitive findings: Not formally assessed but described as possessing a poor memory	Yes
40	Case 21 in McKee et al 2009 [Corsellis et al 1973]	Boxing	62	16	20 (400 bouts)	P	Number: ? Severity: NR	Age and Onset: NR Clinical Features: A few years post retirement he began drinking heavily and became moody and violent. By 54yrs he was unsteady on his feet and fell frequently. He complained of violent headaches, behaved strangely and had 'glassy-looking eyes'. He was doubly incontinent at times and was admitted to a psychiatric hospital at 59yrs old. Cognitive Findings: File notes indicated he was "grossly demented".	Yes
41	Case 22 in McKee et al 2009 [Corsellis et al 1973]	Boxing	71	17	23 (565 bouts)	P	Number: ? Severity: NR	Age and Onset: NR Clinical Features: At age 60yrs deterioration became apparent, he was ataxic and demonstrated left-sided weakness, he had a number of episodes of unconsciousness. He was intolerant of alcohol and was only interested in boxing and gambling. His intellect and behaviour deteriorated and he became violent. A tremor also developed.	Yes
42	Case 23 in McKee et al 2009 [Corsellis et al 1973]	Boxing	72	Unknown	Unknown but > 10yrs	P	Number: ? Severity: NR	Age and Onset: NR Clinical Features: Aged 31 he was noted to have a left hand tremor and slurred and hoarse speech. He began to drink heavily and at age 65yrs he attempted suicide, resulting in psychiatric hospitalisation. A tremor and rigidity of the left upper limb was noted. Cognitive Findings: NR	Yes
43	Case 24 in McKee et al 2009 [Corsellis et al 1973]	Boxing	67	Unknown	Unknown	P	Number: ? Severity: NR	Age and Onset: NR Clinical Features: Known as a violent man and drunk heavily aged 40yrs. By 60yrs, he developed a left hemiparesis. At 63yrs he was admitted to a psychiatric facility, paranoid & deluded, confused and aggressive. Cognitive Findings: Poor memory at age of 40yrs, by 63yrs disoriented, with marked loss of recent memory.	Yes
44	Case 25 in McKee et al 2009 [Corsellis et al 1973]	Boxing	67	Unknown	Retired approx. 35yrs	P	Number: ? Severity: NR	Age and Onset: NR Clinical Features: Limited history but by age 67yrs there was a history of increasing confusion, disorientation, and aggression. Cognitive Findings: NR	Yes
45	Case 26 in McKee et al 2009 [Corsellis et al 1973]	Boxing	91	Unknown	Boxed during youth	P ?	Number: ? Severity: NR	Age and Onset: NR Clinical Features: Little history, aside he spent the last years of his life in a home for the partially disabled. He was solitary and placid but occasionally became aggressive, but considered to be mentally alert. Cognitive Findings: NR	Yes

Case No.	Source [Reference]	Sport / Activity	Age	Exposure				Age and Symptom Onset Clinical Description / Symptoms Reported Cognitive Findings	Pathology Reported[§]
				Age Started	Years of Participation	Level of Play	Number of Concussion(s) & Concussion Severity		
46	Case 27 in McKee et al 2009 [Corsellis et al 1973]	Boxing	57	14	Unknown	A	Number: "Several times" Severity: NR	Age and Onset: NR Clinical Features: By age 43yrs he was vague and spoke more slowly; became intolerant of alcohol. At 53yrs he was admitted to a mental hospital and was found to be mildly confused and complained of blackouts. His personality was reported to have changed. Cognitive Features: His memory, mobility, and speech became progressively worse, eventually he became incontinent, paranoid, and aggressive.	Yes
47	Case 28 in McKee et al 2009 [Corsellis et al 1973]	Boxing	61	Unknown	Unknown	A	Number: ? Severity: NR	Age and Onset: NR Clinical Features: Unremarkable boxing career and post-retirement life. Cognitive Features: NR	Yes
48	Case 29 in McKee et al 2009 [Corsellis et al 1973]	Boxing	58	Unknown	Unknown	A	Number: ? Severity: NR	Age and Onset: NR Clinical Features: Unremarkable boxing career and post-retirement life. Cognitive Features: NR	Yes
49	Case 30 in McKee et al 2009 [Roberts GW et al 1990]	Female; physical abuse	76	Unknown	Unknown	N/A	Number: Unknown Severity: Unknown	Age and Onset: NR Clinical Features: History of a stroke; she had become demented over the past few years, this manifesting predominantly as memory loss and mental confusion. Relatives reported a long standing history of domestic violent. Cognitive Features: Memory loss and mental confusion	Yes
50	Case 31 in McKee et al 2009 [Hof et al 1991]	Female; Autistic head banging	24	7yrs	Approx. 15yrs	N/A	Number: Unknown Severity: Head banging; subconcussive blows.	Age and Onset: NR Clinical Features: She became blind as a bilateral detachment of the retina and dullness of the cornea resulted from repeated head and eye trauma. Head banging behaviour was so severe that she developed a hyperostosis frontalis externa. EEG revealed no epileptic loci, EEG trace was dominated by rapid activity (20 cycle/s) in the anterior areas and showed some theta elements. Cognitive Features: Diagnosed with infantile autism. Did not develop more than three words in her vocabulary and did not develop intellectual abilities. What she had achieved was lost around 11-years of age.	Yes
51	Case 32 in McKee et al 2009 [Hof et al 1992]	Diagnosis: PSP					Number: No reported history of any head trauma Severity: NR	Age and Onset: NR Clinical Features: NR Cognitive features: NR	No
52	Case 33 in McKee et al 2009 [Hof et al 1992]	Diagnosis: PSP					Number: No reported history of any head trauma Severity: NR	Age and Onset: NR Clinical Features: NR Cognitive features: NR	No
53	Case 34 in McKee et al 2009 [Williams & Tannenberg 1996]	Circus Clown	33	Unknown	15yrs in the circus as a clown; also 8-10yrs involved in dwarf throwing.	N/A	Number: "A dozen times" Severity: Never hospitalised but no data recorded on severity.	Age and Onset: NR Clinical Features: Known to abuse alcohol with associated poor eating habit and frequent hospitalisation with withdrawal seizures. Hospital notes recorded aggression, impatience, panic symptoms, and blackouts. Clinical examination had revealed ataxia, nystagmus, mild Rombergism, and brisk reflexes and he had received treatment for Wernicke's encephalopathy. Cognitive Features: Not formally assessed; but the hospital report indicated poor concentration.	Yes
54	Case 35 in McKee et al 2009 [Jordan et al 1995]	Boxing	71	Unknown	>11 (85 bouts, 16 losses)	P	Number: 3 KOs recorded Severity: NR	Age and Onset: 61yrs Clinical Features: At 63yrs he developed an acute right hemiplegia and no longer recognised his family. Cognitive Features: Not formally assessed; although he was described as suffering from "cognitive decline"	Yes

Case No.	Source [Reference]	Sport / Activity	Age	Exposure				Age and Symptom Onset Clinical Description / Symptoms Reported Cognitive Findings	Pathology Reported[§]
				Age Started	Years of Participation	Level of Play	Number of Concussion(s) & Concussion Severity		
55	Case 36 in McKee et al 2009 [Geddes et al 1996; Geddes et al 1999]	Boxing	23	11	12yrs	19 bouts (totalling 120 Rds) / 4yrs P; 80 bouts / 8yrs A	Number: 1 KO; At the age of 10yrs, suffered a concussive HI by falling from a wall. Severity: No severe injury due to his boxing prior to the fatal KO sustained in his final bout. The previous HI at 10yrs-old resulted in transient loss of consciousness, followed by a short period of agitation and then complete recovery. Skull X-rays at the time revealed a right-sided skull fracture.	Age and Onset: NR Clinical Features: There were no neurological symptoms demonstrated on previous assessment. CT scan performed at the time he was granted a professional licence was normal, as was a CT scan 1 week prior to the last fight. He had no history of a severe head injury during his career, until his final fight, as a result of which he developed an acute subdural haematoma; he died 48 h after the contest, despite neurosurgical intervention. Cognitive Features: Not formally assessed; although he was described as being 'somewhat forgetful.'	Yes
56	Case 37 in McKee et al 2009 [Geddes et al 1999]	Boxing	28	16	5yrs (approx. 20 bouts)	A	Number: 0 Severity: He suffered from haematuria after contests but no history of a serious HI during his boxing career.	Age and Onset: NR Clinical Features: History of psychotic illness; diagnosed with paranoid schizophrenia at 20yrs, he was readmitted with an acute psychotic illness at the age of 25, this time more depressive in nature, and then again 2 years later. He died unexpectedly the following year during a grand mal seizure. Cognitive Features: Not formally assessed	Yes
57	Case 38 in McKee et al 2009 [Geddes et al 1999]	Epilepsy & Head Banging	28	Unknown	Unknown	N/A	Number: No history of severe HI History: NR	Age and Onset: NR Clinical Features: A "mentally subnormal" man, who had been slow to achieve childhood developmental milestones, developed grand mal epilepsy at the age of 7 years, at which time he was also diagnosed to be autistic. There was a long history of head banging, but no episode of severe HI. He lived his adult life in residential care, and died 2 days after a fall from a first floor window, in which he sustained a skull fracture, extradural and acute subdural haematomas, and large basal frontal contusions. Cognitive Features: Not formally assessed	Yes
58	Case 39 in McKee et al 2009 [Geddes et al 1999]	Epilepsy	27	2.5yrs	24yrs	N/A	Number: NR Severity: NR	Age and Onset: NR Clinical Features: A "mentally retarded" man who had suffered from intractable complex partial seizures with secondary generalised seizures. He was born 2 months prematurely, suffered from birth trauma and had his first seizure at the age of 2.5 years. The seizure frequency gradually increased, until in recent years he had both "major attacks" seven to ten times a week in which he dropped heavily to the ground and "minor attacks" which occurred once a week. Imaging showed that he had a calcified lesion under the right motor strip. Right frontal lobectomy was performed to include removal of the calcified lesion. Cognitive Features: Not formally assessed	Yes

Case No.	Source [Reference]	Sport / Activity	Age	Exposure				Age and Symptom Onset Clinical Description / Symptoms Reported Cognitive Findings	Pathology Reported[§]
				Age Started	Years of Participation	Level of Play	Number of Concussion(s) & Concussion Severity		
59	Case 40 in McKee et al 2009 [Geddes et al 1999]	Soccer	23	Unknown	Unknown	A	Number: 1 fatal sports HI; sustained 1 other non-sports related HI Severity: He had had a single severe head injury in the past, from which he had made a full recovery (no further details available)	Age and Onset: NR Clinical Features: A regular 'header' of soccer balls; he was reported to have been previously well with no history of neurological disease. He sustained a head injury while playing in a soccer match and developed an acute subdural haematoma and brain swelling, from which he died. Cognitive Features: Not formally assessed	Yes
60	Case 41 in McKee et al 2009 [Newell & Drachman 1999; Drachman & Newell; Schmidt et al 2001 - case 2]	Boxing	67	Unknown	10 (100 bouts); reported to be a "slugger"	P	Number: NR Severity: Had been knocked down 13 times in one fight; otherwise no details regarding severity.	Age and Onset: 64yrs (40yr latency); 'cognitive decline' Clinical Features: Hospitalised due to increasing dementia. 3yrs prior to admission, cognitive decline was noted. One year later, a neurologist diagnosed progressive dementia with Parkinsonism. During the two months before admission, the patient became agitated, experienced transient periods when he stared into space and did not respond to his surroundings, several falls, with apparent loss of consciousness but without obvious injury. One week before admission, physical violence toward family and paranoid behaviour. On admission, found to be oriented only to person, his speech was hypophonic; his facial expression was reduced, and he drooled; posture was slightly stooped, tandem walking was unsteady. MRI: severe, diffuse ventricular and cortical sulcal enlargement, T2-weighted images showed slight thinning of the corpus callosum, atrophy of the mammillary body, a moderately reduced signal in the globus pallidus and putamen, and minimal hyperintensity of periventricular white matter. The pars compacta was thinned on the proton-density-weighted images. A cavum septi pellucidi was noted. EEG findings were consistent with the presence of a generalized disorder of the motor neurons, their axons, or both. Interestingly, severe atrophy of both shoulder girdles and distal muscles, and diffuse fasciculations were present, although muscle strength was reported to be normal, and Babinski signs were absent, an electromyogram showed chronic denervation and re-innervation in all muscle groups, a finding consistent with the presence of a "generalized disorder of motor neurons, their axons, or both." Cognitive Features: Lost concentration when attempting serial tasks; abstract tasks were performed poorly; recalled none of three objects at five minutes, even with cues; left–right confusion was present.	Yes
61	Case 42 in McKee et al 2009 [Schmidt et al 2001]	Boxing	78	NR	NR	NR	Number: NR Severity: NR	Age and Onset: NR Clinical Features: History of dementia with Parkinsonism for several years. Cognitive Features: NR	Yes
62	Case 43 in McKee et al 2009; Case 1 / Omalu et al 2010; Case 1 / Omalu et al 2011	AF	50	16	NFL: 17 (245 games); HS/College: 5	NFL	Number: NR Severity: NR	Age and Onset: NR Clinical Features: Medical history that included atrial fibrillation and coronary atherosclerotic disease (with stenting). A neuropsychiatric history that resembled a dysthymic disorder. A deficit in memory and judgment as well as Parkinsonian symptoms. Anabolic steroid use; history of marked physical abuse; depression; repeatedly stunned himself into unconsciousness with a Taser gun to fall asleep; would not eat for days at a time; chronic use of Ritalin, Dexedrine, Paxil, Prozac, Ultram, Darvocet, Vicodin, Lorcet, and Eldepryl; extensive liver and kidney damage; never treated for a concussion or complained of concussive symptoms during playing career; financial ruin; legal troubles. Cognitive Features: Not conducted - retrospective study.	Yes

Case No.	Source [Reference]	Sport / Activity	Age	Exposure				Age and Symptom Onset Clinical Description / Symptoms Reported Cognitive Findings	Pathology Reported[§]
				Age Started	Years of Participation	Level of Play	Number of Concussion(s) & Concussion Severity		
63	Case 44 in McKee et al 2009; Case 2 / Omalu et al 2010; Case 2 / Omalu et al 2011	AF	45	18	NFL: 8; College: 4; Military: 2	NFL	Number: Reportedly 'sustained repeated mild concussions on numerous occasions' Severity: There was at least one clinically documented severe concussive brain injury during play of football in 1987, which necessitated removal from play for at least 1 week. He was hospitalized for one night and complained of lightheadedness, unsteadiness in gait, and difficulty concentrating.	Age and Onset: 35yrs Clinical Features: Increasingly quiet and that he was afraid and fearful, with paranoid tendencies. In private he occasionally became extremely reclusive. He manifested unpredictable fluctuations in mood and personality. His business activities and decisions were regarded as extraordinarily risky, ambitious, and rather irrational; numerous business failings and he was under federal indictment at time of death. He was diagnosed with adjustment disorder with depressed mood after this first suicide attempt. Suicide by drinking anti-freeze; prior suicide attempt with rat poison. He had been previously admitted for psychiatric treatment three times. He had received a diagnosis of major depressive disorder, which was severe and without psychotic features. There was a documented single episode of a rollover of a sport utility vehicle which he was driving when he swerved to avoid hitting a deer. He experienced a brief loss of consciousness at the scene, but reportedly recovered completely. Other medical history included thyroidectomy for hyperthyroidism, and history of anabolic steroid use. Cognitive Features: Not conducted - retrospective study	Yes
64	Case 45 in McKee et al 2009; Case 3 / Omalu et al 2010; Case 3 / Omalu et al 2011	AF	44	15	NFL: 9; College: 4	NFL	Number: "Lost count at 15" Severity: Once suffered a seizure - hospitalised but practiced 2 days after discharge and played within 7 days.	Age and Onset: 38yrs: Memory problems 3-4 years post-retirement. 5 years post-retirement, he began to get upset and angry if people did not do what he wanted. 8 years post-retirement excessively driven, sleeping little and focused on coaching college football. Clinical Features: Constant headaches and pain, medicated for this at retirement. History of alcohol abuse starting one year post-retirement and lasting approx. 8 years. Progressively avoided social interaction and became a "needy, dependent" man, angry and overreacted to trivial situations with fluctuations in his mood. He exhibited paranoid ideations; persecutory nature, depression, and harboured a fear of financial ruin. A number of suicide attempts prior to his death by gunshot wound to the head. Depression, particularly about low-level college coaching jobs and inability to become NFL coach. Cognitive Features: Not conducted - retrospective study.	Yes
65	Case 46 in McKee et al 2009 [Cajigal 2007]; Case 5 / Omalu et al 2010; Case 6 / Omalu et al 2011	Wrestler	40	18	22yrs	P	Number: None diagnosed but allegedly reported several to his father. Severity: Unknown	Age and Onset: 38yrs Clinical Features: Results limited to neuropathological observation only, no description of clinical correlates. Died via hanging; Xanax, hydrocodone; high levels of synthetic testosterone in blood upon death; history of anabolic steroid use and alcohol abuse. Cognitive Features: Not conducted - retrospective study.	Yes
66	Case 47 in McKee et al 2009; Case 4 / Omalu et al	AF	36	16	NLF: 8; 17 in all	NFL	Number: NR Severity: NR	Age and Onset: 36yrs Clinical Features: "Manifested progressive symptoms and signs of cognitive and neuropsychiatric impairments." Died of brain injury from MVA; history of anabolic steroid use; chronic marijuana use; often excessive alcohol use; no known prior concussion history; depression; possible	Yes

Case No.	Source [Reference]	Sport / Activity	Age	Exposure				Age and Symptom Onset Clinical Description / Symptoms Reported Cognitive Findings	Pathology Reported[§]
				Age Started	Years of Participation	Level of Play	Number of Concussion(s) & Concussion Severity		
	2010; Case 5 / Omalu et al 2011							undiagnosed bipolar disorder/psychosis; extensive psychosocial stressors. Cognitive Features: Not conducted - retrospective study.	
67	Case 48 in McKee et al 2009 [Areza-Fegyveres et al 2007]	Boxing	61	16	14 yrs amateur; 3 yrs Professionally, > 60 bouts.	P	Number: No documented KOs Severity: N/A	Age and Onset: 58yrs Clinical Features: Medical follow up was conducted at least twice a year for seven years. No cerebellar, pyramidal, or extrapyramidal signs were seen during the follow-up period. Cognitive Features: Initial three year history of progressive memory decline. Followed-up over seven years, demonstrating continuous cognitive decline, very similar to that usually observed in Alzheimer's disease. Initial MMSE: 24/30 with NP Ax demonstrating predominately memory problems. His cognitive impairment steadily worsened with progression of the disease, predominant impairment in memory, attention, and executive functions were observed.	Yes
68	Case A in McKee et al 2009; BU CSTE website / John Grimsley / McKee et al (2012) Case 61	AF	45	16	NFL: 10yrs; 16 in all	NFL	Number: 3 in college; 8 or 9 in NFL. Only 1 medically verified. No hospitalisations or residual deficits Severity: Appear to be very mild	Age and Onset: 40yrs Clinical Features: Toward the end of his life, he tended to become angry and verbally aggressive over insignificant issues and was more emotionally labile. He also began to consume more alcohol but did not show other signs or symptoms of depression. Cognitive Features: Retrospective information only; initial minor impairments of short-term memory, attention, concentration, organization, planning, problem-solving, judgment, and multi-tasking. His spatial abilities were mildly impaired, and his language was unaffected.	Yes
69	Case B in McKee et al 2009 / McKee et al (2012) Case 81	Boxing	80	17	5yrs	P	Number: NR; however he sustained a non-sports related mTBI in his teens. Severity: NR	Age and Onset: 63yrs Clinical Features: There was history of alcohol abuse and a family history of Alzheimer's disease. Computed tomographic scan revealed cerebral and cerebellar atrophy. By age 78 years, he was paranoid, his gait was unsteady, his speech slowed, and he frequently fell. He was easily agitated and required multiple hospitalizations for aggressive behaviours. Brother had AD. Cognitive Features: Retrospective information only; he had reportedly suffered from relatively stable cognitive difficulties throughout his life until he developed a marked cognitive deterioration after 70 years of age. By 78yrs his memory loss had increased.	Yes
70	Case C in McKee et al 2009 / McKee et al (2012) Case 75	Boxing	73	11	22 (48 bouts)	P	Number: NR Severity: NR	Age and Onset: 58yrs Clinical Features: Approximately 20 years after retirement, he developed a progressive behavioral disorder with evidence of impairment in all cognitive domains. Neuroimaging showed cerebral atrophy, a cavum septum pellucidum (CSP), and a lacunar infarct in the left globus pallidus. He had a family history of dementia. In his late 50s, he became forgetful with mood swings and restlessness. He changed from his normally happy easy-going self to become apathetic, socially withdrawn, paranoid, irritable, and sometimes violently agitated. During the next 2 years, he began to confuse close relatives and developed increasing anxiety, aggression, and agitation; on occasion, he was verbally abusive toward his wife and tried to strike her. By age 70 years, he had severe swallowing difficulties, diminished upgaze, masked facies, garbled speech, and a slow shuffling gait. Cognitive Features: Neuropsychological testing showed deficits in all cognitive domains, including executive functioning, attention, language, visuospatial abilities, and profound deficits in learning and memory. Repeat neuropsychological testing at age 67 years revealed further global deficits, again with prominent impairments in memory. By age 70 years, MMSE several months before death was 7/30.	Yes
71	BU CSTE website / Lou Creekmur / McKee et al (2012) Case 82	AF	82	High school or younger	NFL: 10yrs	NFL	Number: "16 or 17" (broken nose 13 times) Severity: No LOC or hospitalisations	Age and Onset: NR Clinical Features: A 30-year decline of behavioral issues such as increasingly intensive angry and aggressive outbursts. Cognitive Features: Retrospective information only; 30-year cognitive decline including memory loss, lack of attention and organization skills.	Yes

Case No.	Source [Reference]	Sport / Activity	Age	Exposure				Age and Symptom Onset Clinical Description / Symptoms Reported Cognitive Findings	Pathology Reported[§]
				Age Started	Years of Participation	Level of Play	Number of Concussion(s) & Concussion Severity		
72	BU CSTE website / Mike Borich / McKee et al (2012) Case 60	AF	42	High school or younger	NR	College	Number: Approx. 10 but unconfirmed Severity: NR	Age and Onset: NR Clinical Features: Downward spiral of depression and substance abuse. Died of alcohol, cocaine, and oxycontin overdose; history of alcohol abuse, pain killer abuse, and other drug abuse. Cognitive Features: Not conducted - retrospective study.	Yes
73	BU CSTE website / Thomas McHale; Case 8 Omalu et al 2011 / McKee et al (2012) Case 62	AF	45	High school or younger	NFL: 9yrs	NFL	Number: None during college or NFL according to his wife. Severity: N/A	Age and Onset: NR Clinical Features: Developed such chronic pain in 2005 that he used improperly large doses of the painkiller OxyContin, which exacerbated his lethargy and depression and led him to take cocaine occasionally to offset those effects. Overdose of oxycodone and cocaine as well as alcohol combined with Xanax. Father had bipolar disease. Cognitive Features: Not conducted - retrospective study.	Yes
74	BU CSTE Media Release / Derek Boogaard / McKee et al (2012) Case 45	NHL	28	NR	NHL: 6yrs 277 games Other Professional leagues: 9yrs	NHL	Number: "Bell rung" at least 20 times. Involved in 174 career fights in professional hockey Severity: Twice diagnosed with PCS	Age and Onset: 26yrs; drug addiction, emotional instability, impulsive behaviour, disorientation, poor short-term memory. Clinical Features: Two weeks prior to his final game he had "seen stars" following a fight in which he sustained a concussion. Drug addition, abnormal behaviours, emotional instability. Cognitive Features: Impulsive behaviour, disorientation, poor short-term memory and poor impulse control.	No
75	BU CSTE Media Release / Rick Martin / McKee et al (2012) Case 55	NHL	59	NR	NHL: 12yrs 685 games; Minors: 3yrs	NHL	Number: NR Severity: NR	Age and Onset: NR Clinical Features: NR Cognitive Features: NR	No
76	BU CSTE Media Release / Bob Probert / McKee et al (2012) Case 50	NHL	45	NR	NHL: 15yrs 935 games	NHL	Number: NR Severity: NR	Age and Onset: NR Clinical Features: NR Cognitive Features: NR	No
77	BU CSTE Media Release / Reggie Fleming / McKee et al (2012) Case 97	NHL	73	NR	NHL: 11yrs + 2 Minor Leagues	NHL	Number: NR Severity: NR	Age and Onset: NR Clinical Features: 30 years of worsening behaviour. Diagnosed with dementia. Cognitive Features: 30 years of worsening cognitive difficulties.	No
78	Case 4 Omalu et al 2011	AF	24	NR	NR	NR	Number: NR Severity: NR	Age and Onset: NR Clinical Features: Results limited to neuropathological observation only, no description of clinical correlates. Cognitive Features: Not conducted - retrospective study.	Yes

Case No.	Source [Reference]	Sport / Activity	Age	Exposure				Age and Symptom Onset Clinical Description / Symptoms Reported Cognitive Findings	Pathology Reported[§]
				Age Started	Years of Participation	Level of Play	Number of Concussion(s) & Concussion Severity		
79	Case 7 Omalu et al 2011	Wrestler	38	NR	NR	NR	Number: NR Severity: NR	Age and Onset: NR Clinical Features: Results limited to neuropathological observation only, no description of clinical correlates. Cognitive Features: Not conducted - retrospective study.	Yes
80	Case 9 Omalu et al 2011	AF	52	NR	NR	NR	Number: NR Severity: NR	Age and Onset: NR Clinical Features: Results limited to neuropathological observation only, no description of clinical correlates. Although he was reportedly found dead while intoxicated. Cognitive Features: Not conducted - retrospective study.	Yes
81	Case 10 Omalu et al 2011	AF	39	NR	NR	NR	Number: NR Severity: NR	Age and Onset: NR Clinical Features: Results limited to neuropathological observation only, no description of clinical correlates. However, history of crystal methamphetamine and alcohol abuse, died of acute cocaine and heroin toxicity. Cognitive Features: Not conducted - retrospective study.	Yes
82	Case 11 Omalu et al 2011	MMA	28	NR	NR	NR	Number: NR Severity: NR	Age and Onset: NR Clinical Features: Results limited to neuropathological observation only, no description of clinical correlates. Cognitive Features: Not conducted - retrospective study.	Yes
83	Case 12 Omalu et al 2011	Wrestler	34	NR	NR	NR	Number: NR Severity: NR	Age and Onset: NR Clinical Features: Results limited to neuropathological observation only, no description of clinical correlates. Cognitive Features: Not conducted - retrospective study.	Yes
84	Case 13 Omalu et al 2011	Wrestler	33	NR	NR	NR	Number: NR Severity: NR	Age and Onset: NR Clinical Features: Results limited to neuropathological observation only, no description of clinical correlates. Cognitive Features: Not conducted - retrospective study.	Yes
85	Case 14 Omalu et al 2011	Boxing	50	NR	NR	P	Number: NR Severity: NR	Age and Onset: NR Clinical Features: Results limited to neuropathological observation only, no description of clinical correlates. Cognitive Features: Not conducted - retrospective study.	Yes
86	Case 15 Omalu et al 2011	AF - HS	18	NR	NR	High School	Number: NR Severity: NR	Age and Onset: NR Clinical Features: Results limited to neuropathological observation only, no description of clinical correlates. Cognitive Features: Not conducted - retrospective study.	Yes
87	Case 16 Omalu et al 2011	AF – HS	16	NR	NR	High School	Number: NR Severity: NR	Age and Onset: NR Clinical Features: Results limited to neuropathological observation only, no description of clinical correlates. Cognitive Features: Not conducted - retrospective study.	Yes
88	Case 17 Omalu et al 2011	AF – HS	17	NR	NR	High School	Number: NR Severity: NR	Age and Onset: NR Clinical Features: Results limited to neuropathological observation only, no description of clinical correlates. Cognitive Features: Not conducted - retrospective study.	Yes
89	Saing et al (2012)	Boxing	55	18	13yrs	P	Number: 2 KOs Severity: 1 PTA 72hrs.	Age and Onset: 32yrs memory problems 1 yr post retirement Clinical Features: Behavioural impairments; outbursts of anger, poor judgment, inability to tolerate frustration, fluctuating mood. Initial neurological exam unremarkable aside from bilateral slowing of fine sequential finger movements and mild difficulties with tandem gait. Progressed to include impairments in gait, bilateral paramyotonia and bradykinesia were observed six years post initial examination. Of note there was a significant history of AD in his brother and his father. Cognitive Features: 7 visits: initial presentation he demonstrated mild dementia. Neuropsychological assessment demonstrated a slow but progressive deterioration in cognitive	Yes

Case No.	Source [Reference]	Sport / Activity	Age	Exposure				Age and Symptom Onset Clinical Description / Symptoms Reported Cognitive Findings	Pathology Reported[§]
				Age Started	Years of Participation	Level of Play	Number of Concussion(s) & Concussion Severity		
								abilities; by the final exam (7-year follow up; and approx. 11-mths prior to his death), he was severely demented and unable to perform many of the tasks. Executive dysfunction, particularly disinhibition.	
90	McCrory, Turner, Murray (2004) Punch drunk jockey?	Jockey	48	15 (18yrs prof)	20 (200–250 rides a year)	P	Number: Approx. 10-12 Severity: 10–12 hospitalisations; Cantu grade 1 or Severity: 2. 16yrs 1 LOC approx. 24hrs; In 1988, 2-3hrs LOC.	Age and Onset: Three year history of progressive short-term memory loss. Clinical Features: Developed progressive short-term memory loss about 10 years after retirement. MR brain scan shows cerebral atrophy. Cognitive Features: Progressive short term memory loss; slowed reaction times and processing speed.	No
91	King et al (2010) Case 35	Boxing	76	NR	NR	P	Number: NR Severity: NR	Age and Onset: NR Clinical Features: Diagnosis of dementia Cognitive Features: Not conducted	Yes
92	King et al (2010) Case 36	Boxing	62	NR	NR	P	Number: NR Severity: NR	Age and Onset: NR Clinical Features: Diagnosis of dementia Cognitive Features: Not conducted	Yes
93	King et al (2010) Case 37	Boxing	69	NR	'several years'	Unknown; A or P	Number: NR Severity: NR	Age and Onset: NR Clinical Features: Diagnosis of dementia Cognitive Features: Not conducted	Yes
94	Hazrati et al (2013) Case 1	Canadian Football League	86	5 in the CFL	"Played football from a young age"	P	Number: "multiple" Severity: Unknown	Age and Onset: 70 yrs; memory impairment, apathy, decreased concentration, getting lost, language deficits. Clinical Features: Apathy in early 70s, eating habits changed, restless sleeper, increased irritability and agitation, wheel chair bound at 86 yrs. Family history of AD (brother) and dementia in paternal aunt and grandfather. Cognitive Features: Word finding difficulties and semantic paraphasias, by 85 yrs progressed to a significant expressive aphasia.	Yes
95	Hazrati et al (2013) Case 2	Canadian Football League ice hockey & rugby	61	12 in the CFL	"Played football, hockey and rugby from a young age"	P	Number: "multiple" Severity: Unknown	Age and Onset: 56 yrs; emotional lability and slurred speech Clinical Features: Diagnosis of bulbar ALS. From initial onset progression over next few years to loss of speech and ability to swallow, requiring a feeding tube at 59 yrs and a tracheotomy at 61 yrs. Cognitive Features: mild decline at age 61 yrs, otherwise relatively well preserved.	Yes
96	Hazrati et al (2013) Case 3	Canadian Football League	79	12 in the CFL	NR	P	Number: "multiple" Severity: Unknown	Age and Onset: 50 yrs; flat affect and depressed mood, STM deficits and subtle gait changes Clinical Features: Diagnosed with PD in his 70s. At 62 yrs, subtle changes in gait, he walked more slowly and less steadily. He had major depressive episode that year and underwent ECT. Developed a tremor, rigidity, a Parkinsonian gait, REM sleep behaviour disorder, and lost his sense of olfaction. Apathy and reduced empathy. In his 70s developed hallucinations, episodes of agitation, and aggression. Family history of PD (sister) and both parents suffered from depression. Cognitive Features: STM impairment aged 55 years, in his 60s executive impairment and could no longer manage his business. In his 70s became disinhibited.	Yes
97	Hazrati et al (2013) Case 4	Canadian Football League	67	6 in the CFL	Played HS football	P	Number: "multiple" Severity: Unknown	Age and Onset: 55 yrs; STM difficulties and less able to formulate arguments, apathetic, and depressed Clinical Features: CoD: lung cancer. He developed apathy, agitation, and became depressed. He became a ward of the state following bankruptcy at 66 yrs. He had paranoid delusions. Family history of vascular dementia (paternal grandfather). Cognitive Features: Following initial onset of symptoms he subsequently developed visuospatial impairments and became lost in familiar environments. His loss of judgement reportedly led to bankruptcy at the age of 66 yrs. He developed language deficits and exhibited word substitution,	Yes

Case No.	Source [Reference]	Sport / Activity	Age	Exposure				Age and Symptom Onset Clinical Description / Symptoms Reported Cognitive Findings	Pathology Reported[§]
				Age Started	Years of Participation	Level of Play	Number of Concussion(s) & Concussion Severity		
								and was incoherent at times.	
98	Hazrati et al (2013) Case 5	Canadian Football League	74	6 in the CFL	NR	P	Number: "multiple" Severity: Unknown	Age and Onset: 62 yrs: angry, irritable, poor judgement, and memory deficits Clinical Features: He experienced episodes of hallucinations of strangers in his home and misidentification of others and himself; e.g. he attacked mirrors. He developed delusions that people were stealing from him and had episodes of aggression and agitation and impaired motor function. Family history of late-onset AD (mother) and late-onset 'dementia' (father). Cognitive Features: In the years following onset of symptoms, his memory worsened and he began to get lost.	Yes
99	Hazrati et al (2013) Case 6	Canadian Football League	63	7 in the CFL	Began playing football in HS	P	Number: "multiple" Severity: Unknown	Age and Onset: 48 yrs; withdrawn, anxious, insecure, and lethargic. Motor slowing Clinical Features: At age 50 yrs, he noted his handwriting had become messier, and also complained of some cramping and numbness in his feet and decreased ability to play baseball. His movements progressively slowed. He became obsessed with bladder incontinence, attending the bathroom multiple times a day, yet appeared incongruously unperturbed when accidents did happen. By 55 yrs he had repeated episodes of bladder incontinence. He had vivid dreams he was convinced were real. He became less attentive to hygiene. He had delusions and hallucinations, which ceased with discontinuation of Sinemet. He eventually had episodes of agitation and developed great difficulty ambulating. Cognitive Features: At 50 yrs he began to exhibit memory deficits, which became progressively worse over subsequent years. After a few years his speech became slurred and hypophonic. Concerns regarding his judgement became apparent at 54 yrs, manifest in his poor business decisions. His judgement continued to deteriorate. At 58 yrs he had prosopagnosia. At that time he also displayed difficulty recalling names of his children.	Yes
100	McKee et al (2012) Case 36	AF – HS, HS basketball	10-19	NR	NR	High School	Number: NR Severity: NR	Age and Onset: 17yrs; headaches Clinical Features: CoD: second impact syndrome. Moderate headache. Mild attention deficits. Cognitive Features: Not conducted - retrospective information only.	Yes
101	McKee et al (2012) Case 37	AF – HS, rugby	10-19	NR	NR	High School	Number: NR Severity: NR	Age and Onset: 18yrs: headaches Clinical Features: CoD: cerebral oedema. Moderate headache. Cognitive Features: Not conducted - retrospective information only.	Yes
102	McKee et al (2012) Case 38	IED/explosives, AF – HS, Vet	20-29	NR	NR	High School	Number: NR Severity: NR	Age and Onset: 20yrs: headaches Clinical Features: CoD: ICH. Moderate headache, depression, explosivity and aggression. Mild apathy; diagnosed with PTSD. Cognitive Features: Retrospective information only; moderate attention deficits and mild memory deficits.	Yes
103	McKee et al (2012) Case 39	NFL	20-29	NR	NR	P	Number: NR Severity: NR	Age and Onset: 26yrs: attention deficits, STM, language deficits Clinical Features: CoD: suicide. Mild depression and impulsivity and moderate suicidality, diagnosed with PTSD. Cognitive Features: Retrospective information only; mild executive dysfunction and language difficulties; moderate attention and memory deficits.	Yes
104	McKee et al (2012) Case 40	AF – HS, Vet	20-29	NR	NR	High School	Number: NR Severity: NR	Age and Onset: NR Clinical Features: CoD: suicide. Cognitive Features: Not conducted - retrospective information only.	Yes
105	McKee et al (2012) Case 41	NFL	30-39	NR	NR	P	Number: NR Severity: NR	Age and Onset: 30yrs: headaches, STM Clinical Features: CoD: cardiac. Mild aggression; moderate headache, depression and explosivity. Cognitive Features: Retrospective information only; mild executive dysfunction, attention and memory deficits.	Yes
106	McKee et al (2012) Case 42	NFL	50-59	NR	NR	P	Number: NR Severity: NR	Age and Onset: N/A Clinical Features: CoD: malignancy. Mother had AD. Cognitive Features: Not conducted - retrospective information only.	Yes

Case No.	Source [Reference]	Sport / Activity	Age	Exposure				Age and Symptom Onset Clinical Description / Symptoms Reported Cognitive Findings	Pathology Reported[§]
				Age Started	Years of Participation	Level of Play	Number of Concussion(s) & Concussion Severity		
107	McKee et al (2012) Case 43	AF – college	20-29	NR	NR	College	Number: NR Severity: NR	Age and Onset: N/A Clinical Features: CoD: suicide. Moderate suicidality. Cognitive Features: Retrospective information only; mild impulsivity.	Yes
108	McKee et al (2012) Case 44	Wrestling	20-29	NR	NR	P	Number: NR Severity: NR	Age and Onset: 26yrs: headache, STM Clinical Features: CoD: OD. Moderate headache, depression, explosivity, aggression. Cognitive Features: Retrospective information only; mild memory deficits; moderate attention deficits.	Yes
109	McKee et al (2012) Case 46	AF – college, HS wrestling	30-39	NR	NR	High School / college	Number: NR Severity: NR	Age and Onset: 30yrs: MND Clinical Features: CoD: respiratory failure. Moderate depression, explosivity, aggression, mild apathy and suicidality. Neuropathological diagnosis of CTE-MND. Gait and speech disturbance associated with MND. Cognitive Features: Retrospective information only; mild impulsivity, attention and memory deficits and executive dysfunction.	Yes
110	McKee et al (2012) Case 47	IED, AF-HS, prison guard, Vet	30-39	NR	NR	High School	Number: NR Severity: NR	Age and Onset: 31yrs: STM, depression, PTSD Clinical Features: CoD: OD. Moderate depression. Moderate suicidality and apathy; diagnosed with PTSD. Cognitive Features: Retrospective information only; mild executive dysfunction, language deficits and impulsivity; moderate attention and memory deficits.	Yes
111	McKee et al (2012) Case 48	AF – college	40-49	NR	NR	College	Number: NR Severity: NR	Age and Onset: 40yrs: MND Clinical Features: CoD: respiratory failure. Mild headache; moderate depression and explosivity, gait and speech difficulties associated with MND. Neuropathological diagnosis of CTE-MND. Cognitive Features: Retrospective information only; impulsivity, mild attention and memory deficits.	Yes
112	McKee et al (2012) Case 49	IED, MVA, Vet	40-49	NR	NR	N/A	Number: NR Severity: NR	Age and Onset: 42yrs: headache, depression, attention deficits Clinical Features: CoD: cerebral aneurysm. Moderate headache and depression. Cognitive Features: Retrospective information only; moderate attention deficit..	Yes
113	McKee et al (2012) Case 51	NFL	40-49	NR	NR	P	Number: NR Severity: NR	Age and Onset: 46yrs: headache Clinical Features: CoD: cardiac. Mild depression; moderate headache. Cognitive Features: Not conducted - retrospective information only.	Yes
114	McKee et al (2012) Case 52	AF – HS	40-49	NR	NR	High School	Number: NR Severity: NR	Age and Onset: 47yrs: STM, attention deficits, executive dysfunction, depression Clinical Features: CoD: suicide. Mild explosivity and aggression; moderate depression and suicidality. Father possible AD, bipolar disease. Cognitive Features: Retrospective information only; mild language deficits; moderate attention and memory deficits and executive dysfunction.	Yes
115	McKee et al (2012) Case 53	NFL	40-49	NR	NR	P	Number: NR Severity: NR	Age and Onset: 48yrs: MND Clinical Features: CoD: respiratory failure. Mild explosivity and aggression; moderate depression. Gait and speech difficulties associated with MND. Father possibly undiagnosed dementia. Neuropathological diagnosis of CTE-MND. Cognitive Features: Not conducted - retrospective information only.	Yes
116	McKee et al (2012) Case 54	AF – college	50-59	NR	NR	College	Number: NR Severity: NR	Age and Onset: 52yrs: headaches, STM Clinical Features: CoD: malignancy. Moderate headache, depression, impulsivity, explosivity and aggression. Cognitive Features: Retrospective information only; mild attention, memory, language and visuospatial deficits, mild apathy; moderate executive dysfunction.	Yes
117	McKee et al (2012) Case 56	NFL, Vet	80-89	NR	NR	P	Number: NR Severity: NR	Age and Onset: N/A CoD: cardiac. Mild explosivity. Cognitive Features: Not conducted - retrospective information only.	Yes

Case No.	Source [Reference]	Sport / Activity	Age	Exposure				Age and Symptom Onset Clinical Description / Symptoms Reported Cognitive Findings	Pathology Reported[§]
				Age Started	Years of Participation	Level of Play	Number of Concussion(s) & Concussion Severity		
118	McKee et al (2012) Case 57	NFL	30-39	NR	NR	P	Number: NR Severity: NR	Age and Onset: 34yrs: headache, mood swings, paranoia Clinical Features: CoD: suicide. Mild depression and explosivity; moderate headache, aggression, paranoia and suicidality. Cognitive Features: Retrospective information only; mild attention, memory and language deficits, impulsivity and apathy; moderate executive dysfunction.	Yes
119	McKee et al (2012) Case 58	Boxing	40-49	NR	NR	P	Number: NR Severity: NR	Age and Onset: 37yrs: headache, psychosis, STM Clinical Features: CoD: suicide. Moderate headache, depression, explosivity and aggression, paranoia and suicidality. Cognitive Features: Retrospective information only; moderate impulsivity, mild dementia, gait disturbance and dysarthric speech; moderate attention, memory, language and visuospatial deficits, moderate executive dysfunction.	Yes
120	McKee et al (2012) Case 59	HS - basketball, AF – college, A boxing, Vet	40-49	NR	NR	High School / College	Number: NR Severity: NR	Age and Onset: 27yrs: MDN Clinical Features: CoD: respiratory failure. Mild depression. Gait and speech difficulties associated with MND. Neuropathological diagnosis of CTE-MND. Cognitive Features: Retrospective information only; moderate attention deficits.	Yes
121	McKee et al (2012) Case 63	NFL	50-59	NR	NR	P	Number: NR Severity: NR	Age and Onset: 45yrs: headache, explosivity Clinical Features: CoD: suicide. Mild impulsivity; moderate headache, depression, explosivity and aggression. Suicidality. Father had AD. Cognitive Features: Retrospective information only; Mild dementia with mild language and visuospatial deficits, mild apathy; moderate attention, memory deficits and executive dysfunction.	Yes
122	McKee et al (2012) Case 64	NFL	50-59	NR	NR	P	Number: NR Severity: NR	Age and Onset: 53yrs: STM, attention deficits, executive dysfunction Clinical Features: CoD: cardiac. Mild headache and depression; moderate explosivity. Cognitive Features: Retrospective information only; mild dementia with mild attention, memory language, visuospatial deficits and mild executive dysfunction..	Yes
123	McKee et al (2012) Case 65	Self-injury	50-59	NR	NR	N/A	Number: NR Severity: NR	Age and Onset: Not reported Clinical Features: CoD: respiratory failure. Cognitive Features: Not conducted - retrospective information only.	Yes
124	McKee et al (2012) Case 66	NFL	60-69	NR	NR	P	Number: NR Severity: NR	Age and Onset: 56yrs: STM, apathy Clinical Features: CoD: respiratory failure. Moderate explosivity and aggression. Gait and speech difficulties associated with MND. Neuropathological diagnosis of CTE-MND. Cognitive Features: Retrospective information only; Mild dementia with mild memory and visuospatial deficits; moderate attention deficits, executive dysfunction and apathy.	Yes
125	McKee et al (2012) Case 67	NFL	60-69	NR	NR	P	Number: NR Severity: NR	Age and Onset: 63yrs: STM, executive dysfunction, attention deficits Clinical Features: CoD: OD. Mild depression. Brother mental illness. Cognitive Features: Retrospective information only; mild dementia, with moderate attention, memory, visuospatial deficits and executive dysfunction..	Yes
126	McKee et al (2012) Case 68	NFL	60-69	NR	NR	P	Number: NR Severity: NR	Age and Onset: N/A Clinical Features: CoD: cardiac. Mild depression, explosivity and aggression. Cognitive Features: Retrospective information only; mild visuospatial deficits..	Yes
127	McKee et al (2012) Case 69	NFL	60-69	NR	NR	P	Number: NR Severity: NR	Age and Onset: 52yrs: headaches, STM, depression, impulsivity Clinical Features: CoD: respiratory failure. Moderate headache, depression and impulsivity. Gait and speech difficulties associated with MND. Neuropathological diagnosis of CTE-MND. Father had depression. Cognitive Features: Retrospective information only; mild dementia with mild attention, language and visuospatial deficits, mild executive dysfunction; moderate memory deficits.	Yes
128	McKee et al (2012) Case 70	TBI, PT epilepsy, Vet	70-79	NR	NR	N/A	Number: NR Severity: NR	Age and Onset: NR Clinical Features: CoD: pneumonia. Cognitive Features: Not conducted - retrospective information only.	Yes

Case No.	Source [Reference]	Sport / Activity	Age	Exposure				Age and Symptom Onset Clinical Description / Symptoms Reported Cognitive Findings	Pathology Reported[§]
				Age Started	Years of Participation	Level of Play	Number of Concussion(s) & Concussion Severity		
129	McKee et al (2012) Case 71	MVA, altercation, Vet	70-79	NR	NR	N/A	Number: NR Severity: NR	Age and Onset: NR Clinical Features: CoD: pneumonia. Cognitive Features: Not conducted - retrospective information only.	Yes
130	McKee et al (2012) Case 72	Boxing	50-59	NR	NR	P	Number: NR Severity: NR	Age and Onset: 42yrs: aggression, depression, paranoia Clinical Features: CoD: respiratory failure. Mild explosivity; moderate depression and aggression. Mild language deficit, apathy, gait disturbance and dysarthric speech; and moderate paranoia. Cognitive Features: Retrospective information only; moderate dementia with moderate attention, memory and visuospatial deficits, moderate executive dysfunction.	Yes
131	McKee et al (2012) Case 73	Boxing	60-69	NR	NR	P	Number: NR Severity: NR	Age and Onset: 46yrs: executive dysfunction, impulsivity, paranoia, aggression Clinical Features: CoD: respiratory failure. Moderate depression, impulsivity, explosivity and aggression. Moderate paranoia and suicidality; and gait and speech difficulties associated with MND. Neuropathological diagnosis of CTE-MND. Cognitive Features: Retrospective information only; moderate dementia with moderate attention, memory, and language deficits, moderate executive dysfunction.	Yes
132	McKee et al (2012) Case 74	Boxing	60-69	NR	NR	P	Number: NR Severity: NR	Age and Onset: 64yrs: STM, executive dysfunction, paranoia Clinical Features: CoD: cardiac. Moderate impulsivity, explosivity and aggression. Mild Parkinsonian signs; paranoia; and gait and speech disturbance associated with MND. Neuropathological diagnosis of CTE-MND. Sibling had ALS. Cognitive Features: Retrospective information only; mild language deficits, moderate dementia with moderate attention, memory and visuospatial deficits, moderate executive dysfunction.	Yes
133	McKee et al (2012) Case 76	NFL	70-79	NR	NR	P	Number: NR Severity: NR	Age and Onset: 35yrs: paranoia, impulsivity, bizarre behaviour Clinical Features: CoD: malignancy. Moderate depression, impulsivity, explosivity and aggression, and paranoia. Cognitive Features: Retrospective information only; mild attention deficits; moderate dementia with moderate memory deficits, executive dysfunction.	Yes
134	McKee et al (2012) Case 77	NFL	70-79	NR	NR	P	Number: NR Severity: NR	Age and Onset: 58yrs: depression, aggression Clinical Features: CoD: cardiac. Moderate depression, impulsivity, explosivity and aggression. Mild gait disturbance and suicidality; Mother had bipolar disease. Cognitive Features: Retrospective information only; moderate dementia with moderate attention and memory deficits, moderate executive dysfunction; severe apathy.	Yes
135	McKee et al (2012) Case 78	NFL, Vet	80-89	NR	NR	P	Number: NR Severity: NR	Age and Onset: 60yrs: STM, executive dysfunction, bizarre behaviour Clinical Features: CoD: respiratory failure. Mild Parkinsonian signs. Cognitive Features: Retrospective information only; moderate dementia with moderate attention, memory, language and visuospatial deficits, executive dysfunction, and gait disturbance and dysarthric speech; severe apathy.	Yes
136	McKee et al (2012) Case 79	Boxing, Vet	70-79	NR	NR	P	Number: NR Severity: NR	Age and Onset: NR Clinical Features: CoD: FTT. Cognitive Features: Not conducted - retrospective information only.	Yes
137	McKee et al (2012) Case 80	NFL, Vet	70-79	NR	NR	P	Number: NR Severity: NR	Age and Onset: 76yrs:STM, executive dysfunction, language deficits Clinical Features: CoD: respiratory failure. Mild explosivity and aggression; moderate depression. Cognitive Features: Retrospective information only; Moderate dementia with moderate executive dysfunction, memory and language deficits.	Yes
138	McKee et al (2012) Case 83	NFL, Vet	80-89	NR	NR	P	Number: NR Severity: NR	Age and Onset: 65yrs: executive dysfunction, explosivity Clinical Features: CoD: FFT. Moderate explosivity and aggression. and paranoia. Cognitive Features: Retrospective information only; moderate dementia with moderate executive dysfunction, attention, memory, language and visuospatial deficits, moderate apathy.	Yes
139	McKee et al (2012) Case 84	AF, Vet	80-89	NR	NR	Semi-P	Number: NR Severity: NR	Age and Onset: 74yrs: paranoia Clinical Features: CoD: FFT. Mild explosivity and aggression; moderate headache. Mild apathy and gait disturbance, and paranoia.	Yes

Case No.	Source [Reference]	Sport / Activity	Age	Exposure				Age and Symptom Onset Clinical Description / Symptoms Reported Cognitive Findings	Pathology Reported[§]
				Age Started	Years of Participation	Level of Play	Number of Concussion(s) & Concussion Severity		
								Cognitive Features: Retrospective information only; moderate dementia with moderate executive dysfunction, memory, language and visuospatial deficits.	
140	McKee et al (2012) Case 85	Boxing, Vet	90-99	NR	NR	A	Number: NR Severity: NR	Age and Onset: NR Clinical Features: CoD: FFT. Cognitive Features: Not conducted - retrospective information only.	Yes
141	McKee et al (2012) Case 86	NFL, Vet	90-99	NR	NR	P	Number: NR Severity: NR	Age and Onset: 83yrs: STM, executive dysfunction Clinical Features: CoD: FFT. Moderate dementia. Cognitive Features: Moderate executive dysfunction, attention, memory, language and visuospatial deficits.	Yes
142	McKee et al (2012) Case 87	AF – college	60-69	NR	NR	College	Number: NR Severity: NR	Age and Onset: NR Clinical Features: CoD: FTT. AD. Cognitive Features: Not conducted - retrospective information only.	Yes
143	McKee et al (2012) Case 88	NFL, Vet	60-69	NR	NR	P	Number: NR Severity: NR	Age and Onset: NR Clinical Features: CoD: FTT. AD. Cognitive Features: Not conducted - retrospective information only.	Yes
144	McKee et al (2012) Case 89	AF – college	60-69	NR	NR	P	Number: NR Severity: NR	Age and Onset: NR Clinical Features: CoD: FTT. AD. Cognitive Features: Not conducted - retrospective information only.	Yes
145	McKee et al (2012) Case 90	NFL, Vet	70-79	NR	NR	P	Number: NR Severity: NR	Age and Onset: NR Clinical Features: CoD: FTT. AD. Cognitive Features: Not conducted - retrospective information only.	Yes
146	McKee et al (2012) Case 91	NFL	60-69	NR	NR	P	Number: NR Severity: NR	Age and Onset: NR Clinical Features: CoD: FTT. AD, PD. Cognitive Features: Not conducted - retrospective information only.	Yes
147	McKee et al (2012) Case 92	NFL	70-79	NR	NR	P	Number: NR Severity: NR	Age and Onset: NR Clinical Features: CoD: FTT. AD, LBD. Cognitive Features: Not conducted - retrospective information only.	Yes
148	McKee et al (2012) Case 93	Hockey, Vet	80-89	NR	NR	A	Number: NR Severity: NR	Age and Onset: NR Clinical Features: CoD: FTT. AD, PD. Cognitive Features: Not conducted - retrospective information only.	Yes
149	McKee et al (2012) Case 94	College AF & rugby, Vet	60-69	NR	NR	College	Number: NR Severity: NR	Age and Onset: NR Clinical Features: CoD: FTT. PD. Cognitive Features: Not conducted - retrospective information only.	Yes
150	McKee et al (2012) Case 95	NFL	60-60	NR	NR	P	Number: NR Severity: NR	Age and Onset: NR Clinical Features: CoD: respiratory failure. LBD. Cognitive Features: Not conducted - retrospective information only.	Yes
151	McKee et al (2012) Case 96	NFL	70-79	NR	NR	P	Number: NR Severity: NR	Age and Onset: NR Clinical Features: CoD: cardiac. LBD. Cognitive Features: Not conducted - retrospective information only.	Yes
152	McKee et al (2012) Case 98	NFL, Vet	70-79	NR	NR	P	Number: NR Severity: NR	Age and Onset: NR Clinical Features: CoD: cardiac. PD. Cognitive Features: Not conducted - retrospective information only.	Yes
153	McKee et al (2012) Case 99	NFL, Vet	80-89	NR	NR	P	Number: NR Severity: NR	Age and Onset: NR Clinical Features: CoD: malignancy. LBD. Cognitive Features: Not conducted - retrospective information only.	Yes
154	McKee et al (2012) Case 100	NFL	70-79	NR	NR	P	Number: NR Severity: NR	Age and Onset: NR Clinical Features: CoD: cardiac. PD, FTLD-TDP Cognitive Features: Not conducted - retrospective information only.	Yes

Case No.	Source [Reference]	Sport / Activity	Age	Exposure				Age and Symptom Onset Clinical Description / Symptoms Reported Cognitive Findings	Pathology Reported[§]
				Age Started	Years of Participation	Level of Play	Number of Concussion(s) & Concussion Severity		
155	McKee et al (2012) Case 101	Canadian Football League	70-79	NR	NR	P	Number: NR Severity: NR	Age and Onset: NR Clinical Features: CoD: respiratory failure. PD, PSP Cognitive Features: Not conducted - retrospective information only.	Yes
156	McKee et al (2012) Case 102	NFL	60-69	NR	NR	P	Number: NR Severity: NR	Age and Onset: NR Clinical Features: CoD: FTT. Pick's Cognitive Features: Retrospective information only.	Yes
157	McKee et al (2012) Case 103	NFL	80-89	NR	NR	P	Number: NR Severity: NR	Age and Onset: NR Clinical Features: CoD: FTT. FTLD-TDP Cognitive Features: Not conducted - retrospective information only.	Yes
158	National Institutes of Health, Junior Seau	NFL	43	NR	NFL: 20yrs	P	Number: NR Severity: NR	Age and Onset: NR Clinical Features: CoD: GSW. Demonstrated marked personality change for months prior to his suicide, including depression and irritability. Cognitive Features: Not conducted – retrospective information only; attention problems.	Yes

Definitions: [§]: For further details regarding neuropathology refer to Table 2; *: Original source not checked (not in English); HI: Head Injury; mTBI: mild traumatic brain injury; KOs: Knock Outs; P: professional; A: amateur; B: booths; SP: sparring partner; KO'd: knocked out; LOC: loss of consciousness; yrs: years; dec: decade; AF: American Football; AF - HS: High school American Football; NHL: National Hockey League; MMA: Mixed Martial Arts; CFL: Canadian Football League; Vet: military veteran; IED/explosives: improvised explosive device blast exposure; MVA: motor vehicle accident; PT: post-traumatic; NR: Not Reported; CC: cerebral cortex; SNr: Substantia Nigra; LC: Locus Coeruleus; STM: short-term memory; CTE: chronic traumatic encephalopathy; DP: dementia pugilistica; AD: Alzheimer's disease; PD: Parkinson's disease; FTLD: Frontotemporal lobar degeneration; TDP: TAR DNA-binding protein; LBD: Lewy body disease; ALS: amyotrophic lateral sclerosis; MND: motor neuron disease; PSP: progressive supranuclear palsy; ECT: electroconvulsive therapy; PTSD: post-traumatic stress disorder; PCS: Post-Concussive Syndrome; REM: rapid eye movement; CoD: Cause of death; OD: overdose; ICH: intracerebral haemorrhage; GSW: gunshot wound; FTT: failure to thrive associated with dementia; G&M: The Globe and Mail Newspaper.

Table 2. Cases of reported chronic traumatic encephalopathy: Neuropathology.

Case	Source [Reference]	Reported Pathology; Tau; TDP-43; & Amyloid
1	Case 1 [Roberts 1969]	Pathology: N/A; Tau: N/A; TDP-43: N/A; Amyloid: N/A
2	Case 2 [Roberts 1969]	Pathology: N/A; Tau: N/A; TDP-43: N/A; Amyloid: N/A
3	Case 3 [Roberts 1969]	Pathology: N/A; Tau: N/A; TDP-43: N/A; Amyloid: N/A
4	Case 4 [Roberts 1969]	Pathology: N/A; Tau: N/A; TDP-43: N/A; Amyloid: N/A
5	Case 5 [Roberts 1969]	Pathology: N/A; Tau: N/A; TDP-43: N/A; Amyloid: N/A
6	Case 6 [Roberts 1969]	Pathology: N/A; Tau: N/A; TDP-43: N/A; Amyloid: N/A
7	Case 7 [Roberts 1969]	Pathology: N/A; Tau: N/A; TDP-43: N/A; Amyloid: N/A
8	Case 8 [Roberts 1969]	Pathology: N/A; Tau: N/A; TDP-43: N/A; Amyloid: N/A
9	Case 9 [Roberts 1969]	Pathology: N/A; Tau: N/A; TDP-43: N/A; Amyloid: N/A
10	Case 10 [Roberts 1969]	Pathology: N/A; Tau: N/A; TDP-43: N/A; Amyloid: N/A
11	Case 11 [Roberts 1969]	Pathology: N/A; Tau: N/A; TDP-43: N/A; Amyloid: N/A
12	Case 1 in McKee et al 2009 [Brandenburg & Hallervorden 1954] *	Pathology: Cerebral atrophy, enlarged 2nd & 3rd ventricles. Tau: NFTs severe density in hippocampus; mild density frontal, parietal, temporal, & occipital regions TDP-43: NR Amyloid: Severe diffuse plaques
13	Case 2 in McKee et al 2009 [Grahmann & Ule 1957] *	Pathology: Cerebral atrophy, 2nd ventricle enlargement; cavum septum Tau: NFTs severe density in hippocampus & SNr; mild density frontal, parietal, & temporal regions, thalamus, hypothalamus TDP-43: NR Amyloid: No amyloid plaques observed
14	Case 3 in McKee et al 2009 [Neubuerger et al 1959]	Pathology: Biopsy of Cerebral Cortex. The lower layers of the frontal cortex exhibited a slight numerical reduction of nerve cells. Foci of astrocytes with tangled processes also were noted in the upper cortex. A suggestion of faintly argentophilic structures in the form of thin kinked fibrils was observed in the immediate neighbourhood of small vessels. They vaguely resembled small "senile" plaques; however, typical plaques, fibrillary alteration, and vascular lesions were not found. Tau: NR; TDP-43: NR Amyloid: No amyloid plaques observed.
15	Case 4 in McKee et al 2009 [Neubuerger et al 1959]	Pathology: The embalmed brain weighed 1,130 g. Severe atrophy was evident in the frontal lobes and was more pronounced in the right hemisphere, where it overlapped the medial aspect of the parietal lobe. The convolutions were thin; the sulci were wide; the ventricles were slightly dilated. Focal lesions were absent. Microscopically, the severest changes were present in the cortex of the frontal lobes. However, the cortex of the temporal and occipital lobes exhibited more pronounced atrophy than was anticipated. The cortex was thinned; the stratification was partially lost; numerous nerve cells were absent. A fairly advanced degree of gliosis was observed; many large fibrillary astrocytes were present throughout the cortex, and a network of glial fibres occupied the molecular layer. The hippocampus exhibited loss of nerve cells in the presubiculum, resembling that seen in senile and presenile brain diseases. Tau: NR; TDP-43: NR Amyloid: No amyloid plaques observed
16	Case 5 in McKee et al 2009 [Courville 1962]	Pathology: Brain weight was 1120g, frontal and parietal atrophy, lateral and third ventricle enlargement, NFTs mild density in frontal, parietal, and temporal regions Tau: No NFTs reported TDP-43: NR Amyloid: No amyloid plaques observed
17	Case 6 in McKee et al 2009 [Mawdsley & Ferguson 1963], Case 1	Pathology: NR; Tau: NR; TDP-43: NR; Amyloid: NR
18	Case 7 in McKee et al 2009 [Mawdsley & Ferguson 1963], Case 2	Pathology: N/A; Tau: N/A; TDP-43: N/A; Amyloid: N/A
19	Case 3: Mawdsley & Ferguson 1963	Pathology: N/A; Tau: N/A; TDP-43: N/A; Amyloid: N/A
20	Case 4: Mawdsley & Ferguson 1963	Pathology: N/A; Tau: N/A; TDP-43: N/A; Amyloid: N/A
21	Case 5: Mawdsley & Ferguson 1963	Pathology: N/A; Tau: N/A; TDP-43: N/A; Amyloid: N/A
22	Case 6: Mawdsley & Ferguson 1963	Pathology: N/A; Tau: N/A; TDP-43: N/A; Amyloid: N/A
23	Case 7: Mawdsley & Ferguson 1963	Pathology: N/A; Tau: N/A; TDP-43: N/A; Amyloid: N/A
24	Case 8: Mawdsley & Ferguson 1963	Pathology: N/A; Tau: N/A; TDP-43: N/A; Amyloid: N/A

Case	Source [Reference]	Reported Pathology; Tau; TDP-43; & Amyloid
25	Case 9: Mawdsley & Ferguson 1963	Pathology: N/A; Tau: N/A; TDP-43: N/A; Amyloid: N/A
26	Case 10: Mawdsley & Ferguson 1963	Pathology: Brain weighed only 1,050 g. and there was gross diffuse cortical atrophy, most evident in the frontal lobes. The lateral ventricles were dilated. There was a cavum septi pellucidi. Tau: N/A; TDP-43: N/A; Amyloid: N/A
27	Case 8 in McKee et al 2009 [Constantinidis & Tissot 1967] *	Pathology: Brain weight 1,180g; mild cerebral atrophy, mild cavum septum; severe pallor of SNr. Tau: Severe density NFTs located in hippocampus, entorhinal cortex, amygdala, periventricular gray, tegmentum, SNr, & LC; mild density NFTs in frontal, temporal, & occipital regions. TDP-43: NR Amyloid: No amyloid plaques observed
28	Case 9 in McKee et al 2009 [Payne 1968]	Pathology: Slight general atrophy of frontal lobes, moderate cerebral atheroma, ventricular system was slightly enlarged, cavum septi pellicidi with small fenestration of one of the laminae; thickening of arteriole walls; a small number of argyrophilic plaques in the cortical ribbon with irregular proliferation of the surface layer - most common in the upper corners of the convolutions; Cajal stains revealed small foci of hypotrophy & hyperplasia of astrocytes grey matter of the cortex at the base; Diffuse slight gliosis throughout WM. Tau: NR; TDP-43: NR Amyloid: A number of amyloid bodies scattered throughout the brain with high concentration within the hippocampal gyrus.
29	Case 10 in McKee et al 2009 [Payne 1968]	Pathology: Congestion in the meninges, enlarged ventricles, cavum septi pellucidi with fenestration of the laminae, frontal infarction; parieto-occipital scarring; cystic scarring in the pons and basal ganglia; irregular grey stippling in the left occipital lobe. Widespread arteriolosclerosis and atheroma. Foci of degeneration of myelinated fibres; periventricular glial nodes and irregular areas of gliosis in the centra, CC, & cerebellum. Tau: NR; TDP-43: NR Amyloid: No amyloid plaques observed
30	Case 11 in McKee et al 2009 [Payne 1968]	Pathology: Slightly thickened leptomeninges at the base; minimal cerebral atheroma; small cavum septi pellucidi; thin linear scar in the coronal ribbon in occipital lobe. Cajal stains revealed micro scars scattered in the cortex of the hippocampal gyrus, cerebellum, and medulla. Tau: NR; TDP-43: NR Amyloid: Early NFT changes observed
31	Case 12 in McKee et al 2009 [Payne 1968]	Pathology: Slight thickening of the leptomeninges at the base, right Sylvian fissure, posterior left temporal and parietal lobes. Slight atheroma of vertebral and basilar artery. WM 'congestion' - anterior limb left internal capsule irregular scaring; small scars in left occipital lobe, mainly in the cortex. The superior surface of the left middle temporal gyrus contained linear scar, left lateral ventricle slightly enlarged. Cavum septi pellucidi; four small irregular degenerate areas of left cerebellar hemisphere; in the adjacent WM irregular cystic areas & gliosis. Cajal stain revealed many foci of glial hypertrophy & hyperplasia. Tau: NR; TDP-43: NR; Amyloid: NR
32	Case 13 in McKee et al 2009 [Payne 1968]	Pathology: Few chronic inflammatory cells scattered about the perivascular spaces. Cerebrum micro scars & a few foci of myelin degeneration in the centra and corpus callosum. Tau: NR; TDP-43: NR Amyloid: Early NFT changes observed
33	Case 14 in McKee et al 2009 [Payne 1968]	Pathology: A cavum septi pellucidi was present, a few small areas of glial hyperplasia in the tangential layer of the cerebrum; a few inflammatory cells and some granules of hemosiderin in the perivascular space. WM demonstrated small foci of degenerative changes. Tau: NR; TDP-43: NR; Amyloid: NR
34	Case 15 in McKee et al 2009 [Corsellis et al 1973]	Pathology: Mild septum fenestration; mild cerebellum tonsillar scarring; mild loss of pigmentation in SNr. Tau: Moderate level of NFTs in SNr; severe level of NFTs in CC TDP-43: NR Amyloid: No plaques reported
35	Case 16 in McKee et al 2009 [Corsellis et al 1973]	Pathology: Mild septum fenestration; mild cerebellum tonsillar scarring; moderate loss of pigmentation in SNr. Tau: Severe level of NFTs in SNr & CC TDP-43: NR Amyloid: No plaques reported
36	Case 17 in McKee et al 2009 [Corsellis et al 1973]	Pathology: Mild septum fenestration; mild cerebellum tonsillar scarring; severe loss of pigmentation in SNr. Tau: Severe level of NFTs in SNr & CC TDP-43: NR Amyloid: No plaques reported
37	Case 18 in McKee et al 2009 [Corsellis et al 1973]	Pathology: Mild septum fenestration; cerebellum tonsillar scarring; severe loss of pigmentation in SNr. Tau: Mild level of NFTs in SNr; Moderate level of NFTs in CC TDP-43: NR

Case	Source [Reference]	Reported Pathology; Tau; TDP-43; & Amyloid
		Amyloid: No plaques reported
38	Case 19 in McKee et al 2009 [Corsellis et al 1973]	Pathology: Mild septum fenestration; mild cerebellum tonsillar scarring; mild loss of pigmentation in SNr. Tau: Moderate level of NFTs in SNr & CC TDP-43: NR Amyloid: No plaques reported
39	Case 20 in McKee et al 2009 [Corsellis et al 1973]	Pathology: Mild septum fenestration; mild cerebellum tonsillar scarring; moderate loss of pigmentation in SNr. Tau: Moderate level of NFTs in SNr & CC TDP-43: NR Amyloid: Mild concentration of senile plaques present in cerebral cortex
40	Case 21 in McKee et al 2009 [Corsellis et al 1973]	Pathology: Mild septum fenestration; mild loss of pigmentation in SNr. Tau: Moderate level of NFTs in SNr; severe level of NFTs in CC TDP-43: NR Amyloid: No plaques reported
41	Case 22 in McKee et al 2009 [Corsellis et al 1973]	Pathology: Mild septum fenestration; mild loss of pigmentation in SNr. Tau: Mild level of NFTs in SNr; Moderate level of NFTs in CC TDP-43: NR Amyloid: mild concentration of senile plaques present in cerebral cortex
42	Case 23 in McKee et al 2009 [Corsellis et al 1973]	Pathology: Mild septum fenestration; mild cerebellum tonsillar scarring; moderate loss of pigmentation in SNr. Tau: Moderate level of NFTs in SNr & CC TDP-43: NR Amyloid: No plaques reported
43	Case 24 in McKee et al 2009 [Corsellis et al 1973]	Pathology: Mild septum fenestration; mild cerebellum tonsillar scarring; moderate loss of pigmentation in SNr. Tau: Moderate level of NFTs in SNr & CC TDP-43: NR Amyloid: Mild concentration of senile plaques present in cerebral cortex
44	Case 25 in McKee et al 2009 [Corsellis et al 1973]	Pathology: Mild septum fenestration Tau: Mild level of NFTs in CC TDP-43: NR Amyloid: No plaques reported
45	Case 26 in McKee et al 2009 [Corsellis et al 1973]	Pathology: Unremarkable septum & cerebellar tonsils Tau: Mild level of NFTs in CC TDP-43: NR Amyloid: No plaques reported
46	Case 27 in McKee et al 2009 [Corsellis et al 1973]	Pathology: Mild cerebellum tonsillar scarring; mild loss of pigmentation in SNr. Tau: Moderate level of NFTs in SNr; severe level of NFTs in CC TDP-43: NR Amyloid: Severe concentration of senile plaques present in cerebral cortex
47	Case 28 in McKee et al 2009 [Corsellis et al 1973]	Pathology: Unremarkable septum & cerebellar tonsils Tau: Mild level of NFTs in CC TDP-43: NR Amyloid: Mild concentration of senile plaques present in cerebral cortex
48	Case 29 in McKee et al 2009 [Corsellis et al 1973]	Pathology: Unremarkable septum & cerebellar tonsils Tau: No NFTs reported TDP-43: NR Amyloid: No plaques reported
49	Case 30 in McKee et al 2009 [Roberts GW et al 1990]	Pathology: Mild focal atheroma of the major vessels, gyral atrophy over the cerebral hemispheres, septal cavum with fenestrated leaves, there was some ventricular dilatation, small foci of softening; low numbers of paired helical filament immunoreactive tangles in the frontal cortex and substantial numbers of diffuse p-protein-immunoreactive plaques together with slight numbers of "classic" plaques Tau: Slight and moderate plaque formation in the frontal and temporal lobes, respectively, with NFTs in the hippocampus and brainstem. TDP-43: NR Amyloid: No amyloid angiopathy reported

Case	Source [Reference]	Reported Pathology; Tau; TDP-43; & Amyloid
50	Case 31 in McKee et al 2009 [Hof et al 1991]	Pathology: Brain weight 773 g, gross cerebral atrophy; a cavum in the septum pellucidum; olfactory bulbs and tracts were very fragile and atrophic; some gliosis was observed in the white matter and a few microinfarcts were found, predominantly in the temporal lobe. Tau: Numerous NFTs were found in the inferior temporal neocortex, perirhinal cortex, entorhinal and periamygdaloid cortex; smaller quantities were observed in the amygdala and prepiriform and orbito-frontal cortex. The tangles were located in both layers II and III of the cortex. No NTs observed. The hippocampus proper contained very few NFTs. TDP-43: NR Amyloid: No amyloid plaques observed
51	Case 32 in McKee et al 2009 [Hof et al 1992]	Pathology: NR; Tau: NR; TDP-43: NR, Amyloid: NR
52	Case 33 in McKee et al 2009 [Hof et al 1992]	Pathology: NR; Tau: NR; TDP-43: NR, Amyloid: NR
53	Case 34 in McKee et al 2009 [Williams & Tannenberg 1996]	Pathology: Brain weighed 1,940 g (whole fixed brain weight was 1,833 g) and was externally normal. Lateral and third ventricles were markedly dilated; CC was thin especially caudally, septum pellucidum was fenestrated anteriorly; thalamus subjectively showed shrinkage of the medial dorsal nucleus; cerebellum showed severe superior vermal folial atrophy with virtually total loss of Purkinje cells, florid Bergmann astrogliosis and reduction in number of granular neurones. Tau: The hippocampus showed occasional NFTs in the pyramidal hippocampal neurons. TDP-43: NR Amyloid: No amyloid plaques observed
54	Case 35 in McKee et al 2009 [Jordan et al 1995]	Pathology: Cortical atrophy, a fenestrated septum pellucidum, and two left lobar cerebral hematomas, one of which extended into the lateral ventricle. Tau: Neurofibrillary degeneration was present in the hippocampal CA1 to CA4 regions, dentate, subiculum, oculomotor nuclei, SNr, and LC. TDP-43: NR Amyloid: Diffuse and neuritic plaques were located in moderate numbers in midfrontal, temporal, and inferior parietal cortices. Cerebral amyloid angiopathy involved meningeal and superficial cerebral vessels of the temporal and parieto-occipital cortices; extensive AP immunoreactivity involving leptomeningeal and cortical arteries and arterioles as well as diffuse amyloid plaques and occasional neuritic plaque cores.
55	Case 36 in McKee et al 2009 [Geddes et al 1996; Geddes et al 1999]	Pathology: Brain weighed 1,430 g. There was pronounced mass effect with transtentorial movement of the medial temporal lobe and diencephalon, and secondary brain stem haemorrhage. There was evidence of recent traumatic brain damage, in the form of haematomas producing mass effect, and cerebral swelling, with changes of terminal hypoxia. Recent axonal injury in the splenium of the corpus callosum was also evident. Pathology comprised argyrophilic, numerous neocortical NFTs & NTs sited predominantly around small intracortical blood vessels. Topography of the pathology demonstrated involvement within the basal surfaces of the brain, often the depths of sulci around a penetrating blood vessel, which involved all layers of the cortex. A collection of NFTs was also observed around a vessel in the transentorhinal cortex. Tau: NFTs most numerous in the cortex of the fusiform gyrus, inferior temporal, middle temporal, and orbital gyri, and were to be seen in all neocortical cell layers, although their distribution was patchy in any one gyrus. The supramarginal gyrus of the parietal lobe and the frontal cortex showed focal collections of tangles. NFTs were often grouped round vessels. Rare NFTs were found in the occipital cortex and cingulum. TDP-43: Only a relatively small proportion of the NFTs stained positively on ubiquitin immunostaining – however, the neuroanatomical region was NR. Amyloid: No amyloid plaques observed
56	Case 37 in McKee et al 2009 [Geddes et al 1999]	Pathology: Brain weighed 1,240 g. Macroscopically normal, and there was no structural lesion that might have accounted for the grand mal seizure that was the cause of death. Pathology comprised argyrophilic, numerous neocortical NFTs & NTs sited predominantly around small intracortical blood vessels. Tau: Topography of the NFT & NT pathology demonstrated considerable involvement within the basal surfaces of the brain, often the depths of sulci around a penetrating blood vessel, which involved all layers of the cortex. TDP-43: NR Amyloid: No amyloid plaques observed
57	Case 38 in McKee et al 2009 [Geddes et al 1999]	Pathology: Brain weighed 1,530 g. There was evidence of recent traumatic brain damage, in the form of haematomas producing mass effect, and cerebral swelling, with changes of terminal hypoxia. Tau: Not well reported beyond describing 'less frequent NFTs' demonstrated than the two boxers in this case series TDP-43: NR Amyloid: No amyloid plaques observed
58	Case 39 in McKee et al 2009 [Geddes et al 1999]	Pathology: The right frontal lobectomy specimen (the calcified epileptogenic lesion) was shown to be a hematoma. All the sections of lobectomy specimen showed normal hexilaminar neocortex with underlying white matter. The leptomeninges were mildly thickened. There was evidence of marked subpial and white matter gliosis. Tau: NFTs were frequently arranged in small clusters around small cortical arterial vessels, but scattered NFTs were also found distributed in all cortical layers. TDP-43: NR Amyloid: No amyloid plaques observed

Case	Source [Reference]	Reported Pathology; Tau; TDP-43; & Amyloid
59	Case 40 in McKee et al 2009 [Geddes et al 1999]	Pathology: Brain weighed 1,550g. There was evidence of recent traumatic brain damage, in the form of haematomas producing mass effect, and cerebral swelling, with changes of terminal hypoxia. Tau: Not well reported beyond describing 'less frequent NFTs' demonstrated than the two boxers in this case series. TDP-43: NR Amyloid: No amyloid plaques observed
60	Case 41 in McKee et al 2009 [Newell & Drachman 1999; Drachman & Newell; Schmidt et al 2001 - case 2]	Pathology: Frontal and anterior temporal lobes were slightly atrophic, with a slight reduction of white matter in the frontal lobes and a slight enlargement of the lateral ventricles. Thickening and fenestration of the left septal leaf of an anterior cavum septi pellucidi were seen, and the SNr & LC were pale. Nuclei in the brain stem, cerebellum, and cerebral hemispheres (including the LC, red nucleus, pontine and raphe nuclei, motor nucleus of the fifth cranial nerve, hypoglossal nucleus, arcuate nucleus, inferior olivary nucleus, thalamus, dentate nucleus, caudate nucleus, putamen, globus pallidus, subthalamic nucleus, and amygdala) showed neurofibrillary degeneration. Spinal cord revealed neuronal loss, gliosis, and axonal spheroids in the anterior horns and neurofibrillary tangles in the anterior and posterior horns. Tau: Scattered NFTs most numerous in the superficial cortical layers of the inferior frontal and temporal lobes; abundant tangles in the hippocampus were associated with marked neuronal loss and gliosis; occasional tangles were present in the deep layers of the primary motor cortex. TDP-43: NR Amyloid: Rare senile plaques. No cerebral amyloid angiopathy or acute haemorrhage was detected.
61	Case 42 in McKee et al 2009 [Schmidt et al 2001]	Pathology: Glial tangles were found in neocortical white and gray matter as well as in the brain stem and spinal cord. Tau: NFTs mild density within the inferior frontal cortex, tegmentum, SNr, & pons; moderate density within the hippocampus & entorhinal cortex. Extracellular NFTs released from degenerating neurons were detected in several regions including the hippocampus, entorhinal cortex, neocortex, brain stem, and spinal cord. TDP-43: Occasional LBs were detected in SNr. Amyloid: No diffuse amyloid plaques observed
62	Case 43 in McKee et al 2009; Case 1 / Omalu et al 2010; Case 1 / Omalu et al 2011	Pathology: Formalin-fixed whole brain weighed 1,565 g. overall normal appearing brain on gross inspection. Tau: Sparse-positive NTs, and sparse intraneuronal band-shaped and flame-shaped NFTs in the frontal, temporal, parietal, occipital, and cingulate cortex and the insula. TDP-43: NR Amyloid: Frequent diffuse extracellular (neocortex) amyloid plaques.
63	Case 44 in McKee et al 2009; Case 2 / Omalu et al 2010; Case 2 / Omalu et al 2011	Pathology: Brain weighed 1,535 g. in the fresh state. A cavum septi pellucidi was present. The SNr showed mild pallor. There was mild neocortical neuronal dropout in the frontal, parietal, and temporal lobes, with residual normal laminar and columnar organization. Swollen, achromasic, or ballooned neurons were absent. There was mild extracellular oedema of the cortical gray and white matter. The globus pallidus showed mild neuronal dropout. The LC also revealed mild neuronal dropout. The medulla oblongata revealed mild neuronal dropout and astrogliosis of the dorsal inferior olivary nucleus. There was mild neuronal dropout of the Purkinje neurons. Tau: Sparse to frequent NFTs & NTs in the neocortex, subcortical ganglia and brainstem nuclei. TDP-43: NR Amyloid: No diffuse amyloid plaques observed
64	Case 45 in McKee et al 2009; Case 3 / Omalu et al 2010; Case 3 / Omalu et al 2011	Pathology: Brain weighed 1,140 g. Coronary arteries revealed mild segmental atherosclerosis of the left anterior descending coronary artery and the right coronary artery with approximately 30% and 20% intraluminal occlusion, respectively. Neocortex revealed mild neuronal loss; mild neuronal loss in the Sommer's sector of the hippocampus; cornu ammonis and parahippocampal gray cortex revealed acute contusional microhemorrhages extending to the superficial subcortical white matter; cerebellar cortex revealed focal acute subarachnoidal microextravasations. There was mild neuronal loss of the Purkinje neurons accompanied by mild Bergmann astrogliosis. Tau: Sparse-to-moderate-to-frequent densities of NTs and band-shaped, flame-shaped, and small globose perikaryal NFTs in the neocortex, pyramidal cells of the CA-1, CA-2, and CA-3 regions, the subiculum/ presubiculum, entorhinal cortex, pigmented and nonpigmented neurons of the ventral and tegmental pons and medulla, pontine nuclei and small identifiable fragments of the SNr and LC. Some ghost tangles were noted in the neocortex and hippocampus. TDP-43: NR Amyloid: Hippocampus, neocortex, cerebellum, pons, and medulla revealed no diffuse or neuritic plaques or evidence of cerebral amyloid angiopathy.
65	Case 46 in McKee et al 2009 [Cajigal 2007]; Case 5 / Omalu et al 2010; Case 6 / Omalu et al 2011	Pathology: NR Tau: Sparse to frequent NFTs and NTs throughout the neocortex, subcortical nuclei/basal ganglia, and brainstem. TDP-43: NR Amyloid: No diffuse amyloid plaques observed
66	Case 47 in McKee et al 2009; Case 4 / Omalu et al 2010; Case 5 / Omalu et al 2011	Pathology: Appeared normal on gross inspection. Mild neocortical neuronal loss. Tau: Sparse to frequent NFTs and NTs in the cerebral cortex, brainstem, and few partial sections of subcortical nuclei/basal ganglia in the submitted archival autopsy brain sections. None to sparse NFTs and NTs in the hippocampus. TDP-43: NR Amyloid: No diffuse amyloid plaques observed
67	Case 48 in McKee et al 2009 [Areza-Fegyveres et al 2007]	Pathology: Macroscopic examination of the brain at autopsy showed moderate and symmetric atrophy, particularly of the frontal and temporal lobes, along with moderate enlargement of the lateral ventricles. Total cavum septi pellucidi, and a very thin septum with multiple fenestrations across almost its full extension was evident. Mild-moderate neuronal loss and reactive gliosis in all isocortical structures, predominantly at the frontal and temporal lobes. Intense neuronal loss with reactive gliosis at the CA1 sector was

Case	Source [Reference]	Reported Pathology; Tau; TDP-43; & Amyloid
		evident, along with less intense loss in the CA4 sector of the hippocampus. Tau: NFTs were present in large amounts at the CA4, CA1 sectors of the hippocampus, at the pre-subicullum, subicullum and entorhinal cortex. They were present in moderate amounts at the frontal, cingulate, temporal, and parietal cortices, and absent at the occipital cortex. TDP-43: NR Amyloid: Rare beta-amyloid senile plaques were found only at the subicullum and entorhinal cortex.
68	Case A in McKee et al 2009; BU CSTE website / John Grimsley / McKee et al (2012) Case 61	Pathology: Mild enlargement of the third ventricle otherwise normal on gross inspection. Mild neuronal loss of hippocampal, entorhinal, and amygdala neurons. Tau: Abundant deposition in the amygdala and adjacent temporal cortex; patchy deposition in the frontal cortex. TDP-43: NR Amyloid: No diffuse amyloid plaques observed
69	Case B in McKee et al 2009 / McKee et al (2012) Case 81	Pathology: Brain weight 1,360g. Mild frontal, temporal and parietal atrophy, mild enlargement of 2nd & 3rd ventricles, cavum and fenestrated septum, severe pallor of SNr and LC. Moderate level of neuronal loss within hippocampus and entorhinal cortex; mild level of neuronal loss within the frontal cortex; parietal cortex; temporal cortex; occipital cortex. Tau: Severe level of NFTs observed within the frontal, parietal & temporal cortices; hypothalamus; SNr; nucleus basalis of Meynert; mammillary bodies; hippocampus; entorhinal cortex; amygdala; SNr; LC; olfactory bulb. Moderate levels were detected in the occipital cortex; thalamus; caudate/putamen; periventricular grey; midbrain tegmentum; spinal cord. Mild levels were observed within the globus pallidus; basis pontis; medulla; inferior olive; red nucleus; CN III & IV; cerebellar dentate. TDP-43: NR Amyloid: Moderate level of Aβ diffuse plaques within the frontal, parietal, and temporal cortices
70	Case C in McKee et al 2009 / McKee et al (2012) Case 75	Pathology: Brain weight 1,220g. Moderate frontal, temporal, and parietal atrophy; mild occipital atrophy; moderate enlargement of 2nd & 3rd ventricles, cavum and fenestrated septum, severe pallor of SNr and LC. Severe level of neuronal loss within hippocampus, entorhinal cortex & cerebellum; moderate level of neuronal loss within the frontal cortex, parietal cortex, temporal cortex & occipital cortex. Tau: Severe level of NFTs observed within the frontal, parietal, & temporal cortices; thalamus; hypothalamus; septal nuclei; nucleus basalis of Meynert; mammillary bodies; hippocampus; entorhinal cortex; amygdala; SNr; LC. Moderate levels were detected in the occipital cortex; caudate/putamen; periventricular grey; midbrain tegmentum; basis pontis; medulla; inferior olive; red nucleus; CN III & IV; spinal cord; cerebellar dentate. Mild levels of NFTs were observed within the globus pallidus. TDP-43: NR Amyloid: No diffuse amyloid plaques observed
71	BU CSTE website / Lou Creekmur / McKee et al (2012) Case 82	Pathology: Profound atrophy, tau deposits visible on gross examination. Tau: Dense tau deposits: insula, temporal and frontal cortices, amygdala, and hippocampus TDP-43: NR Amyloid: No diffuse amyloid plaques observed
72	BU CSTE website / Mike Borich / McKee et al (2012) Case 60	Pathology: NR Tau: Extensive tau deposition throughout the frontal and temporal gray matter TDP-43: NR Amyloid: NR
73	BU CSTE website / Thomas McHale; Case 8 Omalu et al 2011 / McKee et al (2012) Case 62	Pathology: NR Tau: McKee: Extensive deposition of tau protein as neurofibrillary tangles and neuropil neurites throughout the neocortex. Dense, patchy deposition of tau protein in the amygdala, inferior orbital cortex, hippocampus, and temporal cortex. Omalu: Sparse to frequent NFTs and NTs in the cerebral cortex, subcortical nuclei/basal ganglia, and hippocampus. No sections of the brainstem in submitted autopsy archival brain sections. Sparse to moderate NFTs and NTs in the hippocampus. TDP-43: NR Amyloid: Sparse to frequent diffuse amyloid plaques in the cerebral cortex.
74	BU CSTE Media Release / Derek Boogaard / McKee et al (2012) Case 45	Pathology: NR; Tau: NR; TDP-43: NR; Amyloid: NR
75	BU CSTE Media Release / Rick Martin / McKee et al (2012) Case 55	Pathology: NR; Tau: NR; TDP-43: NR; Amyloid: NR
76	BU CSTE Media Release / Bob Probert / McKee et al (2012) Case 50	Pathology: NR; Tau: NR; TDP-43: NR; Amyloid: NR
77	BU CSTE Media Release / Reggie Flemming / McKee et al (2012) Case 97	Pathology: NR; Tau: NR; TDP-43: NR; Amyloid: NR

Case	Source [Reference]	Reported Pathology; Tau; TDP-43; & Amyloid
78	Case 4 Omalu et al 2011	Pathology: NR Tau: No evidence of NFTs or NTs in the cerebral cortex, subcortical nuclei/basal ganglia, hippocampus, or cerebellum TDP-43: NR Amyloid: No diffuse amyloid plaques observed
79	Case 7 Omalu et al 2011	Pathology: NR Tau: No evidence of NFTs or NTs in the cerebral cortex, subcortical nuclei/basal ganglia, hippocampus, or cerebellum TDP-43: NR Amyloid: No diffuse amyloid plaques observed
80	Case 9 Omalu et al 2011	Pathology: NR Tau: Moderate to frequent NFTs and NTs in brainstem nuclei. None to sparse NFTs and NTs in the cerebral cortex and subcortical nuclei/basal ganglia. Sparse to moderate NFTs and NTs in the hippocampus. TDP-43: NR Amyloid: No diffuse amyloid plaques observed
81	Case 10 Omalu et al 2011	Pathology: NR Tau: None to sparse NFTs and NTs in neocortex and subcortical nuclei/basal ganglia. None to sparse NFTs and NTs in the hippocampus. None to sparse NFTs and NTs in brainstem nuclei. TDP-43: NR Amyloid: No diffuse amyloid plaques observed
82	Case 11 Omalu et al 2011	Pathology: NR Tau: No evidence of NFTs or NTs in the cerebral cortex, subcortical nuclei/basal ganglia, hippocampus, or cerebellum. TDP-43: NR Amyloid: No diffuse amyloid plaques observed
83	Case 12 Omalu et al 2011	Pathology: NR Tau: Sparse to frequent NFTs and NTs in the cerebral cortex, subcortical nuclei/ basal ganglia, and brainstem nuclei. Sparse to frequent NFTs and NTs in the hippocampus. TDP-43: NR Amyloid: No diffuse amyloid plaques observed
84	Case 13 Omalu et al 2011	Pathology: NR Tau: No evidence of NFTs or NTs in the cerebral cortex, subcortical nuclei/basal ganglia, hippocampus, or cerebellum TDP-43: NR Amyloid: No diffuse amyloid plaques observed
85	Case 14 Omalu et al 2011	Pathology: NR Tau: Moderate to frequent NFTs and NTs in the neocortex, subcortical nuclei/basal ganglia, hippocampus, and brainstem nuclei. TDP-43: NR Amyloid: No diffuse amyloid plaques observed
86	Case 15 Omalu et al 2011	Pathology: NR Tau: None to sparse NFTs and NTs in the neocortex, hippocampus, subcortical nuclei/basal ganglia, and brainstem. TDP-43: NR Amyloid: No diffuse amyloid plaques observed
87	Case 16 Omalu et al 2011	Pathology: NR Tau: No evidence of NFTs or NTs in the cerebral cortex, subcortical nuclei/basal ganglia, hippocampus, or cerebellum TDP-43: NR Amyloid: No diffuse amyloid plaques observed
88	Case 17 Omalu et al 2011	Pathology: NR Tau: No evidence of NFTs or NTs in the cerebral cortex, subcortical nuclei/basal ganglia, hippocampus, or cerebellum TDP-43: NR Amyloid: No diffuse amyloid plaques observed
89	Saing et al (2012)	Pathology: Brain weight: 1115.9g; septum pellucidum was absent and moderately severe ventricular enlargement and thinning of the corpus callosum and was observed. Moderate depigmentation of the SNr and LC. Tau: NFTs - extensive within frontal, temporal, & parietal neocortices and within CA1, subiculum, and entorhinal-transentorhinal region. TDP-43: Fibrils, dense granules, NFT labelling, and coiled body-like comma-shaped TDP-43-positive oligodendrocytes observed in the frontal cortex.

Case	Source [Reference]	Reported Pathology; Tau; TDP-43; & Amyloid
		Amyloid: Plaques were widespread throughout the grey matter; Neuritic plaques - Mild-Moderate within middle frontal & rostral & caudal cingulate cortices; Minimal within superior temporal, inferior parietal, and calcarine/pericalcarine cortices, and within the hippocampal CA1, subiculum, entorhinal-transentorhinal region, and amygdala
90	McCrory, Turner, Murray (2004) Punch drunk jockey?	Pathology: N/A; Tau: N/A; TDP-43: N/A; Amyloid: N/A.
91	King et al (2010) Case 35	Pathology: NR beyond suggestion of a cavum septum pellucidum Tau: Moderate NFT inclusion in neocortex, subpial, depths of sulci, SNr, and perivascular regions. Moderate level of neuritic plaques internal capsule. TDP-43: Mild inclusion within the entorhinal cortex, amygdala, dentate gyrus, limbic system, and neocortex. Inclusion also demonstrated in frontal & temporal cortex, thalamus, internal capsule, SNr, & pons. Amyloid: Moderate level of Aβ diffuse plaques
92	King et al (2010) Case 36	Pathology: NR beyond suggestion of a cavum septum pellucidum Tau: Moderate NFT inclusion in neocortex, subpial, depths of sulci, SNr, and perivascular regions. Moderate level of neuritic plaques internal capsule. TDP-43: Mild inclusion within the entorhinal cortex, amygdala, dentate gyrus, basal ganglia, limbic system and neocortex. Inclusion also demonstrated in frontal & temporal cortex, caudate, thalamus, internal capsule, SNr & pons. Amyloid: Mild level of Aβ diffuse plaques
93	King et al (2010) Case 37	Pathology: NR beyond suggestion of a cavum septum pellucidum Tau: Moderate NFT inclusion in neocortex, subpial, depths of sulci, SNr, and perivascular regions. Moderate level of neuritic plaques internal capsule. TDP-43: Mild inclusion within the entorhinal cortex, amygdala, dentate gyrus, basal ganglia, limbic system and neocortex. Inclusion also demonstrated in frontal & temporal cortex, caudate, thalamus, internal capsule, SNr & pons. Amyloid: Moderate level of Aβ diffuse plaques
94	Hazrati et al (2013) Case 1	Pathology: Diagnosis both CTE & severe AD (Braak Stage VI/VI). Brain weight 1200 g, mild but preferential wasting of the frontal and temporal lobes. The ventricles were moderately enlarged. There was a cavum septi pellucidi, thinning of the corpus callosum, and atrophy of the amygdala and mammillary bodies. Depigmentation of the SNr. Tau: Widespread, NFTs predominantly in the superficial layers in the gray matter and depths of the sulci, deeper layers of the cortex and tau-positive glia in the subpial and patchy areas in gray/white matter. Tau distribution was diffuse throughout the brain involving the frontal, temporal, and inferior parietal lobes, indusium griseum, striate, and cingulate cortices. There was heavy tau staining in the amygdala and throughout the hippocampus, patchy tau-positive inclusions seen throughout the brainstem, the nucleus basalis of Meynert, thalamus, hypothalamus, and mammillary bodies. TDP-43: Not a feature in this case. Amyloid: Numerous senile plaques were observed throughout the brain, most notably in the trans-entorhinal cortex.
95	Hazrati et al (2013) Case 2	Pathology: Diagnosis ALS. Brain weight 1540 g and normal exterior appearance without atrophy. Ventricles were of normal size with no cavum septi pellucidi and the SNr revealed normal pigmentations. Loss of neurons in the motor nuclei of multiple cranial nerves, predominately cranial nerves VII and XII. Tau: Pathological deposition of the hyperphosphorylated tau was very scarce and limited to the trans-entorhinal cortex in the shape of NFTs in neurons. TDP-43: TDP-43 positive intracytoplasmic inclusion, some intracyplasmic TDP-43-positive inclusions, and neuronal loss was also noted in the cranial spinal cord involving the lower motor neurons. Inclusions were also noted in the primary motor cortex, and to a lesser extent, in the dentate gyrus. Amyloid: A few beta-amyloid plaques were noted.
96	Hazrati et al (2013) Case 3	Pathology: Diagnosis diffuse Lewy Body disease & CTE. Brain weight 1090 g, moderate volume loss in the frontal, temporal and parietal lobes, with mild atrophy was noted in the occipital lobe. There was significant enlargement, and thinning of the corpus callosum and cavum septi pellucidi. Coronal sectioning of the brain revealed significant atrophy of the amygdala and hippocampus and pallor of the SNr. NFTs and astrocytic tangles clustering in patches in the superficial layers of the most cortical areas in both the sulci and gyral crowns. There were diffuse astrocytic tangles noted around blood vessels and throughout the parenchyma. Abnormal pallor of the white matter. Tau: Tau-immunopositive neurons were most pronounced in the amygdala and hippocampus. Diffuse astrocytic tangles noted around blood vessels and throughout the parenchyma. Tau-positive inclusions and neurites also populated the subcortical structures including the striatum, globus pallidus, dentate nucleus of the cerebellum, thalamus, subthalamic nucleus, substantia nigra, hypothalamus, septal nuclei, nucleus basalis of Meynert, mammillary bodies, periventricular white matter, locus ceruleus, red nucleus, and the nucleus of the third cranial nerve. Senile plaques were observed in the hippocampus and cortical areas that were tau-positive. TDP-43: Localized TDP-43 staining of the amygdala and hippocampus revealed numerous inclusions. Alpha-synuclein staining revealed numerous Lewy bodies and Lewy neurites throughout the cortex, SNr and LC suggested advanced Lewy body disease. Amyloid: NR.
97	Hazrati et al (2013) Case 4	Pathology: Diagnosis CTE & multiple infarcts. Brain weight 1400 g, with mild atrophy of the frontal and temporal lobes. There were findings consistent with widespread metastatic disease from a lung carcinoma and severe vascular atherosclerotic disease with multifocal brain infarctions. There was also thinning of the olfactory tracts and hypothalamus. Coronal sections of the brain showed an enlarged ventricular system, corpus callosum atrophy, and cavum septi pellucidi. Pigmentation of the SN appeared within normal limits. Mild to moderate neuronal loss and gliosis in CA1, subiculum, entorhinal cortex, amygdala, mammillary bodies, and medial thalamic nuclei. Granulovacuolar degeneration noted in the CA1 and subiculum area with pronounced subpial gliosis in the trans-entorhinal cortex. Tau: Widespread tau-positive NFTs and astrocytic tangles in multiple layers (superficial > deep) of the cortex, especially in the depths of sulci. Some inclusions noted in the

Case	Source [Reference]	Reported Pathology; Tau; TDP-43; & Amyloid
		gyral crowns. These inclusions were consistently found in all cortical areas with a predilection for the medial temporal, hippocampus, and amygdala areas. NFTs were also noted in thalamus, periventricular hypothalamic areas extending into the mamillary bodies, the nucleus basalis of Meynert, and clustering around blood vessels. TDP-43: TDP-43 and alpha-synuclein were not present. Amyloid: Amyloid plaques were reported but the nature of their presence was not described.
98	Hazrati et al (2013) Case 5	Pathology: Diagnosis: AD. Brain weight 1300 g, with moderate ventricular enlargement. Tau: Revealed numerous NFTs in neurons of the deep cortical layers, concentrated to the trans-entorhinal cortex, hippocampus, and isocortex, with significant extension into the primary visual cortex. There was also significant presence of tangles in nucleus basalis of Meynert, amygdala, substantia nigra, and in the Edinger-Westphal nucleus. Supplementing the tangles were numerous dense-core, beta-amyloid positive plaques. TDP-43: No evidence of TDP-43 or alpha-synuclein was observed. Amyloid: NR.
99	Hazrati et al (2013) Case 6	Pathology: Diagnosis PD. Brain weight 1450 g, with mild diffuse cortical atrophy and mildly dilated ventricles. Diffuse Lewy body disease with Lewy bodies and Lewy neuritis in the cerebral cortex, olfactory bulbs, indusium griseum, SNr and limbic system, including the CA2-4 subdivisions of the hippocampus. Extensive neuronal loss in the SNr pars compacta, locus ceruleus, dorsal nucleus of cranial nerve X, and nucleus basalis of Meynert. Tau: Very limited tau labelling in the hippocampus, the amygdala, and peri-amygdala cortex. TDP-43: No TDP-43 was present. Amyloid: Widespread distribution of diffuse amyloid plaques.
100	McKee et al (2012) Case 36	Pathology: Brain weight: N/A. No pathology reported. Tau: Very severe in lateral frontal area. TDP-43: Mild level of TDP-43 Amyloid: NR
101	McKee et al (2012) Case 37	Pathology: Brain weight: N/A. No pathology reported. Tau: Very severe in the dorsolateral and lateral frontal area and moderate in the dorsal medullar nucleus. TDP-43: Mild level of TDP-43 Amyloid: NR
102	McKee et al (2012) Case 38	Pathology: Brain weight: 1360g. Moderate enlargement of the second and third ventricle with mild third ventricle concave. Moderate CC atrophy and mild thalamic atrophy. Tau: Mild in the superior frontal, dorsolateral frontal, lateral frontal, cingulate and inferior frontal areas. TDP-43: NR Amyloid: NR
103	McKee et al (2012) Case 39	Pathology: Brain weight: 1670g. Mild enlargement of the second ventricle. Tau: Severe in the superior frontal, dorsolateral frontal and lateral frontal areas and mild in the LC and inferior frontal areas. TDP-43: Mild level of TDP-43 Amyloid: NR
104	McKee et al (2012) Case 40	Pathology: N/A Tau: Very severe in the lateral frontal area, severe in the dorsolateral frontal area, moderate in the hippocampus and mild in the entorhinal cortex. TDP-43: NR Amyloid: NR
105	McKee et al (2012) Case 41	Pathology: N/A Tau: Very severe in the dorsolateral frontal, lateral frontal areas. TDP-43: Mild level of TDP-43 Amyloid: NR
106	McKee et al (2012) Case 42	Pathology: Brain weight: 1360g. Moderate enlargement of the second ventricle and mild pallor of the SNr. Tau: Very severe in the dorsolateral frontal area and mild in the LC. TDP-43: NR Amyloid: NR
107	McKee et al (2012) Case 43	Pathology: N/A Tau: Very severe in the superior frontal, dorsolateral frontal, lateral frontal and inferior frontal areas, moderate in the hypothalamus and mild in the thalamus. TDP-43: Mild level of TDP-43 Amyloid: NR
108	McKee et al (2012) Case 44	Pathology: Brain weight: 1410g. No pathology reported. Tau: Severe in the thalamus, mild in the hippocampus and entorhinal cortex. TDP-43: NR

Case	Source [Reference]	Reported Pathology; Tau; TDP-43; & Amyloid
		Amyloid: NR
109	McKee et al (2012) Case 46	Pathology: Brain weight: 1460g. Mild thalamic, caudate/putamen, GP, pallor SNr and LC. Tau: Severe in the superior frontal, dorsolateral frontal, lateral frontal, inferior frontal, and inferior parietal, superior temporal areas, severe in the septal area, moderate in the substantial innominata, LC, inferior temporal area, temporal pole, hippocampus, Rolandic area and middle temporal area, mild SNr, dorsal/medial raphe, dorsal medullar nucleus, spinal cord, entorhinal cortex, amygdala, hypothalamus, thalamus, cingulate and insula. TDP-43: Very severe level of TDP-43 Amyloid: NR
110	McKee et al (2012) Case 47	Pathology: Brain weight: 1470g. No pathology reported. Tau: Very severe in the inferior parietal, lateral frontal and inferior frontal areas, moderate in the hippocampus, superior frontal and dorsolateral frontal areas, mild in the substantia innominata, SNr, dorsal/medial raphe, LC, inferior temporal, temporal pole, amygdala, cingulate, septal, insula, superior temporal and middle temporal areas. TDP-43: Mild level of TDP-43 Amyloid: NR
111	McKee et al (2012) Case 48	Pathology: Brain weight: 1680. Cavum SP (0.7mm). Mild enlargement of the third ventricle. Tau: Very severe in the superior frontal, dorsolateral frontal. Lateral frontal, superior temporal, temporal pole and inferior parietal areas, severe in the amygdala, moderate in the substantia innominata, hippocampus, entorhinal cortex and septal areas, mild in the SNr, dorsal/medial raphe, LC, inferior temporal area, hypothalamus, thalamus, Rolandic area, cingulate, inferior frontal area, insula and superior temporal area. TDP-43: Very severe level of TDP-43 Amyloid: NR
112	McKee et al (2012) Case 49	Pathology: N/A Tau: Very severe in the lateral frontal and inferior frontal areas, moderate in the caudate accumbens putamen, substantia innominata temporal pole, hippocampus, hypothalamus and mammillary bodies, mild in the GP, inferior temporal area, entorhinal cortex, thalamus, superior frontal area, dorsolateral frontal area, septal area, insula, and superior temporal area. TDP-43: Absent Amyloid: NR
113	McKee et al (2012) Case 51	Pathology: N/A Tau: Severe in the temporal pole, superior frontal area, dorsolateral frontal area, lateral frontal area and superior temporal area, moderate in the inferior temporal area, inferior frontal area, septal area, insula and middle temporal area, mild in the spinal cord and inferior parietal area. TDP-43: Absent Amyloid: NR
114	McKee et al (2012) Case 52	Pathology: Brain weight: 1600g. Cavum SP (0.2mm), mild enlargement of the third ventricle with mild third ventricle concave. Tau: Very severe in the superior frontal, lateral frontal and superior temporal areas, severe in the temporal pole, dorsolateral frontal area, inferior frontal area, septal area, insula, moderate in the LC, inferior temporal area and middle temporal area, mild in the caudate accumbens putamen, substantia innominata, SNr, dorsal/medial raphe, dorsal medulla nucleus, inferior parietal area, hippocampus, entorhinal cortex, amygdala, hypothalamus, thalamus and cingulate. TDP-43: Mild levels Amyloid: NR
115	McKee et al (2012) Case 53	Pathology: Brain weight: 1360g. Cavum SP (0.3mm), mild enlargement of the second ventricle, mild pallor of the SNr and moderate pallor of the LC. Tau: Very severe in the LC, inferior parietal area, superior frontal, dorsolateral frontal, lateral frontal, inferior frontal areas, severe in the substantia innominata, hypothalamus, thalamus, dorsal/medial raphe, moderate in the SNr, entorhinal cortex, septal area and insula, mild in the dorsal medullar nucleus, spinal cord, inferior temporal area, temporal pole, hippocampus, amygdala, mammillary body, Rolandic area, cingulate, superior temporal and middle temporal areas. TDP-43: Very severe levels Amyloid: NR
116	McKee et al (2012) Case 54	Pathology: Brain weight: 1550g. Mild enlargement of the second and third ventricle with mild third ventricle concave. Mild pallor of the SNr and moderate pallor of the LC. Tau: Very severe in the superior frontal, dorsolateral frontal, lateral frontal areas, severe in the substantia innominata, moderate in the LC, spinal cord, inferior temporal area, temporal pole, thalamus, Rolandic area, superior temporal and middle temporal area, mild in the caudate accumbens putamen, SNr, dorsal/medial raphe, inferior parietal area, hippocampus, entorhinal cortex, amygdala. hypothalamus, mammillary body, cingulate, inferior frontal area, septal area and insula. TDP-43: Mild levels Amyloid: Moderate cerebral angiopathy.
117	McKee et al (2012) Case 56	Pathology: Brain weight: 1460g. Mild enlargement of the second and third ventricle and frontal atrophy. Tau: Very severe in the mammillary body and dorsolateral frontal area, severe in the inferior parietal are, amygdala, superior frontal area and the lateral frontal area, moderate in the substantia innominata, SNr, dorsal/medial raphe, LC, spinal cord, hypothalamus, thalamus and insula, mild in the caudate accumbens putamen, globus pallidus, inferior temporal area, temporal pole, entorhinal cortex, cingulate, inferior frontal area, septal area, superior temporal area and middle temporal area.

Case	Source [Reference]	Reported Pathology; Tau; TDP-43; & Amyloid
		TDP-43: Mild levels Amyloid: Very severe diffuse plaques and mild neuritic plaques.
118	McKee et al (2012) Case 57	Pathology: N/A; Tau: Moderate in the caudate accumbens putamen; TDP-43: Absent; Amyloid: NR.
119	McKee et al (2012) Case 58	Pathology: N/A Tau: Very severe in the inferior temporal area, temporal pole, superior frontal area, dorsolateral frontal area, lateral frontal area, inferior frontal area, superior temporal area, middle temporal area and septal area, severe in the amygdala and insula and moderate in the inferior parietal area. TDP-43: Mild levels Amyloid: NR
120	McKee et al (2012) Case 59	Pathology: Brain weight: 1430g. Moderate third ventricle concave. Tau: Very severe in the superior frontal area, dorsolateral frontal area, lateral frontal area, inferior frontal area, inferior parietal area, entorhinal cortex, cingulate, insula and septal area, severe in the SNr, LC, Rolandic area, inferior temporal area, temporal pole and middle temporal area, moderate in the hippocampus and superior temporal area and mild in the caudate accumbens putamen, GP, substantia innominata, amygdala, dorsal/medial raphe, dorsal medullar nucleus and spinal cord. TDP-43: Severe levels Amyloid: NR
121	McKee et al (2012) Case 63	Pathology: Brain weight: 1300g. Mild fibrotic meninges, cavum SP (0.5mm), mild enlargement of the third ventricle with mild third ventricle concave, mild pallor of the SNr and moderate pallor of the LC. Tau: Very severe in the substantia innominata, LC, inferior temporal area, temporal pole, entorhinal cortex, amygdala, thalamus, superior frontal area, dorsolateral frontal area, lateral frontal area, inferior frontal area, septal area and insula, severe in the nucleus accumbens and SNr, moderate in the dorsal/medial raphe, dorsal medullar nucleus, inferior parietal area, hippocampus, hypothalamus and mammillary body and mild in the Rolandic area, cingulate, superior and middle temporal areas. TDP-43: Mild levels Amyloid: NR
122	McKee et al (2012) Case 64	Pathology: Brain weight: 1550g. Moderate fibrotic meninges, mild enlargement of the second ventricle, moderate enlargement of the third ventricle with mild third ventricle concave, mild hippocampal atrophy, mild thalamic atrophy, mild atrophy of the hypothalamus, moderate atrophy of the corpus callosum, mild pallor of the SNr and moderate pallor of the LC. Tau: Very severe in the substantia innominata, inferior temporal area, temporal pole, hippocampus, amygdala, dorsolateral frontal area, lateral frontal area and the inferior frontal area, severe in the dorsal/medial raphe, LC, entorhinal cortex and hypothalamus, moderate in the SNr, inferior parietal area, superior frontal area, cingulate, septal area, insula and middle temporal area, mild in the caudate accumbens putamen, dorsal medullar nucleus, thalamus, mammillary body and Rolandic area. TDP-43: Mild levels Amyloid: NR
123	McKee et al (2012) Case 65	Pathology: N/A Tau: Severe in the LC, hippocampus, entorhinal cortex and superior temporal area, moderate in the GP, SNr, hypothalamus and thalamus, mild in the caudate accumbens putamen, dorsal/medial raphe and amygdala. TDP-43: Absent Amyloid: NR
124	McKee et al (2012) Case 66	Pathology: Brain weight: 1530g. cavum SP (0.7mm) with fenestration, mild enlargement of the second and third ventricle, moderate atrophy of the mammillary bodies, mild pallor of the SNr and moderate pallor of the LC. Tau: Very severe in the substantia innominata, LC, inferior frontal area, dorsolateral frontal area, lateral frontal area, inferior temporal area, temporal pole, inferior parietal area, superior temporal area, middle temporal area, hippocampus, entorhinal cortex, amygdala, hypothalamus, mammillary body, septal area and insula, severe in the SNr and dorsal/medial raphe, moderate in the spinal cord, thalamus, Rolandic area and cingulate, mild in the caudate accumbens putamen, GP and cerebellar dentate. TDP-43: Very severe levels Amyloid: NR
125	McKee et al (2012) Case 67	Pathology: N/A Tau: Very severe in the inferior temporal area, temporal pole, amygdala, insula, superior and middle temporal areas, severe in the substantia innominata, entorhinal cortex and septal area, moderate in the hippocampus, mild in the caudate accumbens putamen, spinal cord, hypothalamus, thalamus, mammillary body, superior frontal area, dorsolateral frontal area, lateral frontal area and inferior frontal area. TDP-43: Mild levels Amyloid: NR
126	McKee et al (2012) Case 68	Pathology: Brain Weight: 1360g. Cavum SP (0.3mm) with fenestration, moderate enlargement of the second and third ventricle with moderate concave of the third ventricle, mild hippocampal atrophy, mild thalamic atrophy, moderate atrophy of the mammillary bodies, mild pallor of the SNr and LC. Tau: Very severe in the substantia innominata, LC, inferior temporal area, temporal pole, hippocampus, entorhinal cortex, amygdala, superior frontal area, dorsolateral frontal

Case	Source [Reference]	Reported Pathology; Tau; TDP-43; & Amyloid
		area, lateral frontal area, superior temporal area and middle temporal area, severe in the nucleus accumbens, SNr, dorsal/medial raphe, mammillary body, moderate in the inferior parietal area, hypothalamus, thalamus, and Rolandic area, mild in the GP, dorsal medullar nucleus, cerebellar dentate, spinal cord, cingulate, inferior frontal area, septal area and insula. TDP-43: Mild levels Amyloid: NR
127	McKee et al (2012) Case 69	Pathology: Brain weight: 1320g. Moderate fenestrated septum, moderate enlargement of the second ventricle, severe enlargement of the third ventricle with severe third ventricle concave, mild frontal atrophy, mild hippocampal atrophy, moderate atrophy of the thalamus, moderate atrophy of the hippocampus, mild atrophy of the mammillary bodies, moderate atrophy of the CC, and moderate pallor of the LC. Tau: Very severe in the inferior temporal area, temporal pole hippocampus and entorhinal cortex, severe in the LC, amygdala, superior frontal area, dorsolateral area, lateral frontal area, septal area and superior temporal area, moderate in the caudate accumbens putamen, substantia innominata, SNr, dorsal/medial raphe, dorsal medullar nucleus, spinal cord, hypothalamus, thalamus, mammillary body and middle temporal area, mild in the GP, cerebellar dentate, Rolandic area, cingulate, inferior frontal area and insula. TDP-43: Severe levels Amyloid: NR
128	McKee et al (2012) Case 70	Pathology: Brain weight: 1300g. Mild fibrotic meninges, cavum SP (0.3mm), moderate enlargement of the second and moderate third ventricle with third ventricle concave, mild frontal, temporal and parietal atrophy, mild hippocampal, entorhinal cortex, amygdala and mammillary bodies atrophy, moderate CC, thalamus and hypothalamus atrophy, mild pallor of the SNr and moderate pallor of the LC. Tau: Very severe in the inferior temporal area, temporal pole, calcarine, hippocampus, entorhinal cortex, amygdala, thalamus, mammillary body, inferior frontal area, septal area, insula, superior temporal and middle temporal area, severe in the substantia innominata, SNr, dorsal/medial raphe, LC, superior frontal area, dorsolateral frontal, lateral frontal area, Rolandic area and cingulate moderate in the caudate accumbens putamen, dorsal medullar nucleus and inferior parietal area and mild in the GP. TDP-43: Mild levels Amyloid: Moderate diffuse plaques, moderate neuritic plaques, severe cerebral angiopathy.
129	McKee et al (2012) Case 71	Pathology: Brain weight: Unknown. Mild fibrotic meninges, moderate enlargement of the second and moderate third ventricle with moderate third ventricle concave, mild frontal, temporal, parietal and occipital atrophy, mild hippocampal, entorhinal cortex, amygdala, thalamus and hypothalamus atrophy, moderate CC atrophy, moderate pallor of the SNr and LC. Tau: Very severe in the dorsal/medial raphe, LC, spinal cord, inferior temporal area, temporal pole, inferior parietal area, thalamus, superior frontal area, dorsolateral frontal area, lateral frontal area, inferior frontal area, septal area and insula, severe in the SNr and hippocampus moderate in the caudate accumbens putamen, GP, substantia innominata, cerebellar dentate, calcarine, amygdala, hypothalamus, Rolandic area, cingulate, superior and middle temporal area. TDP-43: Mild levels Amyloid: Mild diffuse plaques.
130	McKee et al (2012) Case 72	Pathology: Brain weight: Unknown. Moderate fibrotic meninges, cavum SP (0.7mm), moderate enlargement of the second, severe enlargement of the third ventricle with severe third ventricle concave, mild frontal atrophy, mild hippocampal atrophy, moderate CC atrophy. Tau: Very severe in the substantia innominata, inferior temporal area, temporal pole, hippocampus, entorhinal cortex, amygdala, hypothalamus, superior frontal area, dorsolateral frontal area, lateral frontal area, insula and superior and middle temporal area, severe in the nucleus accumbens, thalamus, mammillary body, inferior frontal area and septal area, moderate in the inferior parietal area and mild in the cingulate. TDP-43: Mild levels Amyloid: NR
131	McKee et al (2012) Case 73	Pathology: Brain weight: 1260g. Moderate fenestrated septum, moderate enlargement of the second and third ventricle with moderate concave of the third ventricle. Moderate frontal and temporal atrophy, mild parietal and occipital atrophy. Moderate hippocampal, entorhinal cortex, amygdala, thalamus and hypothalamus, severe mammillary body atrophy, moderate pallor of the SNr and very severe pallor of the LC. Tau: Very severe in the substantia innominata, SNr, dorsal/medial raphe, LC, inferior temporal area, temporal pole, hippocampus, entorhinal cortex, amygdala, hypothalamus, thalamus, mammillary body, superior frontal area, dorsolateral frontal area, lateral frontal area, inferior frontal area, septal area, insula and superior and middle temporal area, severe in the inferior parietal area, Rolandic area and cingulate, moderate in the caudate accumbens putamen, dorsal medullar nucleus, cerebellar dentate and spinal cord, mild in the GP. TDP-43: Severe levels Amyloid: Mild diffuse plaques, mild neuritic plaques.
132	McKee et al (2012) Case 74	Pathology: Brain weight: Unknown. Cavum SP (1.0mm), with moderate fenestration, moderate enlargement of the second and third ventricles with moderate third ventricle concave, mild frontal and temporal atrophy, moderate hippocampal, entorhinal cortex, amygdala and CC atrophy, moderate pallor of the SNr and LC. Tau: Very severe in the substantia innominata, SNr, dorsal/medial raphe, LC, dorsal medullar nucleus, spinal cord, inferior temporal area, temporal pole, inferior parietal area, hippocampus, entorhinal cortex, amygdala, hypothalamus, thalamus, mammillary body, , superior frontal area, dorsolateral frontal area, lateral frontal area, inferior frontal area, Rolandic area, septal area, insula and superior and middle temporal area, severe in the cingulate, moderate in the , superior frontal area, dorsolateral frontal area, lateral frontal area, inferior frontal area, GP and cerebellar dentate.

Case	Source [Reference]	Reported Pathology; Tau; TDP-43; & Amyloid
		TDP-43: Severe levels Amyloid: Moderate diffuse plaques, mild neuritic plaques
133	McKee et al (2012) Case 76	Pathology: Brain weight: 1380g. Cavum SP (1.0mm) with severe fenestration, moderate enlargement of the second ventricle and severe enlargement of the third ventricle with severe concave of the third ventricle. Moderate frontal and temporal atrophy, mild parietal and occipital atrophy, mild hippocampal, entorhinal cortex and amygdala atrophy, moderate thalamus, hypothalamus, mammillary bodies and CC atrophy. Moderate pallor of the SNr and severe pallor of the LC. Tau: Very severe in the inferior temporal area, temporal pole, hippocampus, entorhinal cortex, superior frontal area, dorsolateral frontal area, lateral frontal area, Rolandic area, septal area, insula and superior and middle temporal area, severe in the caudate accumbens putamen, substantia innominata, SNr, dorsal/medial raphe, amygdala, hypothalamus, thalamus, cingulate and mammillary body, moderate in the LC, spinal cord, inferior parietal area and inferior frontal area and mild in the GP and dorsal medullar nucleus. TDP-43: Severe levels Amyloid: NR
134	McKee et al (2012) Case 77	Pathology: Brain weight: 1420g. Moderate enlargement of the second and third ventricles with moderate concave of the third ventricle, moderate frontal, temporal, parietal and occipital atrophy, moderate hippocampal, amygdala, thalamus and CC atrophy, mild entorhinal cortex atrophy and moderate pallor of the SNr and LC. Tau: Very severe in the mammillary body, moderate in the substantia innominata, SNr, dorsal/medial raphe, LC, dorsal medullar nucleus, cerebellar dentate, spinal cord, entorhinal cortex, amygdala, hypothalamus, thalamus and lateral frontal area, mild in the caudate accumbens putamen, inferior temporal area, temporal pole, inferior parietal area, hippocampus, superior frontal area, dorsolateral frontal area, Rolandic area, cingulate, inferior frontal area, septal area, insula and superior and middle temporal area. TDP-43: Moderate levels Amyloid: NR
135	McKee et al (2012) Case 78	Pathology: Brain weight: 860g. mild fibrotic meninges, severe fenestrated septum, very severe enlargement of the second and third ventricles with very severe third ventricle concave, severe frontal, temporal, parietal and occipital atrophy, very serve hippocampal, entorhinal cortex, and amygdala atrophy, severe thalamus, hypothalamus and mammillary body and CC atrophy, mild caudate/putamen and GP atrophy, very severe pallor of the SNr and LC. Tau: Very severe in the substantia innominata, SNr, dorsal/medial raphe, LC, cerebellar dentate, spinal cord, inferior temporal area, temporal pole, inferior parietal area, hippocampus, entorhinal cortex, amygdala, hypothalamus, thalamus, mammillary body, superior frontal area, dorsolateral frontal area, lateral frontal area, Rolandic area, cingulate, inferior frontal area, septal area, insula and superior and middle temporal area, severe in the caudate accumbens putamen and GP, moderate in the dorsal medullar nucleus and calcarine. TDP-43: Severe levels Amyloid: Mild diffuse plaques, very severe cerebral angiopathy
136	McKee et al (2012) Case 79	Pathology: Brain weight: 1000g. Mild fibrotic meninges, cavum SP (0.7mm) with moderate fenestration, severe enlargement of the second and third ventricles with severe concave of the third ventricle, moderate frontal, temporal, parietal and occipital atrophy, severe hippocampal, entorhinal cortex, amygdala, thalamus, hypothalamus, mammillary body atrophy, moderate CC atrophy, severe pallor of the SNr and LC. Tau: Very severe in the substantia innominata, SNr, dorsal/medial raphe, LC, inferior temporal area, temporal pole, inferior parietal area, hippocampus, entorhinal cortex, amygdala, hypothalamus, thalamus, mammillary body, superior frontal area, dorsolateral frontal area, lateral frontal area, inferior frontal area, septal area, insula and superior and middle temporal area, severe in the caudate accumbens putamen and GP, moderate in the dorsal medullar nucleus, Rolandic area and cingulate, mild in the cerebellar dentate and spinal cord. TDP-43: Severe levels Amyloid: Mild diffuse plaques, mild neuritic plaques.
137	McKee et al (2012) Case 80	Pathology: Brain weight: 1300g. Cavum SP (0.7mm), moderate enlargement of the second and third ventricle with moderate third ventricle concave, moderate hippocampal, entorhinal cortex, amygdala, thalamus, hypothalamus and CC atrophy, mild mammillary body atrophy, mild pallor of the SNr and severe pallor of the LC. Tau: Very severe in the substantia innominata, SNr, inferior temporal area, temporal pole, hippocampus, entorhinal cortex, amygdala, hypothalamus, mammillary body, superior frontal area, dorsolateral frontal area, lateral frontal area, inferior frontal area, septal area, insula and superior and middle temporal area, severe in the caudate accumbens putamen and cingulate, moderate in the dorsal/medial raphe, calcarine and thalamus, mild in the GP, dorsal medullar nucleus, spinal cord, inferior parietal area and Rolandic area. TDP-43: Severe levels Amyloid: Moderate diffuse plaques, mild neuritic plaques, mild cerebral angiopathy.
138	McKee et al (2012) Case 83	Pathology: Brain weight: 1090g. Moderate fibrotic meninges, severe enlargement of the second and third ventricles with severe concave of the third ventricle, severe frontal, and temporal atrophy, moderate parietal and occipital atrophy, severe hippocampal, entorhinal cortex and amygdala atrophy, moderate thalamus, hypothalamus, mammillary body and CC atrophy. Mild pallor of the Snr and severe pallor of the LC. Tau: Very severe in the substantia innominata, SNr, dorsal/medial raphe, LC, inferior temporal area, temporal pole, inferior parietal area, entorhinal cortex, amygdala, hypothalamus, superior frontal area, dorsolateral frontal area, lateral frontal area, inferior frontal area, septal area, insula and superior and middle temporal area, severe in the cingulate, moderate in the caudate accumbens putamen, dorsal medullar nucleus, spinal cord, hippocampus, thalamus and mammillary body, mild in the GP, cerebellar dentate and Rolandic area. TDP-43: Very severe levels

Case	Source [Reference]	Reported Pathology; Tau; TDP-43; & Amyloid
		Amyloid: Mild diffuse plaques, mild neuritic plaques.
139	McKee et al (2012) Case 84	Pathology: Brain weight: 1170g. Severe fenestrated septum, moderate enlargement of the second ventricles, severe enlargement of the third ventricle with severe concave of the third ventricle, moderate frontal and parietal atrophy, mild temporal and occipital atrophy, severe hippocampal and mammillary body atrophy, moderate entorhinal cortex, amygdala, thalamus, hypothalamus and CC atrophy, severe pallor of the SNr and moderate pallor of the LC. Tau: Very severe in the substantia innominata, SNr, dorsal/medial raphe, LC, hippocampus, entorhinal cortex, hypothalamus, thalamus, mammillary body, superior frontal area, dorsolateral frontal area, lateral frontal area and Rolandic area, severe in the calcarine, moderate in the caudate accumbens putamen and dorsal medullar nucleus, mild in the GP, inferior temporal area, temporal pole, inferior parietal, amygdala, cingulate, inferior frontal area, septal area, insula and superior and middle temporal area. TDP-43: Severe levels Amyloid: Very severe diffuse plaques, mild neuritic plaques, mild cerebral angiopathy.
140	McKee et al (2012) Case 85	Pathology: Brain weight: 990g. Severe fibrotic meninges, severe enlargement of the second and third ventricles with severe concave of the third ventricle, severe frontal and temporal atrophy, moderate parietal and occipital atrophy, very severe amygdala atrophy, severe hippocampal, entorhinal cortex, thalamus, hypothalamus, mammillary bodies and CC atrophy, moderate caudate/putamen and GP atrophy, mild pallor of the SNr and very severe pallor of the LC. Tau: Very severe in the LC, amygdala, cingulate and septal area, severe in the substantia innominata, dorsal/medial raphe, inferior temporal area, temporal pole, entorhinal cortex, hypothalamus, insula, superior and middle temporal area, moderate in the caudate accumbens putamen, GP, SNr, spinal cord, inferior parietal, calcarine, hippocampus, thalamus, mammillary body, superior frontal area, dorsolateral frontal area, lateral frontal area, inferior frontal area and Rolandic area, mild in the dorsal medullar nucleus and cerebellar dentate. TDP-43: Very severe levels Amyloid: Moderate diffuse plaques, moderate neuritic plaques, moderate cerebral angiopathy..
141	McKee et al (2012) Case 86	Pathology: N/A Tau: Largely N/A. Very severe in the superior frontal area, dorsolateral frontal area, lateral frontal area, inferior frontal area, superior temporal area and middle temporal area, severe in the cingulate, moderate in the thalamus and Rolandic area. TDP-43: Very severe levels Amyloid: NR
142	McKee et al (2012) Case 87	Pathology: Brain weight: 1250g. Moderate fenestrated septum, moderate enlargement of the second and third ventricles with moderate concave of the third ventricle, mild frontal, temporal, parietal and occipital atrophy, moderate thalamus atrophy, mild hippocampus, entorhinal cortex, amygdala and CC atrophy, severe pallor of the SNr and moderate pallor of the LC. Tau: Very severe in the substantia innominata, SNr, dorsal/medial raphe, LC, inferior temporal area, temporal pole, inferior parietal, hippocampus entorhinal cortex, amygdala, superior frontal area, dorsolateral frontal area, lateral frontal area, Rolandic area, cingulate, inferior frontal area, septal area, insula superior temporal area and middle temporal area, severe in the hypothalamus, moderate in the caudate accumbens putamen, dorsal medullar nucleus and thalamus, mild in the GP, cerebellar dentate, spinal cord, calcarine and mammillary body. TDP-43: Mild levels Amyloid: Very severe diffuse plaques, very severe neuritic plaques, moderate cerebral angiopathy.
143	McKee et al (2012) Case 88	Pathology: Brain weight: 1270g. Cavum SP (1.0mm) with severe fenestration, mild enlargement of the second ventricle, moderate enlargement of the third ventricle with moderate concave, mild frontal, temporal, parietal and occipital atrophy, moderate thalamus and hypothalamus atrophy, mild hippocampal, entorhinal cortex, amygdala and CC atrophy, severe pallor of the LC. Tau: Very severe in the substantia innominata, dorsal/medial raphe, LC, inferior temporal area, temporal pole, inferior parietal area, entorhinal cortex, amygdala, hypothalamus, superior frontal area, dorsolateral frontal area, lateral frontal area, Rolandic area, cingulate, inferior frontal area, septal area, insula superior temporal area and middle temporal area, severe in the SNr, hippocampus and thalamus, moderate in the caudate accumbens putamen and the mammillary body mild in the GP, dorsal medullar nucleus and cerebellar dentate. TDP-43: Mild levels Amyloid: Very severe diffuse plaques, severe neuritic plaques, moderate cerebral angiopathy.
144	McKee et al (2012) Case 89	Pathology: Brain weight: 1200g. Moderate enlargement of the second and third ventricle with mild concave of the third ventricle, moderate frontal and occipital atrophy, mild temporal and parietal atrophy, mild hippocampal, entorhinal cortex, amygdala and thalamus atrophy, mild pallor of the SNr and moderate pallor of the LC. Tau: Very severe in the substantia innominata, dorsal/medial raphe, LC, inferior temporal area, temporal pole, inferior parietal, calcarine, hippocampus, entorhinal cortex, hypothalamus, thalamus, mammillary body, superior frontal area, dorsolateral frontal area, lateral frontal area, Rolandic area, cingulate, inferior frontal area, septal area, insula superior temporal area and middle temporal area, severe in the amygdala, moderate in the caudate accumbens putamen, mild in the GP and SNr. TDP-43: Mild levels Amyloid: Very severe diffuse plaques, very severe neuritic plaques, severe cerebral angiopathy.
145	McKee et al (2012) Case 90	Pathology: Brain weight: 1375g. Mild enlargement of the second and third ventricle, mild frontal, temporal, parietal and occipital atrophy, mild hippocampal, entorhinal cortex and amygdala atrophy. Tau: Very severe in the caudate accumbens putamen, GP, substantia innominata, SNr, dorsal/medial raphe, LC, inferior temporal area, temporal pole, inferior parietal, calcarine,

Case	Source [Reference]	Reported Pathology; Tau; TDP-43; & Amyloid
		hippocampus, entorhinal cortex, amygdala, hypothalamus, thalamus, mammillary body, superior frontal area, dorsolateral frontal area, lateral frontal area, Rolandic area, cingulate, inferior frontal area, septal area, insula superior temporal area and middle temporal area, moderate in the dorsal medullar nucleus and spinal cord, mild in the cerebellar dentate. TDP-43: Severe levels Amyloid: Severe diffuse plaques, moderate neuritic plaques, moderate cerebral angiopathy.
146	McKee et al (2012) Case 91	Pathology: Brain weight: 1240g. Mild fibrotic meninges, severe enlargement of the second and third ventricle with severe concave of the third ventricle, moderate frontal, temporal, parietal and occipital atrophy, severe hippocampal, entorhinal cortex, amygdala and CC atrophy, moderate thalamus, hypothalamus and mammillary body atrophy, severe pallor of the SNr and moderate pallor of the LC. Tau: Very severe in the substantia innominata, SNr, dorsal/medial raphe, LC, inferior temporal area, temporal pole, inferior parietal, entorhinal cortex, amygdala, hypothalamus, thalamus, mammillary body, superior frontal area, dorsolateral frontal area, lateral frontal area, Rolandic area, cingulate, inferior frontal area, septal area, insula, superior temporal area and middle temporal area, severe in the hippocampus, moderate in the dorsal medullar nucleus, mild in the caudate accumbens putamen, GP and cerebellar dentate. TDP-43: Mild levels Amyloid: Severe diffuse plaques, moderate neuritic plaques, moderate cerebral angiopathy.
147	McKee et al (2012) Case 92	Pathology: Brain weight: 1260g. No other pathology reported. Tau: Very severe in the LC, inferior temporal area, temporal pole, hippocampus, entorhinal cortex, amygdala, lateral frontal area, cingulate and middle temporal area, severe in the substantia innominata, SNr, dorsal/medial raphe, calcarine, inferior frontal area, septal area, insula and superior temporal area moderate in the caudate accumbens putamen, hypothalamus, thalamus, superior frontal area, dorsolateral frontal area and Rolandic area, mild in the inferior parietal area and mammillary body. TDP-43: Moderate levels Amyloid: Severe diffuse plaques, moderate neuritic plaques.
148	McKee et al (2012) Case 93	Pathology: Brain weight: 1260g. Moderate enlargement of the second ventricles, severe enlargement of the third ventricle with severe concave, moderate frontal and temporal atrophy, mild parietal and occipital atrophy, severe hippocampal and mammillary body atrophy, moderate entorhinal cortex, amygdala, thalamus and hypothalamus atrophy, mild CC atrophy, severe pallor of the SNr and moderate pallor of the LC. Tau: Very severe in the inferior temporal area, temporal pole, inferior parietal area, mammillary body, superior frontal area, dorsolateral frontal area, lateral frontal area, Rolandic area, cingulate, inferior frontal area, septal area, insula superior temporal area and middle temporal area, severe in the substantia innominata, SNr, hippocampus and hypothalamus moderate in the caudate accumbens putamen, GP, dorsal/medial raphe, LC, dorsal medullar nucleus, calcarine, entorhinal cortex, amygdala and thalamus. TDP-43: Mild levels Amyloid: Severe diffuse plaques, severe neuritic plaques, moderate cerebral angiopathy.
149	McKee et al (2012) Case 94	Pathology: Brain weight: 1260g. Moderate enlargement of the second and third ventricles with severe concave of the third ventricle, moderate frontal and temporal atrophy, mild parietal and occipital atrophy, severe hypothalamus and mammillary body atrophy, moderate hippocampal, entorhinal cortex, amygdala, thalamus, and CC atrophy, very severe pallor of the SNr and moderate pallor of the LC. Tau: Very severe in the substantia innominata, SNr, LC, inferior temporal area, temporal pole, inferior parietal area, entorhinal cortex, amygdala, hypothalamus thalamus superior frontal area, dorsolateral frontal area, lateral frontal area, Rolandic area, cingulate, inferior frontal area, septal area, insula superior temporal area and middle temporal area, severe in the calcarine and hippocampus, moderate in the caudate accumbens putamen, GP, dorsal/medial raphe, dorsal medullar nucleus, cerebellar dentate, spinal cord and mammillary body. TDP-43: Very severe level of TDP-43 Amyloid: Mild diffuse plaques, mild neuritic plaques.
150	McKee et al (2012) Case 95	Pathology: Brain weight: 1390g. Mild enlargement of the second and third ventricles, mild frontal and temporal atrophy, moderate mammillary body atrophy, mild hippocampal, entorhinal cortex, amygdala, thalamus and hypothalamus atrophy, moderate pallor of the SNr and LC. Tau: Very severe in the dorsal medullar nucleus, inferior temporal area, temporal pole, hippocampus, superior frontal area, dorsolateral frontal area, lateral frontal area, severe in the LC, entorhinal cortex and amygdala, moderate in the caudate accumbens putamen, substantia innominata, dorsal/medial raphe, hypothalamus, mammillary body and insula, mild in the GP, SNr, spinal cord, inferior parietal area, thalamus, cingulate, inferior frontal area, septal area, insula and superior and middle temporal area. TDP-43: Mild level of TDP-43 Amyloid: Mild diffuse plaques, mild neuritic plaques, mild cerebral angiopathy
151	McKee et al (2012) Case 96	Pathology: Brain weight: 1550g. Moderate enlargement of the second and third ventricles with moderate concave of the third ventricle, moderate hippocampal, entorhinal cortex, amygdala, thalamus, hypothalamus, mammillary body and CC atrophy, mild caudate/putamen and GP atrophy, mild pallor of the SNr and moderate pallor of the LC. Tau: Very severe in the SNr, LC, superior temporal area, temporal pole, inferior parietal area, entorhinal cortex, amygdala, hypothalamus, superior frontal area, dorsolateral frontal area, lateral frontal area, inferior frontal area and superior temporal area, severe in the cingulate, septal area and insula, moderate in the substantia innominata, dorsal medullar nucleus, spinal cord, thalamus, mammillary body and middle temporal area, mild in the dorsal/medial raphe, hippocampus and Rolandic area. TDP-43: Mild levels Amyloid: Severe diffuse plaques, mild neuritic plaques, mild cerebral angiopathy

Case	Source [Reference]	Reported Pathology; Tau; TDP-43; & Amyloid
152	McKee et al (2012) Case 98	Pathology: Brain weight: 1300g. Moderate enlargement of the second ventricle, severe enlargement of the third ventricle with severe concave, moderate frontal and temporal atrophy, mild parietal and occipital atrophy, severe hippocampal, entorhinal cortex and amygdala atrophy, moderate thalamus, hypothalamus and CC atrophy, mild mammillary body atrophy, moderate pallor of the SNr and severe pallor of the LC. Tau: Very severe in the superior temporal area, temporal pole, entorhinal cortex, amygdala, hypothalamus, lateral frontal area, septal area, insula and superior and middle temporal area, severe in the substantia innominata, SNr, LC, spinal cord, inferior parietal area, thalamus, superior frontal area, dorsolateral frontal area and cingulate, moderate in the nucleus accumbens, dorsal/medial raphe, dorsal cerebellar nucleus, mammillary body, Rolandic area and inferior frontal area, mild in the GP, cerebellar dentate and hippocampus. TDP-43: Mild levels Amyloid: Mild diffuse plaques, mild cerebral angiopathy
153	McKee et al (2012) Case 99	Pathology: Brain weight: 1410g. Mild enlargement of the second and third ventricle with mild concave of the third ventricle, mild frontal, temporal, parietal and occipital atrophy. Tau: Very severe in the inferior temporal area, temporal pole, hippocampus and lateral frontal area, severe in the amygdala and middle temporal area, moderate in the substantia innominata, SNr, dorsal/medial raphe, LC, hypothalamus and mammillary body, mild in the nucleus accumbens, GP dorsal medullar nucleus, spinal cord, entorhinal cortex, thalamus, superior frontal area, dorsolateral frontal area, cingulate, inferior frontal area, septal area, insula and superior temporal area. TDP-43: Mild levels Amyloid: Severe diffuse plaques, mild neuritic plaques.
154	McKee et al (2012) Case 100	Pathology: Brain weight: 1240g. Cavum SP (0.3mm), moderate enlargement of the second ventricles, severe enlargement of the third ventricles with severe concave, moderate frontal and temporal atrophy, mild parietal and occipital atrophy, severe mammillary body atrophy, moderate hippocampal, thalamus, hypothalamus and CC atrophy, mild entorhinal cortex and amygdala atrophy, moderate pallor of the SNr and severe pallor of the LC. Tau: Very severe in the dorsal/medial raphe, LC, dorsal medullar nucleus, inferior temporal area, temporal pole, hippocampus, amygdala, lateral frontal area, septal area, insula and middle temporal area, severe in the substantia innominata, SNr, entorhinal cortex, hypothalamus, thalamus, superior frontal area and dorsolateral frontal area, moderate in the caudate accumbens putamen, GP, mammillary body, inferior frontal area and superior parietal area, mild in the spinal cord, inferior parietal area, Rolandic area and cingulate. TDP-43: Very severe levels Amyloid: Mild diffuse plaques, mild neuritic plaques.
155	McKee et al (2012) Case 101	Pathology: Brain weight: 1450g. Cavum SP (0.3mm), moderate enlargement of the second ventricles, mild enlargement of the third ventricles with mild concave, mild frontal, temporal, parietal and occipital atrophy, mild thalamus and hypothalamus atrophy, very severe pallor of the SNr and Moderate pallor of the LC. Tau: Severe in the SNr, dorsal medullar nucleus, thalamus and Rolandic area, moderate in the substantia innominata, dorsal/medial raphe, LC, cerebellar dentate, temporal pole, amygdala, hypothalamus, mammillary body, and superior and middle temporal area, mild in the spinal cord, inferior temporal area, inferior parietal area, hippocampus, entorhinal cortex superior frontal area, dorsolateral frontal area, lateral frontal area, cingulate, inferior frontal area, septal area and insula. TDP-43: Mild levels Amyloid: NR
156	McKee et al (2012) Case 102	Pathology: Brain weight: 820g. Very severe enlargement of the second and third ventricles, very severe frontal and temporal atrophy, severe parietal and occipital atrophy, very severe hippocampal, entorhinal cortex and amygdala atrophy, severe thalamus, hypothalamus, mammillary body, and CC atrophy, moderate caudate/putamen and GP atrophy, severe pallor of the SNr and LC. Tau: Severe in the cerebellar dentate, moderate in the dorsal/medial raphe, spinal cord, and lateral frontal area, mild in the substantia innominata, SNr, LC, inferior temporal area, temporal pole, inferior parietal area, entorhinal cortex, amygdala, superior frontal area, dorsolateral frontal area, Rolandic area, cingulate, inferior frontal area, septal area, insula and superior and middle temporal area. TDP-43: Mild levels Amyloid: Mild cerebral angiopathy
157	McKee et al (2012) Case 103	Pathology: Brain weight: 1140g. Cavum SP (1.2mm), moderate enlargement of the second ventricles, severe enlargement of the third ventricle with severe concave, very severe temporal atrophy, severe frontal atrophy, moderate parietal and occipital atrophy, very severe hippocampal, entorhinal cortex and amygdala atrophy, severe mammillary body, caudate/putamen and GP atrophy, moderate thalamus atrophy, moderate pallor of the SNr and severe pallor of the LC. Tau: Very severe in the SNr, dorsal/medial raphe, LC, inferior temporal area, temporal pole, entorhinal cortex, amygdala, hypothalamus, thalamus, mammillary body, superior frontal area, dorsolateral frontal area, lateral frontal area, cingulate and superior and middle temporal area, severe in the substantia innominata, septal area and insula, moderate in the GP, inferior parietal, hippocampus, Rolandic area and inferior frontal area, mild in the caudate accumbens putamen, dorsal medullar nucleus, cerebellar dentate and spinal cord. TDP-43: Very severe levels Amyloid: Severe diffuse plaques, mild neuritic plaques, moderate cerebral angiopathy

Case	Source [Reference]	Reported Pathology; Tau; TDP-43; & Amyloid
158	National Institutes of Health, National Institute of Neurological Disorders and Stroke (NINDS), Junior Seau	Pathology: Adult six layer cytoarchitectonics in the neocortex, occasional NFTs were identified in the CA4 of the hippocampus, pyriform, and insular cortex, nucleus accumbens, basal forebrain, hippocampus, midbrain, and pons, a region in left frontal lobe with focal rarefaction (pallor) of white matter with a few foci of hemosiderin around blood vessels with a mild accompanying gliosis, sections of the cerebellum and medulla were unremarkable, mild generalised pallor of the subcortical white matter, pigmented neurons of the SNr and LC without depopulation, but several globoid NFTs in intact neurons, no neuritic (senile) plaques were observed in the neocortex, no appreciable neuronal loss, no Lewy bodies ; Tau: NR; TDP-43: NR; Amyloid: No amyloid deposits.

Note: N/A: Not applicable; g: grams; N/A: not available; CC: corpus callosum; SNr: substantia nigra; GP: globus pallidus; SP: septum pellucidum; NFTs: neurofibrillary tangles; NTs: neuritic threads; LC: locus coeruleus; CN: cranial nerve; WM: white matter.