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Does Second Impact Syndrome Exist?

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Abstract: Second impact syndrome (SIS) is a widely feared complication of traumatic brain injury. Although postulated to occur after repeated concussion, the evidence for such a premise is not compelling. This paper reviews the published evidence for and against the existence of this controversial entity. Rather than SIS being a complication of recurrent concussion, it is far more likely that the clinical condition represents "diffuse cerebral swelling," a well-recognized complication of traumatic brain injury. This condition is more common in children and adolescents, which reflects the known demographics of so-called "second impact syndrome." We propose that clinicians abandon the misleading term second impact syndrome and refer to the syndrome as diffuse cerebral swelling.

Key Words: Concussion—Cerebral edema—Second impact syndrome.

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INTRODUCTION

In the United States, belief in the so-called "second impact syndrome" (SIS) has reached almost mythical proportions. SIS has been defined as occurring when

> "...an athlete who has sustained an initial head injury, most often a concussion, sustains a second head injury before symptoms associated with the first have fully cleared."[1]

It is postulated that this second impact sets in motion cerebral vascular congestion, which in turn causes cerebral swelling. Death usually follows rapidly due to transtentorial brainstem herniation. While there is no doubt that brain swelling may occur in response to a head injury,[2] the issue of whether recurrent concussive injury is a risk factor for this condition is disputed. This point is critical for team physicians because it is the fear of this entity that underpins concussion guidelines regarding return to sport.[4,19]

BACKGROUND

Diffuse cerebral swelling (in the absence of repeated concussion) is a rare but well-recognized cause of delayed catastrophic deterioration in children and adolescents resulting in death or persistent vegetative state after a minor head injury.[3–10] The etiology of this condition is said to be due to disordered cerebral autoregulation following brain injury. This condition is often loosely termed "malignant brain edema."[5]

SIS is said to share a similar pathology to this phenomenon differing only in the risk factor of repeated concussive injury. If SIS represents a real clinicopathologic entity, then there are potentially major consequences for the management of minor head injury in sport. Belief in the concept of SIS currently dictates management strategies for use in all minor sport-related injuries.[4,11–16] Moreover, scientific study of the causes of posttraumatic cerebral swelling, which undoubtedly does occur, could be misdirected. Given the rarity of these conditions, a case-control study would be the only feasible means to establish the risk factors.[17]

There are also medicolegal implications that limit the ability to challenge existing concussion guidelines for fear of litigation. In recent times, however, many team physicians have begun to raise concerns over the widespread belief in this syndrome, given the high incidence of concussion in most collision sports and the scarcity of published SIS cases.[18,19]

EVIDENCE AGAINST THE EXISTENCE OF SIS

Interpretation of Case Reports

The concept of SIS largely rests on the interpretation of anecdotal case reports. In addition to the published cases described below, a further 35 cases from the U.S. National Center for Catastrophic Sport Injury Research have been cited as probable cases of SIS, but not published due to lack of confirmatory details.[1,20]

In 1998, McCrory and Berkovic published an analysis and reinterpretation of the published cases of this entity.[19] To provide a consistent framework by which published case reports could be analyzed, four arbitrary diagnostic criteria were defined by the authors based on the clinicopathophysiological features and temporal profile of SIS.

These criteria were:

A. Medical review following a witnessed first impact
B. Documentation of ongoing symptoms following the initial impact up to the time of the second impact

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TABLE 1. *Number of cases satisfying diagnostic criteria*

Criteria	Definition	Number
A	Medical review after a witnessed first impact	5/17
B	Documentation of ongoing symptoms following the first impact up to the time of the second impact	7/17
C	Witnessed second head impact with a subsequent rapid cerebral deterioration	6/17
D	Neuropathological or neuroimaging evidence of cerebral swelling without significant intracranial hematoma or other cause for edema	13/17

C. Witnessed second head impact with a subsequent rapid cerebral deterioration
D. Neuropathologic or neuroimaging evidence of cerebral swelling without significant intracranial hematoma or other cause for cerebral edema (e.g., encephalitis)

All published reports were classified by two independent reviewers according to the above criteria as: *definite SIS* (criteria A, B, C, and D); *probable SIS* (criteria C and D plus either A or B); *possible SIS* (criteria C and D only); or *not SIS* (criteria C or D absent).

Seventeen published cases were described[1,4,10,21–23] or subsequently quoted[3,24] examples of SIS. See Table 1 for cases satisfying the proposed diagnostic criteria.

The amount of clinical documentation varied considerably in the published reports. In most cases, evidence of previous trauma was based on team mate-recalled episodes rather than video-documented reports. In only two cases, immediate medical evaluation after the initial impact was documented in the reports, but these two cases failed to fulfill the other criteria of SIS. Surprisingly, there was no evidence at all of a "second" impact in 11 cases, including 4 of the cases described by Schneider, which are frequently cited as classic examples of SIS.[24] Diffuse cerebral swelling was documented in 14 cases; however, in 1 case, there was another plausible neuropathologic cause for brain swelling (encephalitis), leaving 13 cases satisfying criterion D.

Under the classification, there were no cases of "definite SIS." There were five cases of "probable SIS" (Table 2), and the remaining 12 cases were "not SIS." SIS was excluded in these 12 cases on the basis of absence of neuroimaging or neuropathologic evidence of unexplained cerebral swelling (criterion D) in 4 of 12 cases and absence of a witnessed second impact (criterion C) in 11 of 12 cases. Both criteria C and D were lacking in 3 of 12 cases.

Recall Bias

Given that team mate recall is often the basis on which a "first impact" is documented, a further study was published testing the reliability of this method of data collection.[19] Statistical analysis demonstrated a significant ($p = 0.001$) difference between team mate-recalled and self-reported/video-documented episodes of major and minor concussion, where Australian football players consistently over-reported recalled episodes of major (associated with loss of consciousness [LOC]) and minor (no LOC) concussive brain injury in their team mates when compared with self-reported and video-documented episodes. The rationale therefore of reliance of this method of ascertaining previous concussive injuries in athletes dying from cerebral swelling/SIS is dubious.

Geographic Variation

It is surprising that there are virtually no reports of SIS outside the United States, despite the fact that similar (or greater) concussion rates occur in the other sports played throughout the world. A recent study was published analyzing all deaths due to football in the State of Victoria, Australia, during the period 1968–1999.[25] The aim of this study was to determine whether cases of SIS might have occurred in this setting.

TABLE 2. *Probable second impact syndrome cases*

Ref	Age/sex	Sport	1st episode	Ongoing symptoms	2nd episode	Pathology	Criteria satisfied
(3)	16/M	Hockey	Struck back of head on ice; brief loss of consciousness; eyewitness description	Headache, unsteady, weakness	Checked heavily, causing loss of consciousness	Path: Occipital contusion (days), cerebral edema, small SDH, SAH	B, C, D
(4)	17/M	Football	Cantu Grade 1 concussion during football game; no loss of consciousness; headache post game	Headache	Head struck during successive plays; light head contact during next play and collapsed	Path: cerebral swelling, obstructive hydrocephalus, small SDH/SAH	B, C, D
(1)	17/M	Boxer	Headache after boxing match 2 days prior; using aspirin ++; motor vehicle accident causing head impact on morning of fight	Yes	Collapsed round 2; no knockdowns in fight	Path: small L frontal SDH, cerebral edema	B, C, D
	19/M	Boxer	Knocked down in fight; post fight headache	Yes	Collapsed round 2 after "minor" blows	Path: Small R SDH, cerebral edema ++	B, C, D
	17/M	Boxer	Several standing counts after being stunned by head blows; post fight psychiatric disturbance	Yes	Fight stopped in round 2 after several "standing counts"; collapsed minutes later	Path: Cerebral edema with brainstem herniation	B, C, D

SAH, subarachnoid hemorrhage; SDH, subdural hematoma.

In the 32-year time frame of the study, a total of 25 player deaths were identified. Nine were due to neurotrauma and the remaining 16 deaths were due to other causes not related to neurologic injury, predominantly unrecognized ischemic or congenital heart disease. The nine player deaths due to brain injury were predominantly due to either intracerebral hematoma or traumatic subarachnoid hemorrhage due to vertebral artery trauma. Diffuse cerebral edema was noted in three cases in conjunction with surgically treated subdural hematomata, one case with an extradural hematoma and one case following a middle cerebral arterial territory stroke. No cases of SIS were noted in the coronial findings and none would fit the diagnostic criteria discussed above.

For registered players, the crude risk of death from all causes in Australian football is approximately 22 per 240 million player games or 1 per 11 million player games. The risk of death from brain injury is therefore 1 per 30 million player games.

DISCUSSION

The medical literature clearly describes many causes of delayed cerebral deterioration after traumatic brain injury. The earliest description of such a syndrome is credited to Otto Bollinger, who in 1891, coined the term "traumatische spät-apoplexie."[26] Patients who suffer a delayed deterioration or who "talk and die" after closed head injury represent approximately 15% of all patients sustaining severe head injuries. Intracranial hematoma is the cause of this syndrome in approximately 75% of these patients.[27–32] In some cases, hematomas are evident on initial imaging studies, but in other cases, hematomas develop after a delay.[33,34] There is a smaller subgroup of patients who deteriorate due to causes other than mass lesions who have evidence of posttraumatic diffuse cerebral swelling.

It is important to note that cerebral swelling may occur with or without structural brain injury[35], and that deterioration may be rapid following an acute injury.[36]

The Pathophysiology of Posttraumatic Brain Swelling

Posttraumatic cerebral swelling may be due to two separate pathophysiological mechanisms. The first of these is thought to be due to increased cerebral blood volume that in turn is secondary to a failure of cerebral vascular autoregulatory mechanisms.[5,6,27,37] Animal models, as well as evidence from human cases, demonstrate the extreme rapidity by which these vascular changes can occur.[38,39] In one case report, massive traumatic cerebral swelling, documented on computed tomographic scanning, occurred within 20 minutes of cerebral injury.[36]

The second mechanism of posttraumatic brain swelling is due to true cerebral edema. The characteristic feature of this entity is that the cut brain at autopsy "wept fluid."[2] The classic study of Klatzko identified two forms: vasogenic and cytotoxic edema.[40] Experimental evidence demonstrates that both of these entities can occur within hours of head trauma although more typically are seen after several days.[2,41,42] Their precise contribution to the morbidity and mortality of closed head injury remains unknown.

Does SIS Exist?

In the SIS literature, we found 13 reports that clearly describe sport-related catastrophic brain injury associated with unexplained cerebral swelling. In many of these cases, the players did not have a second impact; rather they either collapsed during sport participation or walked off and collapsed without any further injury occurring.[1,4,21–24] Indeed, the index case that used the label of "second impact syndrome," did not have a described second impact.[22] The analysis of the published cases shows that by using strict criteria for the definition of SIS, only five of the cases would be considered "probable SIS" with the remainder being excluded. None of the published cases fulfilled the criteria for "definite SIS." In many published case reports, there was a paucity of medical details presented.

In most cases, evidence of previous trauma is based on recalled eyewitness accounts or circumstantial evidence. The proposed criteria where an initial documented witnessed impact must occur, while strict, emphasizes the fundamental issue. This degree of diagnostic certainty may seem unrealistic to some observers; however, the central basis of this condition rests on the verification of this particular aspect of the published cases. It is assumed that other team players' recall of head injury events in such circumstances will be reliable. The dangers of this form of retrospective case ascertainment should be obvious. The recall study demonstrates the limitations of using teammate-recalled injury.

In contrast to the view that SIS probably does not exist, or at best has been over-diagnosed, there has been suggestion that the rarity of this condition does not reflect its true incidence with cases going unreported.[20] This seems implausible since most sport-related deaths in children and adolescents are likely to be investigated and/or be the subject of coronial inquests. Given that these episodes seem noteworthy in their own right, one can assume that virtually all cases would be documented. This is supported by the Australian football fatality study where no case of SIS was demonstrated over a 32-year period in spite of the high participation rate for this sport and a concussive injury rate that is approximately eight times that of American football.

Risk Factors for Cerebral Swelling in Sports

Are boxers at greater risk?

Particular note of the cases of cerebral swelling reported in boxers should be made. With the propensity to numerous head impacts during a single bout, it makes it very difficult to determine what is in fact a "first" or "second" impact. Some published cases suggest that both may occur during the course of a single bout.[1] Should these cases be included with other sports? If SIS is a real entity, the repetitive head impacts in boxing should make boxers much more likely to suffer from this entity. Boxers do suffer more frequently from other forms of cata-

strophic brain injury, such as subdural hematoma, than other sports.[35,43–47] Given that concussive episodes occur in virtually every bout fought, why then is SIS not more frequently seen in boxing?

Are children at greater risk?

The striking feature of these published cases of "SIS" is that virtually all are adolescents. Excluding boxing, only two cases exist of "probable" SIS, one being in a 16-year-old ice hockey player and the other in a 17-year-old gridiron football player.[4] In boxing, the majority of cases are also noted in teenagers. In children, given the apparent higher risk of cerebral swelling after minor head injury and the propensity for structural injury (e.g., subdural hematomas) with relatively mild injury, some authors have argued that there may be a different cerebral autoregulatory response to trauma than in adults.[5–9,37]

Is There a Sex Bias?

All the reported cases of SIS are in young males. Whether this represents a true sex difference or an exposure bias has not been clarified. Given the nature of the sports from which cases are reported (gridiron, ice hockey, and boxing), the male bias is not wholly unexpected. In the related medical literature on neurosurgical catastrophic brain injury after minor trauma, approximately 30% of the cases were female.[23,27–30,32,35] Once again, given that motor vehicle accidents, gunshot trauma, and sport injury are the major patient sources, it is not surprising that males predominate. There is however some indirect evidence to suggest that female sex hormones may play a role in memory function postinjury.[48] Whether a true sex difference exists in terms of cerebral response to trauma remains unsubstantiated at this stage.

Prevention

Although extremely rare, sport-related diffuse cerebral swelling has a mortality approaching 100%. Many of the published case reports[21,22] and most notably the guidelines of the Colorado Medical Society and the American Academy of Neurology suggest that prevention of this syndrome should be based on a policy of not allowing individuals to return to sport until postconcussive symptoms have fully resolved.[4,12,49] In addition, the Colorado and Academy guidelines define arbitrary periods of exclusion from sport following concussive injury. The reasons for these practices relate to the belief that

> "individuals who are symptomatic from a concussion, even without LOC, are at risk for developing diffuse brain swelling after a second impact to the head"

and that the risk of cerebral swelling is lessened with time.[4] No scientific data is provided as to the rationale by which arbitrary exclusion periods were established.

We agree that athletes should not return to sport until all postconcussive symptoms have resolved. The danger of prematurely returning to sport relates to the risk of sustaining further injury. It is known that neuropsychologic measures of speed of information processing and reaction times are slowed in the early stages postinjury.[50–55] In this setting, an athlete participating in a collision sport (such as football) or high-risk sport (such as motor car racing) may not be able to respond appropriately to dangers in the sporting situation and therefore sustain further injury. Unfortunately, there is no evidence that these strategies reduce the risk of posttraumatic cerebral swelling.

As already discussed, the risk factors for posttraumatic acute brain swelling are not understood at present. Our current limited knowledge suggests that children and adolescents are at higher risk, and increased clinical vigilance and perhaps more aggressive investigational strategies may be necessary after all head injuries in this age group. Certainly the presence of postconcussive symptoms should be an important factor prompting further medical assessment.

Recent discussion as to the potential role of genetic markers influencing outcome from traumatic brain injury has raised further issues. While the apolipoprotein E4 phenotype has been demonstrated to be associated with poor outcome after moderate-to-severe brain injury and with the development of traumatic encephalopathy in boxers, its role in the genesis of cerebral edema remains speculative.[58,59]

CONCLUSION

From the discussion above, we recognize an extremely rare catastrophic complication of single brain impact, namely diffuse cerebral swelling. This entity is typically but not exclusively associated with structural brain injury (e.g., cerebral contusion or subdural hematoma) and is more common in children and adolescents. Its causes are unknown but may involve disordered cerebral vascular autoregulation.

Most cases of traumatic cerebral swelling, whether associated with a structural brain injury or not, have no prior evidence of head injury with ongoing symptoms that would support the concept of second impact syndrome as defined in the literature. In those cases that are presumed to represent SIS, the evidence that a prior head injury is a risk factor for this pathophysiological entity is not compelling. Case-control studies are required to determine if prior head injury is relevant in some instances of posttraumatic cerebral swelling and to identify other risk factors so that correct preventative strategies can be instituted.

While repeated concussion is not necessarily associated with diffuse cerebral swelling (i.e., the so-called "second impact syndrome"), nevertheless clinicians need to be aware of the possibility that cerebral swelling may rarely occur following a head injury. The presence of postconcussive symptoms should be seen as a significant risk factor for this to occur, and any symptoms should mandate restriction from further sports participation until the symptoms fully resolve.

Is early return to play following concussion, in the sports medicine sense, therefore inherently dangerous? We know from the large body of research on the neuropsychologic effects of sport-related concussions that the principal cognitive deficits in the postinjury period relate

to reduced reaction times and impaired speed of information processing.[51,56,57] Premature return of a concussed athlete would presumably lead to an increase in injury rates, consequent on the fact that the athlete's ability to respond appropriately to the demands and threats of the sport would be slowed—not an increase in mortality due to the so-called second impact syndrome.

Arbitrary exclusion periods based on a fear of a nonexistent entity are not the answer in this era of evidence-based medicine. We need to prospectively assess return-to-play strategies based on symptom resolution and neuropsychologic recovery, and determine that the outcomes of this approach are safe for the player concerned and appropriate for the sport played. Until such studies are performed, the management of concussion should follow the experience of most team physicians who safely treat concussed athletes with a combination of good common sense and clinical judgement.

REFERENCES

1. Cantu RC, Voy R. Second impact syndrome: a risk in any contact sport. *Phys Sportsmed* 1995;23:27–34.
2. Kimelberg H. Current concepts of brain edema. *J Neurosurg* 1995; 83:1051–1059.
3. Fekete JF. Severe brain injury and death following minor hockey accidents: the effectiveness of the safety helmets of amateur hockey players. *Can Med Assoc J* 1968;99:1234–1239.
4. Kelly JP, Nichols JS, Filley CM, et al. Concussion in sports. Guidelines for the prevention of catastrophic outcome. *JAMA* 1991;266:2867–2869.
5. Bruce DA, Alavi A, Bilaniuk L, et al. Diffuse cerebral swelling following head injuries in children: the syndrome of "malignant brain oedema." *J Neurosurg* 1981;54:170–178.
6. Bruce DA. Delayed deterioration of consciousness after trivial head injury in childhood. *B Med J* 1984;289:715–716.
7. Pickles W. Acute general edema of the brain in children with head injuries. *N Eng J Med* 1950;242:607–611.
8. Nee PA, Phillips BM, Bannister CM. Extradural haematoma in a child after an apparently mild head injury. *Br Med J* 1993;306: 1665–1666.
9. Schnitker MT. A syndrome of cerebral concussion in children. *J Paediatr* 1949;35:557–560.
10. Centre for Disease Control. Sports-related recurrent brain injuries—United States. *MMWR* 1997;46:224–227.
11. Kelly J, Rosenberg J. Diagnosis and management of concussion in sports. *Neurology* 1997;48:575–580.
12. American Academy of Neurology. Practice parameter: the management of concussion in sports (summary statement). *Neurology* 1997;48:581–585.
13. Hugenholz H, Richard MT. The on-site management of athletes with head injuries. *Phys Sportsmed* 1983;11:71–80.
14. Kulund D. Athletic injuries to the head, neck and face. In: Kulund D, ed. *The Injured Athlete*. Philadelphia: J.B. Lippincott, 1982:225–257.
15. Nelson WE, Jane JA, Gieck JH. Minor head injury in sports: a new system of classification and management. *Phys Sportsmed* 1984; 12:103–107.
16. Torg JF, ed. *Athletic Injuries to the Head, Neck and Face. 2nd Ed*. St Louis: Mosby Year Book, 1991:54–76.
17. Sackett D, Haynes R, Guyatt G, et al. *Clinical Epidemiology: A Basic Science For Clinical Medicine. 2nd Ed*. Boston: Little, Brown and Company, 1991:126–155.
18. Rice SG. Head injury rules: based on one tragedy? *Sports Med Prim Care* 1995;1:9–12.
19. McCrory PR, Berkovic SF. Second impact syndrome. *Neurology* 1998;50:677–83.
20. Mueller FO, Cantu RC, Van Camp SP. Catastrophic Injuries In High School And College Sports. Champaign, IL: Human Kinetics, 1996.
21. McQuillen JB, McQuillen EN, Morrow P. Trauma, sport and malignant cerebral edema. *Am J Forensic Med Pathol* 1988;9:12–15.
22. Saunders RL, Harbaugh RE. The second impact in catastrophic contact-sports head trauma. *JAMA* 1984;252:538–539.
23. Shell D, Carico GA, Patton RM. Can subdural hematoma result from repeated minor head injury? *Phys Sportsmed* 1993;21:74–84.
24. Schneider RC. Head and neck injuries in football: mechanisms, treatment and prevention. Baltimore: Williams and Wilkins, 1973.
25. McCrory P, Berkovic S, Cordner S. Deaths due to brain injury among footballers in Victoria, from 1968 to 1998. *Med J Aust* 2000;172:217–220.
26. Bollinger O. Uber traumatische spät-apoplexie; ein Beitrag zur lihr von der Hirnerschütterung. In: Virchow R, editor. *Internationale Beitrage zur Weissenschaftlichen Medizin*. Berlin: Auttirschwald, 1891:457–470.
27. Lobato RD, Rivas JJ, Bilaniuk L. Head injured patients who talk and deteriorate into coma. *J Neurosurg* 1991;75:256–261.
28. Marshall LF, Gautille T, Klauber MR. The outcome of severe closed head injury. *J Neurosurg* 1991;75:S25-S36.
29. Marshall LF, Toole BM, Bowers SA. The national traumatic coma databank. Part 2: patients who talk and deteriorate. *J Neurosurg* 1983;59:285–288.
30. Rockswold GL, Pheley PJ. Patients who talk and deteriorate. *Ann Emerg Med* 1993;22:1004–1007.
31. Rockswold GL, Leonard PR, Nagib MG. Analysis of management in 33 closed head injury patients who "talked and deteriorated." *Neurosurg* 1987;21:51–55.
32. Reilly PL, Adams JH, Graham DI. Patients with head injury who talk and die. *Lancet* 1975;2:375–377.
33. Wilberger JE, Deeb Z, Rothfus W. Magnetic resonance imaging in cases of severe head injury. *Neurosurg* 1987;20:571–576.
34. Mellion BT, Narayan RK. Delayed traumatic intracerebral hematomas and coagulopathies. In: Barrow DL, editor. *Complications and Sequelae of Head Injury*. Park Ridge, IL: American Association of Neurological Surgeons, 1992:51–59.
35. Dacey RG, Alves WM, Rimel RW, et al. Neurosurgical complications after apparently minor head injury. *J Neurosurg* 1986;65: 203–210.
36. Kobrine AI, Timmins E, Rajjour RK, et al. Demonstration of massive traumatic brain swelling within 20 minutes after injury. *J Neurosurg* 1977;46:256–258.
37. Snoek JW, Minderhoud JM, Wilmink JT. Delayed deterioration following mild head injury in children. *Brain* 1984;107:15–36.
38. Corales RL, Miller JD, Becker DP. Intracranial pressure and water content in acute graded experimental trauma. In: Shulman K, Marmarou A, Miller JD, et al. eds. *Intracranial Pressure IV*. Berlin: Springer-Verlag, 1980:280–283.
39. Wako N, Shima K, Marmarou A. Time course of brain tissue pressure in temporal fluid percussion injury. In: Hoff JT, Betz AL, eds. *Intracranial Pressure VII*. Berlin: Springer-Verlag, 1989:593–597.
40. Klatzko I. Neuropathological aspects of brain edema. *J Neuropathol Exp Neurol* 1967;26:1–13.
41. Bullock R, Maxwell W, Graham D. Glial swelling following cerebral contusion: an ultrastructural study. *J Neurol Neurosurg Psych* 1991;54:427–434.
42. Bullock R, Sakas D, Patterson J, et al. Early post traumatic cerebral blood flow mapping: correlation with structural damage after focal injury. *Acta Neurochir* 1992;55(Suppl):14–17.
43. Cantu RC, ed. *Boxing and Medicine*. Champaign, IL: Human Kinetics, Inc., 1995.
44. Jordan BD. Neurologic injury in boxing. *Hosp Med* 1991;27:93–105.
45. Jordan B, ed. *Medical Aspects of Boxing*. Boca Raton: CRC Press, 1993.
46. Jordan BD, Campbell EA. Acute injuries among professional boxers in New York: a two year survey. *Phys Sportsmed* 1988;16:87–91.
47. Jokl E. *The Medical Aspects of Boxing*. Pretoria: Van Schaik Publishers, 1941.
48. Joseph R. Traumatic amnesia, repression, and hippocampus injury due to emotional stress, corticosteroids and enkephalins. *Child Psychiatry Hum Dev* 1998;29:169–185.

49. Colorado Medical Society. *Report of the Sports Medicine Committee: Guidelines for the Management of Concussions in Sport (Revised)*. Denver: Colorado Medical Society, 1991.
50. Gronwall D, Wrightson P. Delayed recovery of intellectual function following minor head injury. *Lancet* 1974;ii:605–609.
51. Gronwall D, Wrighson P. Memory and information processing capacity after closed head injury. *J Neurol Neurosurg Psych* 1981; 44:889–895.
52. Gronwall D. Paced auditory serial addition task: a measure of recovery from concussion. *Percep Motor Skills* 1977;44:367–373.
53. Maddocks D, Saling M. Neuropsychological sequelae following concussion in Australian rules footballers. *J Clin Exp Neuropsychol* 1991;13:439–441.
54. Levin H, Eisenberg HM, Benton AL, eds. *Mild Head Injury*. Oxford: Oxford University Press, 1989.
55. McCrea M, Kelly JP, Kluge J, et al. Standardized assessment of concussion in football players. *Neurology* 1997;48:586–588.
56. Maddocks D, Saling M. Neuropsychological deficits following concussion. *Brain Inj* 1996;10:99–103.
57. Barth JT, Alves WM, Ryan TV, et al. Mild head injury in sports: neuropsychological sequelae and recovery of function. In: Levin HS, Eisenberg HM, Benton AL, eds. *Mild Head Injury*. New York: Oxford University Press, 1989:257–275.
58. Jordan B, Relkin N, Ravdin L. Apolipoprotein E epsilon 4 associated with chronic traumatic brain injury in boxing. *JAMA* 1997; 278:136–140.
59. Teasdale G, Nicol J, Murray G. Association of apolipoprotein E polymorphism with outcome after head injury. *Lancet* 1997;350: 1069–1071.