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Chronic post-traumatic encephalopathy in boxing Prevention and follow-up: review article

Summary

Chronic post-traumatic encephalopathy is a neurodegenerative disease resulting from the accumulation of numerous craniocerebral traumas, for which there is no definitive pre-mortem diagnosis or specific treatment. Risk factors associated with chronic post-traumatic encephalopathy include: exposure to contact sports, the presence of apolipoprotein E4, and advanced age. Histopathological, although it shares certain characteristics with Alzheimer's disease, it has a more specific presentation (deposition of phosphorylated tau protein in the form of neurofibrillary tangles, associated with an accumulation of neuropil elements, sometimes accompanied by beta-amyloid plaques). Clinically, it is characterized by a slow course that begins with mild cognitive and emotional symptoms, and progresses towards the appearance of parkinsonian symptoms and dementia. Although there are promising diagnostic elements, they are not currently a reality, and the key to managing this disease is prevention and early detection of its first symptoms.

Keywords: dementia, encephalopathy, knockout, boxing

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Introduction

Chronic post-traumatic encephalopathy (CPE) is a nosological entity that is defined as a progressive neurological deterioration, secondary to the accumulation of repeated head traumas.[1,2] Within the broad spectrum that constitutes CPE, dementia pugilistica (DP) is a neurodegenerative condition resulting from the accumulation of phosphorylated tau protein in certain locations of the CNS, the result of repeated traumatic brain injuries (TBI) suffered by athletes who practice contact sports. It was initially described in boxers as "punch drunk syndrome", specifically in 1928 by Dr. Harrison Martland,[3] and it was during the 1960s that the term "pugilistic dementia" was coined. For simplicity of understanding, we will consider the terms CPE and DP as interchangeable. The term "concussion", although ambiguous, is defined by the Center for the Control and Detection of Mild Cranial Trauma as a mild TBI with a score on the Glasgow Coma Scale between 13 and 15, which is associated with a loss of consciousness of a duration considered to last, amnesia of the episode and/or immediate confusion after the trauma.

In recent years, there has been growing popular interest in the impact that mild TBI has on the development of neurocognitive activities and the possible degree of disability associated in the long term. This interest has been transferred to the scientific community, and although there are some reported cases whose purpose is to describe histopathological alterations, as well as other studies carried out in animals, the material we have on the physiological bases, diagnostic methods and prognostic factors and protectors is still scarce. Our objective will be to analyze, through an exhaustive review of the literature, the predictive and risk factors for the development of CPE, as well as the current diagnostic methods that allow the physician to correctly identify the initial phases of the disease, prevent its development.

Epidemiology

Mild TBI is one of the most common neurological disorders, constituting 90% of all attacks that occur on the brain parenchyma.[4] Epidemiological studies that allow us to determine the true frequency of CPE or PD are simply non-existent.[5] It is estimated that approximately 17% of retired professional boxers have CPE,[6] being a rare disease in the subgroup of amateur boxers.[5] In a review carried out by McKee et al.[7] of the 51 cases diagnosed with DBS, 46 (90%) were professional athletes. For the most part, these athletes participated in contact sports, especially boxing and American football, beginning their practice at an early age.[7] However, the appearance of symptoms rarely occurs before its withdrawal.[5]

Risk factors

Several risk factors in CPE have been described, including retirement after the age of 28, a long professional career or having participated in a high number of combats.[6] Episodes of concussion and head trauma expose the athlete to the risk of suffering from this disease.[7] There is a clear relationship between the number of out of combat episodes-also known as knockouts or K.O.-with the probability of developing DP.[8] In a study carried out by Crisco et al.[9] on university American football players, they observed that the severity of the impacts received by the athletes varied depending on the position they had on their team. These results are in line with the histopathological study developed by McKee et al.[7] in which the 5 soccer players who were diagnosed with CPE played in similar positions, that is, in those positions that They suffered from less energy in each impact, but withstood a greater number of blows.[9] Likewise, it is our hypothesis that these variations are also likely to be found in boxing, depending on the category in which the fighters compete. With this assumption, and extracting the results of Crisco et al.[9] and McKee et al., the lighter weight fighters would be those exposed to a greater number of blows (although these were of lower intensity) and, therefore, it would be This category is the most susceptible to developing a neurological condition compatible with CPE in the long term. It seems reasonable that to develop CPE it is necessary for the individual to suffer head trauma. However, not all players who are subjected to these traumas develop this disease. Therefore, it would be interesting to elucidate the factors associated with this progression.

One of the big questions raised by the study of PD or CPE is whether a single blow is capable of causing it. Johnson et al.[10] observed that one third of individuals who had suffered a head injury had neurofibrillary deposits, while this finding was exceptional in healthy controls who had not been subjected to any trauma. In a study carried out on an animal model, Laurer et al.[11] determined that the changes that occur in neurocognitive studies, as well as in histopathological findings, occurred both in individuals who had been subjected to a single trauma and in those who suffered repeated traumas in less than 24 hours, although these changes were much more pronounced in the second group. Therefore, it is logical to think that the severity and presentation of this disease requires repeated head trauma, and that its risk increases when said trauma is shortened in time. Age is another possible risk factor. Although at an early age a TBI would trigger neuro-destructive enzymatic cascades that will continue throughout their professional career,[12] young individuals have greater neuronal plasticity, and, therefore, it is the older patients who present a higher risk.[13]

Among the genetic factors involved, the apolipoprotein E (apoE) gene deserves special mention. ApoE is a protein of 299 amino acids that is encoded in a gene (ApoE) for which there are 3 allelic variables (E2, E3 and E4) that occur with a frequency of 7, 78 and 15%, respectively in white subjects.[14] ApoE is produced in glial cells and is the major transporter of lipids through the cerebrospinal fluid. It is also responsible for maintaining the structural integrity of microtubules within the axon and neuron. The apoE4 allele is involved in the prognosis and presentation of certain neurological disorders, such as Alzheimer's disease (AD),[15] subarachnoid hemorrhage,[16] head trauma,[17,18] as well as ischemia that occurs after head trauma.[19] The presence of the apoE4 allele is also associated with larger intracerebral hematomas.[19] The brain that has suffered trauma is especially sensitive to ischemia, so the secondary insults that occur will condition a worse evolution. Various studies have shown a poorer prognosis in TBI due to the existence of the E4 allele.[18,20] Jordan et al.[21] demonstrated, in a study carried out on professional boxers, that subjects who had worse scores on neurocognitive tests had at least one apoE4 allele. These authors concluded that the apoE4 allele may be associated with greater severity of long-term TBI damage in highly exposed boxers.[22–35]

Pathophysiology

The first studies on the biophysics of head trauma and concussion, carried out on primates, concluded that the phenomenon of concussion was fundamentally produced by rotational acceleration and shear forces, with the phenomenon of impact and countercoup being less important.[36,37] Although the model in primates is quite similar to concussion in humans, these studies are limited by the small number of the sample. In recent years, progress has been made in experiments based on telemetry data obtained from the helmets of athletes from different professional and university contact sports leagues.[38,39] The results of these investigations determined that the greatest tension forces were imparted on the region corresponding to the central structures of the diencephalon and telencephalon,[40] in such a way that these forces applied to structures such as the midbrain (ascending reticular substance), corpus callosum and fornix They are responsible for the episode of loss of consciousness, amnesia and cognitive dysfunction.[7,40] Crisco et al.[9] determined that the impacts that occurred on the cranial vertex presented the lowest rotational force, but a significant linear force, and these traumas were associated with fractures of the cervical spine. On the contrary, blows that occurred on the side subjected the head to a large rotational acceleration force, which was responsible for the concussion and loss of consciousness. The concept of "cognitive reserve" refers to the ability of the nervous system to develop alternative systems or pathways that allow it to compensate for initial deficits.[41] When certain associated degenerative mechanisms (age, toxins, trauma, etc.) are present, cognitive capacity is overwhelmed and compensation mechanisms become insufficient, facilitating a decrease in the performance of neurocognitive parameters.

Clinical manifestations

While concussion and the post-concussive episode represent temporary states of neuronal and axonal deterioration, CPE is a neurodegenerative disease that occurs years or decades after recovery from the acute and subacute symptoms of head trauma. Although the symptoms of post-concussion syndrome can remain for long periods of time, they usually resolve in the first 3 months.[13] On the other hand, the symptoms of CPE evolve over time and are, therefore, degenerative. The symptoms of CPE usually begin in the middle ages of life, typically when the athlete has already retired from his professional career, although in some individuals they may begin to manifest cognitive alterations early. In fact, memory and attention failures, as well as deficits in frontal and executive functions, are the first symptoms, all of them neurocognitive, to manifest in this spectrum of the disease, and they are present in almost all patients at certain times initials of this illness.[7] Subsequently, neuropsychological alterations tend to be noticeable, although many of these manifestations are present from the initial phases, although they usually go unnoticed, given that they are often difficult to differentiate from the individual's premorbid personality traits.[5] In particular, these changes in mood and behavior are defined by family and friends as apathy, aggressiveness, irritability and unjustified anger, and are reported in up to a third of patients who suffer from a condition compatible with CPE.[7]

The use of neuropsychological tests is of special importance in the early diagnosis of the disease and the monitoring of players exposed to contact sports, since psycho-cognitive changes usually persist longer, despite the disappearance of the most obvious motor neurological symptoms in the post-concussive period, and can determine management and the decision to return to play if psychological and behavioral symptoms are still present.[42] In a similar way, motor symptoms may appear, being clearly present in up to 40% of subjects with DBS, according to the series by McKee et al.[7] Within this type of alterations, mild dysarthria and discrete stability alterations are usually early, which are usually revealed very early with the Romberg test5.As the symptoms progress, ataxia, coordination disorders, spasticity and parkinsonism appear.[43] In very rare cases, dementia develops in the context of CPE13. The relative infrequency of this last phase could be due to the early mortality associated with suicide, although this association is not clearly established in the literature.[44]

Diagnosis

MRI

The role of conventional magnetic resonance imaging (MRI) in preventing the deleterious effects of head trauma is quite limited. In conventional MRI sequences, CPE shows a series of nonspecific changes. Without However, these changes occur once there is established structural damage to the brain parenchyma, which will most likely inevitably lead (if it has not already) to CPE. Nuclear medicine: positron emission tomography-computed tomography.[45–59]

Using glucose labeled with fluorine-18 we can estimate cerebral metabolic consumption59. Functional neuroimaging techniques have

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excellent sensitivity for detecting alterations after TBI, in addition to offering good anatomoclinical correlation.[60] In a study carried out on animals[61], a triphasic temporal pattern was identified regarding the metabolic consumption of glucose in individuals who had suffered a head injury. An initial brief response of hyperglycolysis was followed by a relatively prolonged period of metabolic depression associated with neurological deficits. Finally, in the third phase, a recovery of metabolic function took place in the most relevant areas. A similar triphasic pattern has been found in humans.[62,63] Several studies show that patients with good neurological recovery have greater metabolic consumption of glucose.[63,64] Studies based on photon emission tomography (SPECT) have not shown the same consistency in their results.[65] The usefulness of these imaging tests is currently controversial, although there seems to be a trend in which these studies could identify athletes with a greater chance of developing PD-CPE.

Therapeutics and prevention

Currently, there are few proven lines of treatment that stop the development of this disease, and most efforts are aimed at "relieving" or "palliating" the presence of motor, neuropsychological and cognitive symptoms. The use of selegiline has been proposed by Colosimo and Albanese as a treatment aimed at preventing the progression of the disease in a boxer, but its use is not widespread.[66] The empirical use of antiparkinsonian drugs (levodopa) is recommended in patients who present disabling motor symptoms.[5] It is not clear that the use of cholinergic agents stops or improves cognitive symptoms.[67,68] The bulk of preventive strategies are aimed at avoiding prolonged exposure to contact sports, as well as detecting those individuals who have an individualized susceptibility to presenting CPE5. For this, genetic detection tests that allow determining the presence of the apoE4 allele are of special importance. The use of appropriate neuropsychological tests selects those individuals who present incipient symptoms and, therefore, allows guiding the management of these patients, guiding the moment at which athletes can join the game.[69]

Conclusion

CPE is a neurological deterioration associated with the deposition of phosphorylated tau protein caused by the repeated load of numerous head traumas that shares findings with neurodegenerative diseases such as AD, with a clinical course that is sometimes indistinguishable, and whose final diagnosis can only be established postmortem. Neuropsychological tests seem to be the most sensitive to detect the initial symptoms of CPE, and allow management rules to be established to guide reintroduction to sports practice. The new MRI sequence techniques (gradient echo, diffusion) and Nuclear Medicine are promising techniques, but they are not a reality in the accurate diagnosis of this disease. Given that there are no specific therapeutic targets, the most plausible strategy currently lies in prevention, avoiding prolonged exposure and determining the most susceptible individuals (genetic study to detect the -apoE4 allele). In boxing, very close monitoring of the participants must be carried out in order to identify early clinical manifestations in athletes who have received many blows to the skull, as well as those who began the practice of boxing at a very early age.

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None.

Conflicts of interest

The authors declare that there are no conflicts of interest.

References

1. Thurman DJ, Branche CM, Sniezek JE. The epidemiology of sports-related traumatic brain injuries in the United States: recent developments. *J Head Trauma Rehabil*. 1998;13(2):1–8.
2. Lacava G. Boxer's encephalopathy. *J Sports Med Phys Fitness.* 1963;168:87–92.
3. Martland HS. Punch drunk. *JAMA*. 1928;91:1103–1107.
4. Fourtassi M, Hajjioui A, Ouahabi AE, et al. Long term outcome following mild traumatic brain injury in Moroccan patients. *Clin Neurol Neurosurg*. 2011;113(9):716–720.
5. Jordan BD. Chronic traumatic brain injury associated with boxing. *Semin Neurol*. 2000;20(2):179–185.
6. Roberts AH. Brain damage in boxers: A study of the prevalence of traumatic encephalopathy among ex-professional boxers. London: Pitman Medical & Scientific Publishing Co., Ltd.; 1969.
7. McKee AC, Cantu RC, Nowinski CJ, et al. Chronic traumatic encephalopathy in athletes: Progressive tauopathy after repetitive head injury. *J Neuropathol Exp Neurol.* 2009;68(7):709–735.
8. Jordan BD, Jahre C, Hauser WA, et al. CT of 338 active professional boxers. *Radiology*. 1992;185(2):509–512.
9. Crisco JJ, Wilcox BJ, Beckwith JG, et al. Head impact exposure in collegiate football players. *J Biomech*. 2011;44(15):2673–2678.
10. Johnson VE, Stewart W, Smith DH. Widespread tau and amyloidbeta pathology many years after a single traumatic brain injury in humans. *Brain Pathol*. 2012;22(2):142–149.
11. Laurer HL, Bareyre FM, Lee VM, et al. Mild head injury increasing the brain's vulnerability to a second concussive impact. *J Neurosurg.* 2001;95(5):859–870.
12. Wall SE, Williams WH, Cartwright-Hatton S, et al. Neuropsychological dysfunction following repeat concussions in jockeys. *J Neurol Neurosurg Psychiatry*. 2006;77(4):518–520.
13. Saulle M, Greenwald BD. Chronic traumatic encephalopathy: A review. *Rehabil Res Pract.* 2012;2012:816069.
14. Xia Z, Dickens M, Raingeaud J, et al. Opposing effects of ERK and JNK-p38 MAP kinases on apoptosis. *Science*. 1995;270(5240):1326–1331.
15. Seto-Salvia N, Clarimon J. Genetics of Alzheimer's disease. *Rev Neurol.* 2010;50(6):360–364.
16. Leung CH, Poon WS, Yu LM, et al. Apolipoprotein e genotype and outcome in aneurysmal subarachnoid hemorrhage. *Stroke.* 2002;33(2):548–552.
17. Zhou W, Xu D, Peng X, et al. Meta-analysis of APOE4 allele and outcome after traumatic brain injury. *J Neurotrauma.* 2008;25(4):279–290.
18. Teasdale GM, Nicoll JA, Murray G, Fiddes M. Association of apolipoprotein E polymorphism with outcome after head injury. *Lancet.* 1997;350(9084):1069–1071.
19. Liaquat I, Dunn LT, Nicoll JA, et al. Effect of apolipoprotein E genotype on hematoma volume after trauma. *J Neurosurg*. 2002;96(1):90–96.
20. Kutner KC, Erlanger DM, Tsai J, et al. Lower cognitive performance of older football players possessing apolipoprotein E epsilon4. *Neurosurgery.* 2000;47:651–657, discussion 657–658.
21. Jordan BD, Relkin NR, Ravdin LD, et al. Apolipoprotein E epsilon4 associated with chronic traumatic brain injury in boxing. *JAMA.* 1997;278(2):136–140.

22. Omalu B, Bailes J, Hamilton RL, et al. Emerging histomorphologic phenotypes of chronic traumatic encephalopathy in American athletes. *Neurosurgery.* 2011;69:173–83, discussion 183.
23. Blaylock RL, Maroon J. Immunoexcitotoxicity as a central mechanism in chronic traumatic encephalopathy-A unifying hypothesis. *Surg Neurol Int*. 2011;2:107.
24. Gavett BE, Stern RA, McKee AC. Chronic traumatic encephalopathy: A potential late effect of sport-related concussive and subconcussive head trauma. *Clin Sports Med.* 2011;30(1):179–188, xi.
25. DeKosky ST, Ikonomovic MD, Gandy S. Traumatic brain injury: Football, warfare, and long-term effects. *Minn Med*. 2010;93(12):46–47.
26. Chen H, Richard M, Sandler DP, et al. Head injury and amyotrophic lateral sclerosis. *Am J Epidemiol*. 2007;166(7):810–816.
27. Omalu BI, DeKosky ST, Minster RL, et al. Chronic traumatic encephalopathy in a National Football League player. *Neurosurgery.* 2005;57(1):128–34, discussion 134.
28. Kane MJ, Angoa-Pérez M, Briggs DI, et al. A mouse model of human repetitive mild traumatic brain injury. *J Neurosci Methods*. 2012;203(1):41–49.
29. Bennett RE, Mac Donald CL, Brody DL. Diffusion tensor imaging detects axonal injury in a mouse model ofrepetitive closed-skull traumatic brain injury. *Neurosci Lett.* 2012;513(2):160–165.
30. Kanayama G, Takeda M, Niigawa H, et al. The effects of repetitive mild brain injury on cytoskeletal protein and behavior. *Methods Find Exp Clin Pharmacol.* 1996;18(2):105–115.
31. Longhi L, Saatman KE, Fujimoto S, et al. Temporal window of vulnerability to repetitive experimental concussive brain injury. *Neurosurgery*. 2005;56(2):364–374.
32. Mortimer JA, French LR, Hutton JT, et al. Head injury as a risk factor for Alzheimer's disease. *Neurology.* 1985;35:264–247.
33. Giza CC, Hovda DA. The neurometabolic cascade of concussion. *J Athl Train*. 2001;36(3):228–235.
34. Serbest G, Burkhardt MF, Siman R, et al. Temporal profiles of cytoskeletal protein loss following traumatic axonal injury in mice. *Neurochem Res*. 2007;32(12):2006–2014.
35. Spillantini MG, Bird TD, Ghetti B. Frontotemporal dementia and Parkinsonism linked to chromosome 17: A new group of tauopathies. *Brain Pathol.* 1998;8(2):387–402.
36. Ommaya AK. Nervous system injury and the whole body. *J Trauma.* 1970;10:981–990.
37. Masuzawa H, Nadamura N, Hirakawa K, et al. Experimental head injury & concussion in monkey using pure linear acceleration impact. *Neurol Med Chir (Tokyo)*. 1976;16(PT1):77–90.
38. Duhaime AC, Beckwith JG, Maerlender AC, et al. Spectrum of acute clinical characteristics of diagnosed concussions in college athletes wearing instrumented helmets: Clinical article. *J Neurosurg*. 2012;117:1092–1099.
39. Rowson S, Duma SM, Beckwith JG, et al. Rotational head kinematics in football impacts: An injury risk function for concussion. *Ann Biomed Eng*. 2012;40(1):1–13.
40. Pellman EJ, Viano DC, Tucker AM, et al. Concussion in professional football: reconstruction of game impacts and injuries. *Neurosurgery*. 2003;53(4):799–812.
41. Allen JS, Bruss J, Damasio H. The aging brain: The cognitive reserve hypothesis and hominid evolution. *Am J Hum Biol.* 2005;17(6):673–689.
42. Erlanger DM, Kutner KC, Barth JT, et al. Neuropsychology of sports-related head injury: Dementia pugilistica to post concussion syndrome. *Clin Neuropsychol.* 1999;13:193–209.
43. Mendez MF. The neuropsychiatric aspects of boxing. *Int J Psychiatry Med.* 1995;25:249–262.
44. Wortzel HS, Shura RD, Brenner LA. Chronic traumatic encephalopathy and suicide: A systematic review. *Biomed Res Int.* 2013;2013:424280.
45. Bruce JM, Echemendia RJ. History of multiple self-reported concussions is not associated with reduced cognitive abilities. *Neurosurgery.* 2009;64(1):100–106.
46. De Beaumont L, Theoret H, Mongeon D, et al. Brain function decline in healthy retired athletes who sustained their last sports concussion in early adulthood. *Brain*. 2009;132(Pt 3):695–708.
47. Gaetz M, Goodman D, Weinberg H. Electrophysiological evidence for the cumulative effects of concussion. *Brain Inj*. 2000;14(12):1077–1088.
48. Cavanaugh JT, Guskiewicz KM, Giuliani C, et al. Recovery of postural control after cerebral concussion: New insights using approximate entropy. *J Athl Train*. 2006;41(3):305–313.
49. McCrea M, Guskiewicz KM, Marshall SW, et al. Acute effects and recovery time following concussion in collegiate football players: The NCAA Concussion Study. *JAMA*. 2003;290(19):2556–2563.
50. De Beaumont L, Lassonde M, Leclerc S, et al. Longterm and cumulative effects of sports concussion on motor cortex inhibition. *Neurosurgery.* 2007;61(12):329–367.
51. De Beaumont L, Henry LC, Gosselin N. Long-term functional alterations in sports concussion. *Neurosurg Focus*. 2012;33(6):E8:1–7.
52. Scheid R, Walther K, Guthke T, et al. Cognitive sequelae of diffuse axonal injury. *Arch Neurol*. 2006;63(3):418–424.
53. Hughes DG, Jackson A, Mason DL, et al. Abnormalities on magnetic resonance imaging seen acutely following mild traumatic brain injury: Correlation with neuropsychological tests and delayed recovery. *Neuroradiology.* 2004;46(7):550–558.
54. Mac Donald CL, Dikranian K, Song SK, et al. Detection of traumatic axonal injury with diffusion tensor imaging in a mouse model of traumatic brain injury. *Exp Neurol.* 2007;205(1):116–131.
55. Arfanakis K, Haughton VM, Carew JD, et al. Diffusion tensor MR imaging in diffuse axonal injury. AJNR *Am J Neuroradiol.* 2002;23(5):794–802.
56. Tirapu-Ustárroz J, Luna-Lario P, Hernáez-Goni P, et al. Relation between white matter and cognitive functions. *Rev Neurol*. 2011;52:725–742.
57. Liston C, Watts R, Tottenham N, et al. Frontostriatal microstructure modulates efficient recruitment of cognitive control. *Cereb Cortex.* 2006;16(4):553–560.
58. Niogi SN, Mukherjee P, Ghajar J, et al. Structural dissociation of attentional control and memory in adults with and without mild traumatic brain injury. *Brain*. 2008;131(Pt 12):3209–3221.
59. Carnero-Pardo C. Systematic review of the value of positron emission tomography in the diagnosis of Alzheimer's disease. *Rev Neurol.* 2003;37(9):860–870.
60. De la Cueva-Barrao L, Noé-Sebastián E, Sopena-Novales P, et al. The clinical relevance of FDG-PET imaging in severe traumatic brain injuries. *Rev Neurol.* 2009;49(2):58–63.
61. Hovda D. Metabolic dysfunction. En: Narayan RK, Wiberger JE, Povlishock JT, editors. *Neurotrauma.* New York: Mc Graw Hill; 1996. p. 1459–1478.
62. Yamaki T, Yoshino E, Fujimoto M, et al. Chronological positron emission tomographic study of severe diffuse brain injury in the chronic stage. *J Trauma*. 1996;40(1):50–56.
63. Bergsneider M, Hovda DA, McArthur DL, et al. Metabolic recovery following human traumatic brain injury based on FDG-PET: Time course and relationship to neurological disability. *J Head Trauma Rehabil*. 2001;16(2):135–148.

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64. Tenjin H, Ueda S, Mizukawa N, et al. Positron emission tomographic studies on cerebral hemodynamics in patients with cerebral contusion. *Neurosurgery.* 1990;26(6):971–979.

65. Kant R, Smith-Seemiller L, Isaac G, et al. Tc-HMPAO SPECT in persistent post-concussion syndrome after mild head injury: Comparison with MRI/CT. *Brain Inj.* 1997;11(2):115–124.

66. Colosimo C, Albanese A. Boxer disqualified for taking selegiline. *Lancet.* 1995;346(8975):647.

67. Goldberg E, Gerstman LJ, Mattis S, et al. Effects of cholinergic treatment on posttraumatic anterograde amnesia. *Arch Neurol.* 1982;39(9):581.

68. Taverni JP, Seliger G, Lichtman SW. Donepezil medicated memory improvement in traumatic brain injury during post acute rehabilitation. *Brain Inj*. 1998;12(1):77–80.

69. Erlanger D, Feldman D, Kutner K, et al. Development and validation of a web-based neuropsychological test protocol for sports-related return-to-play decision-making. *Arch Clin Neuropsychol.* 2003;18(3):293–316.

Citation: Zavala JGG. Chronic post-traumatic encephalopathy in boxing Prevention and follow-up: review article. *J Neurol Stroke.* 2024;14(6):180–184. DOI: 10.15406/jnsk.2024.14.00605