

RECOMMENDATIONS

- Future research should focus on determining the pathophysiological characteristics of patients who will have a better response to amantadine, the most effective dosage and duration of treatment and timing of its initiation.
- With insufficient evidence to establish guidelines for optimal pharmacological treatment in TBI care must be taken when choosing pharmacological interventions and If the decision is made to use medications to promote the recovery, clinicians should thoroughly document the goals of pharmacotherapy and closely monitor for side effects.
- TBI is not an “event” but it is an ongoing process in any patient, so assessment must be dynamic in nature to accommodate the evolving nature of TBI.
- In addition to pharmacotherapy, nonpharmacologic interventions also should be a mainstay of treatment. Compensatory training and cognitive exercise may improve patients’ cognitive deficits and return some sense of control. Individual and family psychotherapy, including cognitive-behavioral therapy, also may be beneficial.
- Results of this trial and additional similarly designed trials will be necessary to develop evidence based recommendations for amantadine therapy in TBI.

REFERENCES

1. Faul M, Xu L, Wald MM, Coronado VG. Traumatic brain injury in the United States: emergency department visits, hospitalizations, and deaths. Atlanta (GA): Centers for Disease Control and Prevention, National Center for Injury Prevention and Control 2010.
2. Langlois JA, Kegler SR, Butler JA. Traumatic brain injury-related hospital discharges. Results from a 14-state surveillance system. *MMWR SurveillSumm*2003;52:1–20.
3. Coronado VG, Thomas KE, Sattin RW, Johnson RL. The CDC traumatic brain injury surveillance system: characteristics of persons aged 65 years and older hospitalized with a TBI. *J H Tra Rehabil*2005;20:215–28.
4. Cicerone KD, Dahlberg C, Malec JF. Evidence-based cognitive rehabilitation: updated review of the literature from 1998 through 2002. *Arch Phys Med Rehabil*2005;86: 1681–92.
5. The Brain Trauma Foundation. The American Association of Neurological Surgeons. The Joint Section on Neurotrauma and Critical Care. Indications for intracranial pressure monitoring. *NeurotraumaJ* 2000;17: 479–91.
6. Povlishock JT, Katz DI. Update of neuropathology and neurological recovery after traumatic brain injury. *J H Tra Rehabil* 2005;20:76–94.
7. Rees PM. Contemporary issues in mild traumatic brain injury. *Arch Phys Med Rehabil*2003; 84(12):1885–94.
8. Maas AI, Stocchetti N, Bullock R. Moderate and severe traumatic brain injury in adults. *Lancet Neuro* 2008; 7(8): 728–41.
9. Parikh S, Koch M, Narayan RK. Traumatic brain injury. *Inter AnesthesiolClin*2007; 45(3): 119–35.
10. Saatman KE, Duhaime AC Workshop Scientific Team Advisory Panel Members. Classification of traumatic brain injury for targeted therapies. *NeurotraumaJ* 2008; 25 (7): 719–38.
11. Hannay HJ, Howieson DB, Loring DW, Fischer JS, Lezak MD. Neuropathology for neuropsychologists. In: Lezak MD, Howieson DB, Loring DW ed. *Neuropsychological Assessment*. Oxford University Press 2004; 158–62.
12. Smith DH, Meaney DF, Shull WH. Diffuse axonal injury in head trauma. *J H Tra Rehabil*2003; 18 (4): 307–16.
13. Kraus MF, Susmaras T, Caughlin BP, Walker CJ, Sweeney JA, Little DM. White matter integrity and cognition in chronic traumatic brain injury: A diffusion tensor imaging study 2007; 130 (10): 2508–19.
14. Melvin JW, Lighthall JW, Nahum AM, Melvin JW. [Accidental Injury: Biomechanics and Prevention](#). Berlin: Springer 2008; 280–1.

15. Mattson AJ, Levin HS. Frontal lobe dysfunction following closed head injury. A review of the literature. *J Nerv&MentDis*1990; 178(5): 282–91.
16. Hardman JM, Manoukian A. Pathology of head trauma. *NeuroimagClin N Am* 2002; (2): 175–87.
17. Collins C, Dean J. [Acquired brain injury](#). In Turner A, Foster M, Johnson SE ed. *Occupational Therapy and Physical Dysfunction: Principles, Skills and Practice*. Edinburgh: Churchill Livingstone 2008; 395–6.
18. Valadka AB. [Injury to the cranium](#). In Moore EJ, Feliciano DV, Mattox KL ed. *Trauma*. New York: McGraw-Hill, Medical Pub. Division 2008; 385–406.
19. Shaw NA. The neurophysiology of concussion. *Progress in Neurobiology* 2002; 67 (4): 281–344.
20. Morrison AL, King TM, Korell MA, Smialek JE, Troncoso JC. [Acceleration-deceleration injuries to the brain in blunt force trauma](#). *Am Fore Med PathoJ* 1998; 19 (2): 109–12.
21. Poirier MP. [Concussions: Assessment, management, and recommendations for return to activity](#) 2003; 4 (3): 179–85.
22. [Arlene L. Polaski, Suzanne E. Tatro. Core Principles and Practice of Medical-Surgical Nursing: Harcourt Publishers Ltd, a subsidiary of Harcourt International Ltd 1996;235.](#)
23. Scalea TM. Does it matter how head injured patients are resuscitated?In Valadka AB, Andrews BT ed. *Neurotrauma: Evidence-Based Answers to Common Questions*. Thieme2005; 3–4.
24. Silver JM, McAllister TW, Yudofsky SC. *Textbook of Traumatic Brain Injury*. Washington, DC: American Psychiatric Association 2005; 27–33.
25. Porth, Carol. [Essentials of Pahtophysiology: Concepts of Altered Health States](#). Hagerstown, MD: Lippincott Williams & Wilkins 2008; 838.
26. Pitkänen A, McIntosh TK. Animal models of post-traumatic epilepsy. *Neurotrauma J* 2006; 23 (2): 241–61.
27. LaPlaca MC, Simon CM, Prado GR, Cullen DR. [CNS injury biomechanics and experimental models](#). In: Weber JT ed. *Neurotrauma: New Insights Into Pathology and Treatment*. Elsevier 2008; 13–9.
28. Zink BJ, Walsh RF and Feustel PJ. Effects of alcohol in traumatic brain injury. *J Neurotrauma*1993; (10): 275.
29. Hovda DA, Lee SM, Smith ML. The neurochemical and metabolic cascade following brain injury: moving from animal models to man, *Neurotrauma J*1995; (12): 903.

30. Patt S and Brodhun M. Neuropathological sequelae of traumatic injury in the brain: an overview. *Exp Toxicol Pathol* 1999; (51): 119.
31. Bullock R, Zauner A, Woodward JJ. Factors affecting excitatory amino acid release following severe human head injury. *J Neurosurg* 1998; 507.
32. C. Werner K. Engelhard. Pathophysiology of traumatic brain injury. *Br J Anaesth* 2007; (99):4-9.
33. Sullivan PG, Rabchevsky AG, Hicks RR, Gibson TR, Fletcher-Turner A, Scheff SW. [Dose response curve and optimal dosing regimen of cyclosporin A after traumatic brain injury in rats](#). *Neuroscience* 2000; 101 (2): 289–95.
34. Sauaia A, Moore FA, Moore EE. [Epidemiology of trauma deaths: A reassessment](#). *J Trauma* 1995; 38 (2): 185–93.
35. Narayan RK, Michel ME, Ansell B. [Clinical trials in head injury](#). *Neurotrauma J* 2002; 19 (5): 503–57.
36. Andrews BT. [Head injury management](#). In Andrews BT ed. *Intensive Care in Neurosurgery*. New York: Thieme Medical Publishers 2008; [125-44](#).
37. Schultz W. Multiple dopamine functions at different time courses. *Annu Rev Neurosci* 2007; (30): 259–88.
38. A. Dahlström and K Fuxe . Evidence for the existence of monoamine-containing neurons in the central nervous system. Demonstration of monoamines in the cell bodies of brain stem neurons. *Actaphysiologica Scandinavica Supplementum* 1964; (232): 1–55.
39. Christine CW, Aminoff MJ. Clinical differentiation of parkinsonian syndromes: prognostic and therapeutic relevance. *Am J Med* 2004; 117 (6): 412–9.
40. Robbins TW, Arnsten AF. The neuropsychopharmacology of fronto-executive function: monoaminergic modulation. *Annu Rev Neurosci* 2009; 32: 267–87.
41. Paulus W, Schomburg ED. Dopamine and the spinal cord in restless legs syndrome: does spinal cord physiology reveal a basis for augmentation? . *Sleep Med Rev* 2006; 10 (3): 185–96.
42. Ben-Jonathan N, Hnasko R. [Dopamine as a Prolactin \(PRL\) Inhibitor](#). *Endocrine Reviews* 2001; 22(6): 724–63.
43. James W, Bales Amy K, Wagner Anthony E, Kline C, Edward Dixon. Persistent cognitive dysfunction after traumatic brain injury: A dopamine hypothesis. *Neuroscience and Biobehavioral Reviews* 2009; 33: 981–1003
44. Chudasama Y, Robbins TW. Functions of frontostriatal systems in cognition: comparative neuropsychopharmacological studies in rats, monkeys and humans. *Biol Psychol* 2006; 73: 19–38.

45. Donnemiller, E, Brenneis C, Wissel J, Scherfler C, Poewe W, Riccabona G, Wenning GK. Impaired dopaminergic neurotransmission in patients with traumatic brain injury: a SPECT study using 123I-beta-CIT and 123I-IBZM. *Eur J Nucl Med* 2000; 27: 1410–4.
46. McIntosh TK, Yu T, Gennarelli TA. Alterations in regional brain catecholamine concentrations after experimental brain injury in the rat. *Neurochem J* 1994; 63:1426–33.
47. Massucci JL, Kline AE, Ma X, Zafonte RD, Dixon CE. Time dependent alterations in dopamine tissue levels and metabolism after experimental traumatic brain injury in rats. *NeurosciLett* 2004; 372: 127–31.
48. Wagner AK, Ren D, Conley YP, Ma X, Kerr ME, Zafonte RD, Puccio AM, Marion DW, Dixon CE. Sex and genetic associations with cerebrospinal fluid dopamine and metabolite production after severe traumatic brain injury. *Neurosurg J* 2007; 106: 538–47.
49. Williams GV, Castner SA. Under the curve: critical issues for elucidating D1 receptor function in working memory. *Neuroscience* 2006; 139(1): 263-76.
50. Goldberg TE, Bigelow LB, Weinberger DR, Daniel DG, Kleinman JE. Cognitive and behavioral effects of the coadministration of dextroamphetamine and haloperidol in schizophrenia. *Am J Psychiatry* 1991; 148(1): 78-84.
51. Arnsten AF, Goldman PS. Noise stress impairs prefrontal cortical cognitive function in monkeys: evidence for a hyperdopaminergic mechanism. *Arch Gen Psychiatry* 1998; 55(4): 362-8.
52. Clausen F, Hanell A, Bjork M, Hillered L, Mir AK, Gram H, Marklund N. Neutralization of interleukin-1beta modifies the inflammatory response and improves histological and cognitive outcome following traumatic brain injury in mice. *Eur J Neurosci* 2009, 30(3): 385-96.
53. Ekdahl CT, Kokaia Z, Lindvall O. Brain inflammation and adult neurogenesis: the dual role of microglia. *Neuroscience* 2009; 158(3): 1021-9.
54. Farber K, Kettenmann H. Physiology of microglial cells. *Brain Res Rev* 2005; 48: 133-43.
55. Kim YS, Joh TH. Microglia major player in the brain inflammation: their roles in the pathogenesis of Parkinson's disease. *Exp Mol Med* 2006; 38(4): 333-47.
56. Mastroeni D, Grover A, Leonard B, Joyce JN, Coleman PD, Kozik B, Bellinger DL, Rogers J. Microglia responses to dopamine in a cell culture model of Parkinson's disease. *Neurobiol Aging* 2009; 30(11):1805-17.
57. Brustolim D, Ribeiro dos Santos R, Kast RE, Altshuler EL, Soares MB. A new chapter opens in anti-inflammatory treatments: the antidepressant bupropion lowers production of tumor necrosis factor-alpha and interferon-gamma in mice. *Int. Immunopharmacol* 2006; 6(6), 903-07.

58. James W Bales, Anthony E, Kline Amy K. Wagner and C. Edward Dixon. Targeting Dopamine in Acute Traumatic Brain Injury *The Open Drug Discovery J* 2010; 2: 119-28.
59. Arlinghaus KA, ShoaibAM. Neuropsychiatric assessment. In Silver JM, McAllister TW, Yudofsky SC. *Textbook of Traumatic Brain Injury*. Washington, DC: American Psychiatric Association. 2005; 63–5.
60. "[NINDS Traumatic Brain Injury Information Page](#)". National Institute of Neurological Disorders and Stroke. September 15, 2008. Retrieved 2008-10-27
61. McDonald S, Flanagan S, Rollins J, Kinch J. TASIT. A new clinical tool for assessing social perception after traumatic brain injury. *J H TraRehabil* 2003; 18 (3): 219–38.
62. Ponsford J, K. Draper and M Schonberger. Functional outcome 10 years after traumatic brain injury: its relationship with demographic, injury severity, and cognitive and emotional status. *Neuropsychological Society J* 2008; 14 (2): 233–42.
63. Zink BJ. Traumatic brain injury outcome: Concepts for emergency care. *Annals of Emergency Medicine* 2001;37 (3): 318–32.
64. Valadka AB. [Injury to the cranium](#). In Moore EJ, Feliciano DV, Mattox KL ed. *Trauma*. New York: McGraw-Hill, Medical Pub. Division 2004; 385–406.
65. Office of Communications and Public Liaison. [Traumatic brain injury: Hope through research](#). NIH Publication No. 02-2478. National Institute of Neurological Disorders and Stroke, National Institutes of Health 2008.
66. Moppett IK. [Traumatic brain injury: Assessment, resuscitation and early management](#). *British AnaesthesiolJ* 2007; 99 (1): 18–31.
67. Ghajar J .Traumatic brain injury.*Lancet* 2000; 356 (9233): 923–9.
68. Alderson, Roberts I. Corticosteroids for acute traumatic brain injury. *Neurosurgery* 2005; 32 (4):523-45.
69. Tasker RC. Head and spinal cord trauma. In Nichols DG ed. *Roger's Textbook of Pediatric Intensive Care* 4th ed. PA: Lippincott Williams & Wilkins 2008; 887–911.
70. Marshall LF. Head injury: Recent past, present, and future. *Neurosurgery* 2000; 47 (3): 546–61.
71. Salomone JP, Frame SB. [Prehospital care](#). In Moore EJ, Feliciano DV, Mattox KL. *Trauma*. New York: McGraw-Hill, Medical Pub. Division 2008;117–8.
72. O'Leary R, McKinlay J. Neurogenic pulmonary oedema. [Continuing Education in Anaesthesia, Critical Care & Pain](#) 2011; 11 (3): 87–92.

73. Dunn IF, Ellegala DB. Decompressive hemicraniectomy in the management of severe traumatic brain injury. In Bhardwaj A, Ellegala DB, Kirsch JR ed. *Acute Brain and Spinal Cord Injury: Evolving Paradigms and Management*. Informa Health Care. 2008; 1–2.
74. Turner-Stokes L, Disler PB, Nair A, Wade DT. *Multi-disciplinary rehabilitation for acquired brain injury in adults of working age* 2005.
75. Arciniegas DB, The cholinergic hypothesis of cognitive impairment caused by traumatic brain injury. *Curr Psychiatry Rep* 2003; 5: 391-9.
76. Aaron Talsky, Laura R. Pacione, Tammy Shaw, Lori Wasserman, Adam Mark Lenny, Amol Verma, Gillian Hurwitz, Robyn Waxman, Andrew Morgan, Shree Bhalerao. *Pharmacological interventions for traumatic brain injury*. *BC Medical J*. 2011; 53: 1.
77. David A. Hounshell and John Kenly Smith. *Science and Corporate Strategy: Du Pont R&D, 1902-1980*. Cambridge University Press 1988: 469.
78. Moiseev I K, Doroshenko R I, Ivanova V I. Synthesis of amantadine via the nitrate of 1-adamantanol. *PharmaChemi J* 1976; 10(4): 450.
79. Wilson WW, Rajput AH. Amantadine-Dyazide Interaction. *Can Med Assoc J* 1983; 129:974-5.
80. Macchio GJ, Ito V, Sahgal V. Amantadine-induced coma. *Arch Phys Med Rehabil* 1993; 74: 1119–20.
81. Gualtieri T, Chandler M, Coons TB, Brown LT. Amantadine: A clinical profile for traumatic brain injury. *Clin Neuropharmacol* 1989; 12: 258–70.
82. Aoki FY, Sitar DS. Clinical pharmacokinetics of amantadine hydrochloride. *Clin Pharmacokinet* 1988; 14:35–51.
83. Jing X, Ma C, Ohigashi Y, et al. Functional studies indicate amantadine binds to the pore of the influenza A virus M2 proton-selective ion channel. *Proc Natl Acad Sci USA* 2008; 105 (31): 10967–72.
84. Blanpied TA, Clarke RJ, Johnson JW. Amantadine inhibits NMDA receptors by accelerating channel closure during channel block. *Neuroscience J* 2005; 25 (13): 3312–22.
85. Gilman AG, Goodman L, Gilman A. *The Pharmacological Basis of Therapeutics* 8th ed. New York: Macmillan; 1989: 472–3.
86. Zafonte RD, Lexell J, Cullen N. Possible applications for dopaminergic agents following traumatic brain injury: Part 2. *J Head Tr Rehabil* 2001; 16:112–6.
87. Toide K. Effects of amantadine on dopaminergic neurons in discrete regions of the rat brain. *Pharm Res* 1990; 7:670–2.

88. Gianutsos G, Stewart C, Dunn JP. Pharmacological changes in dopaminergic systems induced by long-term administration of amantadine. *Eur J Pharmacol* 1985; 110:357–61.
89. Schwab RS, Poskanzer DC, Englander AC, Young RR. Amantadine in Parkinson's disease. Review of more than two years experience. *JAMA* 1972; 222:792–5.
90. Crosby, Niall J, Deane, Katherine; Clarke, Carl E. Amantadine in Parkinson's disease. In Clarke, Carl E. *Cochrane Database of Systematic Reviews* 2003;15:3.
91. Deyde, Varough M Xu, Xiyan, Bright, Rick A, Michael Smith, Catherine B, Zhang Ye Shu, YuelongGubareva, Larisa V Cox, Nancy J Klimov, Alexander I. Surveillance of Resistance to Adamantanes among Influenza A(H3N2) and A(H1N1) Viruses Isolated Worldwide. *Infectious Diseases J* 2007; 196 (2): 249–57.
92. Cohen RA, Fisher M .Amantadine treatment of fatigue associated with multiple sclerosis. *Archives of neurology* 1989; 46 (6): 676–80.
93. Shrivastava RK, Shrivastava S, Overweg N, Schmitt M. Amantadine in the treatment of sexual dysfunction associated with selective serotonin reuptake inhibitors. *Clinical psychopharmacolJ* 1995; 15(1): 83–4.
94. Singhal KC, Rahman SZ. Stevens Johnson Syndrome induced by Amantadine. *Rational Drug Bulletin* 2002; 12(1): 6.
95. Cook PE, Dermer SW, Mc Gurk, T. Fatal overdose with amantadine . *Canadian Psych J* 1986; 31 (8): 757–8.
96. David W. Corthell, Ed D. *Traumatic Brain Injury and Vocational Rehabilitation, the Research and Training Center University ofWisconsin Stout* 1990; 1(2):21-67
97. Ylviaker M & Gobble E MR .*Community re-entry for head injured adults*. Boston: Little, brown and Company 1987; 3(2):54-8.
98. Strub R L & Black F W. *Neurobehavioral disorders; A clinically approach*. Philadelphia F A Davis 1988;22(7):123-34.
99. Walsh. K. *Neuroshology; A clinical approach (2nd Ed.)*. Edin burgh: Churchill Livangatone; 1987;13(9):223-34.
100. Prigatano et al. *Neuropsychological rehabilitation after brain injury* Baltimore: Johns Hopkins University Press 1986;6(14):55-9.
101. Wood R L. *Brain injury rehabilitation: A neurobehaviouralapproach*. Rockville MD Aspen Publishers 1987; 15:110-9.
102. Meier M, Benton A, & Diller L. *Neuropsychological rehabilitation*. New York: Guilford Press 1987; 5(2):36-49.
103. Miller. E. *Recovery and management of Neuropsychological impairments*. Chichester: John Wiley and Sons 1984; 19:149-60.

104. Brooks N (Ed). Closed head injury: Psychological, Social and family consequences. Oxford: Oxford University Press 1984; 8(3)210-22.
105. Kay T, Ezrachi O, Cavallo M. Annotated bibliography of research on vocational outcome following head trauma 2nd ed. New York: New York University Medical Center, Research and Training Center on Head Trauma and Stroke 1988; 4(2):65-70.
106. Ylviaker M. (Ed). Head injury rehabilitation Children and adolescents San Diego: College-Hill Press 1985; 6(12):92-165.
107. Levin H S, Grafman j, Eisenberg H M. Neurobehavioral recovery from head iniury. New York: Oxford University Press 1987; 20: 220-36.
108. Ben-Yishay. Working approaches to remediation of cognitive deficits in brain injured persons. New York: N.Y.U. Medical Center, Rehabilitation Monographs 1978-1983;46: 1124-68.
109. Trexler LE. Cognitive rehabilitation: Conceptualization and intervention. New York: Plenum Pre 1982;17: 22-65.
110. Kreutze J, Kolokowsky-Hayner S, Kemm S, Meade M. A structured approach to family intervention after brain injury. J H Tra Rehab 2002; 17 (4): 349–67.
111. Campbell K, Millu C. From the a.sh: A head iniury self advocacy guide options. KiritandWA 1989;6:102-29.
112. Kay T, Silver S. The contribution of the neuropsychological evaluation to the vocational rehabilitation of the head injured adult. J H TrRehab 1988; 3:65-76.
113. Bullock J, Chestnut RM, Clifton G, et al. Guidelines for the Management of Severe Traumatic Brain Injury. J Neurotrauma 2000; 17:451-627.
114. Goldstein LB. Pharmacologic modulation of recovery after stroke: Clinical data. J Neuro Rehabil 1991; 5:129-40.
115. Wright, J. The Disability Rating Scale. The Center for Outcome Measurement in Brain Injury 2000.
116. Crum RM, Anthony JC, Bassett SS, Jolstein MF. Population-bases norms for the mini-mental state examination by age and educational level. JAMA 1993; 269:2386-91.
117. Chandler MC, Barnhill FB, Gaultieri CT. Amantadine for the agitated head-injury patient. Brain Injury 1988; 2:309-11.
118. Safar P. Cerebral resuscitation after cardiac arrest: research initiatives and future directions. Ann Emerg Med 1993; 22: 324–49.
119. Brown JIM. Clinical significance of CSF glutamate concentrations following severe traumatic brain injury in humans. J Neurotrauma 1998; 15: 253–63.

120. Whyte J, Hart T, LaBorde A, Rosenthal M. Rehabilitation of the patient with traumatic brain injury. In: DeLisa JA, ed. *Rehabilitation Medicine: Principles and Practice*, 3rd ed. Philadelphia: Lippincott; 1998; 1191–239.
121. Meythaler JM, Peduzzi-Nelson J, Eleftheriou E, Novack T. Current concepts: diffuse axonal injury associated traumatic brain injury. *Arch Phys Med Rehabil*. 2001; 82:1461–71.
122. Povlishock JT. Pathobiology of traumatically induced axonal injury in animals and man. *Ann Emerg Med*. 1993; 22:980–6.
123. Zafonte RD, Watanabe T, Mann NR. Amantadine: a potential treatment for the minimally conscious state. *Brain Inj* 1998; (12): 617–21.
124. Wu TS, Garmel GM. Improved neurological function after amantadine treatment in two patients with brain injury. *J Emerg Med* 2005; (28):289-92.
125. Nickels JL, Schneider WN, Dombovy ML, Wong TM. Clinical use of amantadine in brain injury rehabilitation. *Brain Injury* 1994; (8):709-18.
126. Hughes S, Colantonio A, Santaguida PL, Paton T. Amantadine to enhance readiness for rehabilitation following severe traumatic brain injury. *Brain Injury* 2005; (19): 1197-206.
127. Saniova B, Drobny M, Kneslova L, Minarik M. The outcome of patients with severe head injuries treated with amantadine sulphate. *J Neural Transm* 2004; (111):511- 4.
128. Schneider WN, Drew-Cates J, Wong TM, Dombovy ML. Cognitive and behavioral efficacy of amantadine in acute traumatic brain injury: an initial double-blind placebo-controlled study. *Brain Injury* 1999; (13):863-72.
129. Meythaler JM, Brunner RC, Johnson A, Novack TA. Amantadine to improve neurorecovery in traumatic brain injury–associated diffuse axonal injury: a pilot double-blind randomized trial. *J Head Trauma Rehabil* 2002; (17):300-13.
130. Elizabeth Sawyer, Laurie S Mauro, Martin J Ohlinger. Amantadine Enhancement of Arousal and Cognition after Traumatic Brain Injury: *Ann Pharmacother* 2008; 42: 247-52.
131. Whyte J. Treatments to enhance recovery from the vegetative and minimally conscious states: ethical issues surrounding efficacy studies. *Am J Phys Med Rehab* 2007; (86):86-92.
132. Gualtieri Th, Chandler M, Coons TB, Brown LT: Amantadine: A New Clinical Profile for Traumatic Brain Injury. *ClinNeuropharm* 1989; 12: 170-258.
133. Gianutsos G, Chute S, Dunn JP. Pharmacological changes in dopaminergic systems induced by long-term administration of amantadine. *Euro J Pharmacol* 1985; 110: 357-61.
134. Allen RM. Role of amantadine in the management of neuroleptic induced extrapyramidal syndromes: overview and pharmacology. *ClinNeuropharmacol* 1983; 6: 64-73.