Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 9, Issue, 05, pp.49994-49998, May, 2017

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

ISSN: 0975-833X

RESEARCH ARTICLE

EARLY AND LATE POSTTRAUMATIC SEIZURES: AGE, COMPUTERIZED TOMOGRAPHY FEATURES, AND FUNCTIONAL OUTCOME

***Mathias O N Nnadi**

Division of Neurosurgery, Department of Surgery, University of Calabar Teaching Hospital, Calabar, Nigeria

ARTICLE INFO

Article History:
Received 22nd February, 2017
Received in revised form
20th March, 2017
Accepted 24th April, 2017
Published online 19th May, 2017

Key words:

Age, early,
CT features,
Late, outcome,
Posttraumatic seizure.

ABSTRACT

Traumatic brain injury devastates our young adults, leaving on its trail mortalities and morbidities. One of the morbidities, seizure, leaves the patients battling in three fronts: the seizure itself, the antiepileptic drugs, and the societies the patients belong. Patients managed for early and late posttraumatic seizures in our center were compared in age, computerized tomography (CT) features and functional outcome. The study was done over a six year period.

Objective: To compare patients with early and late posttraumatic seizures in age, computerized tomography scan features and functional outcome at three months post injury.

Methods: It was a prospective, comparative and observational study of patients managed in our center for early and late posttraumatic seizures from traumatic brain injuries from August 2010 to July 2016. Patients were resuscitated in accident and emergency using Advanced Trauma Life Support protocols. Brain computerized tomography (CT) scan and other relevant investigations were done. Patients who had seizures were given Phenytoin for one week. After a week we used Carbamazepine. The functional outcome was assessed at three months post-injury.

Data were collected using structured proforma and analyzed with Environmental Performance Index info 7 software.

Results: There were 63 patients, 46 early and 17 late posttraumatic seizures. There were 47 males. The mean age was 27.5 years. There were significant difference between early and late posttraumatic seizures in terms of age ($P = 0.0289$) and CT findings ($P = 0.0221$).

Conclusion: There was significant difference between early and late posttraumatic seizures in age and CT features.

Citation: Mathias O N Nnadi. 2017. "Early and late posttraumatic seizures: age, computerized tomography features, and functional outcome", *International Journal of Current Research*, 9, (05), 49994-49998.

INTRODUCTION

Seizure is the physical manifestation of abnormal electrical discharge in the brain (Acharya *et al*., 2013; Labate *et al*., 2013). It makes the patient battle in three fronts. First, seizure reduces the oxygen supply to the brain, increases intracranial pressure and brain's metabolic demands, thus increasing secondary injury to the injured brain. It also prevents the patient from enjoying some social activities such as cooking, driving and swimming. Second, the antiepileptic drugs and the poor seizure patient in our environment is akin to the story of the buffalo and the stream. The buffalo told the stream that when he came during the rainy season to quench his thirst, the mud in its bank would be holding his legs. When he came during the dry season, the water had dried up, leaving him at the mercy of thirst.

****Corresponding author: Mathias O N Nnadi***
Division of Neurosurgery, Department of Surgery, University of Calabar Teaching Hospital, Calabar, Nigeria

When the money is there to buy the drugs the side effects of the drugs give the patient a lot of problems. When the money is not there, he will be at the mercy of the seizure. Third, the society poses another challenge for the patient. A young lady's marriage crashed when she had seizure in the presence of her young husband. A young man called off the relationship with his girl when she had seizure in the market. The male patient with seizure finds it difficult to get married as ladies avoid him. When seizure occurs due to traumatic brain injury, it is called posttraumatic seizure (Frey, 2003). The risk of developing seizure after traumatic brain injury ranged from 2% to 5% in the general population (Annegers *et al*., 1980; Jennet, 1974). When seizure occurs within seven days of traumatic brain injury, it is called early seizure, and when it occurs after seven days, it is called late posttraumatic seizure (Haddad and Arabi, 2012; Bratton *et al*., 2007). Posttraumatic seizure early in the injury worsens primary brain injury by causing hypoxia, increased intracranial pressure, cardiac arrhythmias and increased metabolic demand of the brain (Bullock *et al*., 2007;

Treiman *et al*., 1998; Vespa *et al*., 2007). Early seizure is being attributed to inflammatory changes with cellular, chemical and metabolic events that occur early in the injury (Majores *et al*., 2004; Ravizza *et al*., 2008) while late posttraumatic seizure is being attributed to a fall out of imbalance in excitatory and inhibitory changes that occur during neuroplasticity and brain reorganization occurring during the reparative process (Dudek and Spitz, 1997; McCormick and Contreras, 2001; Nadler, 2003).This study compared age, CT features and functional outcome of early and late posttraumatic seizure patients from traumatic brain injuries managed in our center from 1st August 2010 to 31st July 2016.

MATERIALS AND METHODS

Setting/approval

The study was carried out in young neurosurgical center in the hinterland of a developing country. It was a component of prospective data bank that was approved by our research and ethics committee.

Inclusion criteria

All traumatic brain injury patients who had posttraumatic seizures and were admitted, treated, and followed up to three months post-injury.

Exclusion criteria

All traumatic brain injury patients who did not develop seizure and those who developed seizure after three months post-injury. Patients with history of seizure before the traumatic brain injury. Patients who discharged against medical advice. Those who ran away while being treated and those who did not attend clinic at three months post-injury and could not be reached through phone.

Protocols

Patients were managed in accident and emergency unit using Advanced Trauma Life Support protocols. We ensured patent airway and breathing aiming at oxygen saturation of ≥95%. This was achieved in some cases by augmenting with oxygen via face mask, nasal prongs or endotracheal intubation with ventilation. Normotension with euvolemia was achieved by use of Normal Saline and/or 5%Dextrose in Saline given at one liter every 8 hours for adult and 4.3%Dextrose/1/5Saline for children based on their weights. Vitamin C and Vitamin B/complex were added 1ml each in every 500ml of the fluid. Phenytoin infusion 14mg/kg for adults and 21mg/kg for children was given in 100ml Normal saline over one hour as loading dose, and 300mg for adult and 5mg/kg (not more than 300mg) for children in 100ml Normal saline over one hour daily as maintenance doses. Those who were conscious were given the oral doses. The drug was given for one week for early posttraumatic seizures. Late posttraumatic seizure patients and early cases who continued to have seizures after one week were given Carbamazepine 200mg twice daily for adults and 5mg/kg twice daily for children. They continued the drug on discharge. Patients who did not have seizure were not given antiepileptic drugs. Cranial CT scan, full blood count, serum electrolyte/urea/creatinine and random blood sugar were done. Those whose Glasgow Coma Scale scores were ≤8 were admitted in intensive care unit (when functional). Others were admitted in the wards. Those requiring surgery were operated and admitted into the appropriate wards. Those requiring other specialist care were co-managed with the appropriate specialist unit. We fed unconscious patients with high energy/high protein diet from third day post-injury. The diet is constituted with pap 500ml, soya bean powder two tablespoonful, powdered milk two tablespoonful, crayfish powder one tablespoonful, and red oil one tablespoonful. Patients were given five to six times daily via nasogastric tube. The daily fluid requirement for each patient was calculated and factored into the diet. Oral drugs were given via the tube. We gave them Encephabol, Vitamin C, Vitamin B/complex, and Multivitamin one tablet each three times daily. On discharge we followed them up in the surgical out-patient clinic. The functional outcome was assessed three months post injury using Glasgow Outcome Score (GOS).

Data were collected using structured proforma which was component of our prospective data bank that was approved by our research and ethics committee. The biodata, etiology, time and number of seizures, Glasgow Coma Scale (GCS) scores after resuscitation and other physical findings, as well as investigation results were documented in accident and emergency. The GCS score prior to surgery, type of surgery and findings were documented in theater. The progress of the patients and length of hospital stay were documented in the wards. The GOS was documented in the clinic at three months post-injury or via phone contact for those who did not attend clinic at three months. Data were analyzed with Environmental Performance Index (EPI) info 7 software (Center for Disease Control and Prevention, Atlanta, Georgia, USA). We used ad-analysis component of the Visual Dashboard to analyze the data. The mean component was used for continuous variables such as age and hospital stay. Frequency and chart components were used frequencies of some variables such as etiology. The MXN/2X2 component was used for univariate analysis, while its advanced component was used for multivariate analysis. At 95% confidence interval, $P < 0.05$ was considered significant.

RESULTS

There were 63 patients in the study. Forty six (73.02%) were early posttraumatic seizures, while seventeen (26.98%) were late posttraumatic seizures (PTS). Males were 47 (74.6%) while females were 16 (25.4%). The mean age was 27.53 years with a range of seven months to 72 years. The mean age of those with early seizures was 22.35 years with range of seven months to 70 years. The mean age for late seizures was 41.53 years with a range of three years to 72 years. The age group most affected was 0-10 years, and 84.13% of all the patients were less than 50 years, Table 1. There was significant relationship between seizure type and age, with early seizure seen mainly in children and young adults, $P = 0.0289$, table 2. The most common etiology was road traffic accident, fig 1. There was no significant relationship between etiology and seizure type, $P = 0.132$.Thirty four patients had mild, eleven had moderate, while eighteen had severe traumatic brain injuries. There was no significant relationship between the type of seizure and severity of injuries, $P = 0.7502$.Fifty two patients did cranial Computerized Tomography (CT) scan. The most common CT finding was multiple lesions, table 3. Most of the CT lesions were more in early seizures, while subdural hematoma was more in late seizures. There was significant relationship between CT findings and seizure type $P = 0.0221$,

Table 4. The overall favorable outcome (GOS ≥4) was 92.07%, Table 5.

Table 1. Age group frequency

Age group	Number	Percent (%)
0 - <10	15	23.82
10 - <20	9	14.29
20 - <30	14	22.22
30 - <40	11	17.46
40 - <50	4	6.35
50 - <60	2	3.17
60 - <70	6	9.52
70 - <80	2	3.17
Total	63	100

Table 2. Age group vs Seizure type

Age group	Seizure period		
	Early (%)	Late (%)	Total (%)
0 - <10	14 (93.33)	1 (6.67)	15 (100)
10 - <20	9 (100)	0 (0)	9 (100)
20 - <30	10 (71.43)	4 (28.57)	14 (100)
30 - <40	7 (63.64)	4 (36.36)	11 (100)
40 - <50	2 (50)	2 (50)	4 (100)
50 - <60	0 (0)	2 (100)	2 (100)
60 - <70	3 (50)	3 (50)	6 (100)
70 - <80	1 (50)	1 (50)	2 (100)
Total	46 (73.02)	17 (26.98)	63 (100)

P= 0.0289

Table 3. CT findings

CT findings	Number	Percent (%)
Contusions/ICH	8	15.38
DAI	7	13.46
Edema	4	7.69
EDH	2	3.58
Multiple	14	26.92
None	2	3.85
Others	1	1.92
SDH	7	13.46
Skull fractures	7	13.46
Total	52	100

Abbreviations: ICH (intracerebral hematoma), DAI (diffuse axonal injuries), EDH (extradural hematoma), SDH (subdural hematoma).

Table 4. CT findings vs Seizure type

CT Findings	Seizure Period		
	Early (%)	Late (%)	Total (%)
Contusion/ICH	5 (62.5)	3 (37.5)	8 (100)
DAI	5 (71.43)	2 (28.57)	7 (100)
Edema	3 (75)	1 (25)	4 (100)
EDH	0 (0)	2 (100)	2 (100)
Multiple	13 (92.86)	1 (7.14)	14 (100)
None	2 (100)	0 (0)	2 (100)
Others	0 (0)	1 (100)	1 (100)
SDH	2 (28.57)	5 (71.43)	7 (100)
Skull fractures	6 (85.71)	1 (14.29)	7 (100)
Total	36 (69.23)	16 (30.77)	52 (100)

P = 0.0221

Table 5. Glasgow Outcome Score (GOS) Frequency

GOS	Number	Percent (%)
1	1	1.59
3	4	6.35
4	5	7.49
5	53	84.13
Total	63	100

Among those with early seizure 93.48% (43) had favorable outcome, 4.35% (2) had severe disability, while mortality was 2.17% (1). Among the patients with late seizures, the favorable outcome was 88.23% (15) while11.76% (2) had severe disability. There was no significant difference between them in functional outcome, *P =0.6645*. The mean hospital stay was 22.51 days with range of one day to 132 days. For early seizures, the mean hospital stay was 20.26 days with range of one day to 97 days. For late seizures the mean hospital stay was 28.59 days with a range of 12 days to 132 days. There was no significant difference between them in terms of hospital stay, *P =0.3491*.

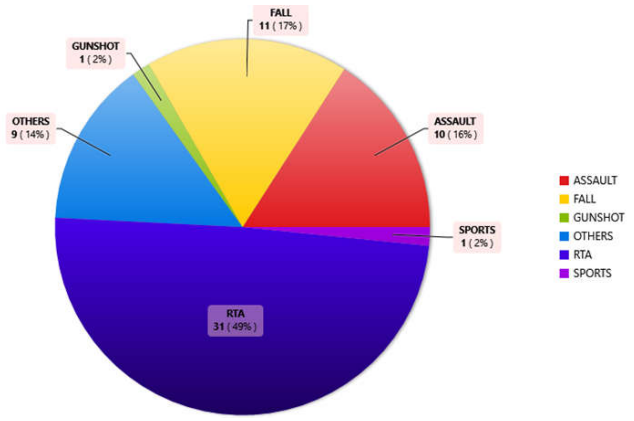

Fig. 1. Etiology frequency

DISCUSSION

There were more males than females with majority of the patients being less than fifty years. The most common etiology was road traffic accident. In our environment and many developing countries, traumatic brain injury is a disease of young males. They are very active group of the society trying to make a living from the environment to ensure sustainability of their families. They engage in activities such as commercial vehicle driving, motorcycle driving, carpentry, wine tapping, and many other occupations that predispose them to traumatic brain injuries (TBI). Due to high unemployment rate in our country and other developing countries, the number of young men engaged in commercial motorcycle and vehicle driving has been increasing, causing a rise in TBI among them. Emejulu *et al*. (2010) in their study of traumatic brain injury in the accident and emergency department of a tertiary hospital in Nigeria found that males were 79.2% and those ≤40 years were 75.1%; road traffic accident formed 80.8% with motorcycle accidents forming 58.8% while vehicular accidents formed 22%. Jasper *et al*. (2014) studied the epidemiology of hospital-referred head injury in northern Nigeria and found that males formed 79.9%; those ≤50 years formed 89.95%, and road traffic accident formed 71.7%. In their study of early and late posttraumatic seizure following traumatic brain injuries in Iran, Najafi *et al*. (2015) found that75.91% were males, the mean age was 33.6 years, and 63.7% were from motor vehicular accident.

Forty six patients had early, while seventeen had late posttraumatic seizures (PTS). There was significant difference between early and late posttraumatic seizures in terms of age with early seizures seen among children and young adult. In children and young adults, the brain cortex is closely applied to the meninges and the cranium. In the older adults the brain weighs less with increase in extra-cerebral volume due to brain atrophy with age (Misra *et al*., 1996). When there is traumatic brain injury with its attendant inflammation, the pressure

builds up which will compress the cortex against the cranium in the young, while volume of extra-cerebral space helps the older adults to compensate. The inflammatory process leads to cascade of events and production of many chemicals such as reactive oxygen species that results in oxidative stress. Reactive oxygen species can cause oxidative damage to several components of mitochondria, including the electron transport chain (Dencher *et al*., 2007; Lesnefsky and Hoppel, 2006; Van Remmen and Richardson, 2001) lipid membranes (Hoch, 1992) and DNA (Richter, 1995). Other authors also noted that mitochondria display a significant amount of dysfunction early after traumatic brain injury (Gilmer *et al*., 2009; Lifshitz *et al*., 2004; Sullivan *et al*., 2002). There is also decrease in oxygen utilization in traumatic brain injuries with attendant decrease in ADP respiration and resultant decrease in ATP production (Glimmer *et al*., 2010). The Na^+-K^+ ATPase pump malfunctions in the presence of low ATP with resultant lowering of threshold for action potential generation. It had also been found that after the injury there was extracellular increase in excitatory amino acids with increased level of glutamic and aspartic acids (Katayama *et al*., 1990). The traumatized cells tend to assume excitatory amino acids more readily than normal cells and present increase expression of the sodium-coupled neutral amino acid transporters subtypes1 and subtype 2 (Tani *et al*., 2007). These predispose to early PTS. Wang *et al*. (2008) in their study of factors predictive of outcome in posttraumatic seizures found that 126 (74.12%) of their 170 patients had early posttraumatic seizures. Singh *et al*. (2015) in their study of 70 patients with posttraumatic seizures found that 57 (81.43%) of the patients had early posttraumatic seizure and 56 (80%) were ≤50 years. Thapa *et al*. (2010) in their study of posttraumatic seizures in India found that in 59 patients with posttraumatic seizures, 45 (76.27%) had early posttraumatic seizures and the average age among the patients with seizure was 26.3 years.

There was also significant relationship between CT findings and type of seizure. Subdural hematoma was seen more in late PTS, while other lesions were more in early PTS. Just like age the subdural hematoma was seen in older adults while other lesions occur in children and younger adults. The pressure from subdural hematoma in acute stage in older adults was compensated by extra-cerebral space volume early after the injury, hence the pressure on the cortical cells were not much. With the hematoma lysing and going into subacute and chronic stage from 3rd day, the volume increase exerts pressure on the cortical cells leading to malfunction of the cells and late PTS. It had also been found that mitochondrial respiration decline with ageing, and this is more pronounced with pathological conditions (Finsterer, 2008) such as TBI. Higher levels of oxidative damage to machinery inside mitochondria of aged people, particularly in the synaptic fraction (Gilmer *et al*., 2010) may impede their ability to produce ATP, resulting in greater cellular dysfunction. During the reparative period, there was decrease in inhibitory neurons relative to excitatory neurons with tendency to seizure productions. Avramescu *et al*. (2009) found that this relative decrease in inhibitory GABAergic neurons became significant from two weeks post injury, and worsened in 4th and 6thweek post injury (the periods they studied). This relative decrease in inhibitory neurons predispose patients to late seizures.

Conclusion

The study showed that early PTS occurred mainly in children and young adults with various brain injuries. It also showed that late PTS occurred in older adults with chronic subdural hematoma.

Financial support: No financial support

Conflict of interest: There was no conflict of interest

REFERENCES

Acharya, R.U., Sree, V.S., Swapna, G., Martis, R.I., Suri, J.S. 2013. Automated EEG analysis of epilepsy: a review. Knowledge-based Systems., 45:147-65

Annegers, J.F., Grabow, J.D., Groover, R.V., Laws, E.R. Jr, Elveback, L.R., Kurland, L.T. 1980. Seizures after head trauma: a population study. *Neurology*, 30:683-9

Avramescu, S., Nita, D.A., Timofeev, I. 2009. Neocortical posttraumatic epileptogenesis associated with loss of GABAergic neurons. *J Neurotrauma,* 26:779-812

Bratton, S.L., Chestnut, R.M., Ghajar, J., McConnell, H.F.F., Haris, O.A., Hartl, R., *et al*. 2007. Guidelines for the management of severe traumatic brain injury. VI. Indications for intracranial pressure monitoring. *J Neurotrauma,* 24(Suppl1):S37- 44

Bullock, M.R., Povlishock, J.T. 2007. Guidelines for the management of severe traumatic brain injury. Editor's Commentary. *J Neurotrauma*, 24(Suppl1):2

Dencher, N.A., Frezel, M., Reifschneider, N.H., Sugawa, M., Krause, F. 2007. Proteome alterations in rat mitochondria caused by ageing. *Ann N Y Acad Sci.,* 1100:291-8

Dudek, F.E., Spitz, M. 1997. Hypothetical mechanism for the cellular and neurophysiologic basis of secondary epileptogenesis: proposed role of synaptic reorganization. *J Clin Neurophysiol.,* 14:90-101

Emejulu, J.K.C., Isiguzo, C.M., Agbasoga, CE, Ogbuagu CN. 2010. Traumatic brain injury in the emergency department of a tertiary hospital in Nigeria. East and Central Africa *Journal of Surgery*, 15:28-38

Finsterer, J. 2008. Cognitive decline as a manifestation of mitochondrial disorders (mitochondrial dementia). *J Neurol Sci*., 272:20-33

Frey, L.C. 2003. Epidemiology of posttraumatic epilepsy: a cortical review. *Epilepsia*, 44(Suppl.10):11-17

Gilmer, L.K., Ansari, M.A., Roberts, K.N., Scheff, S.W. 2010. Age-related mitochondrial changes after traumatic brain injury. *J Neurotrauma*, 27:939-50

Gilmer, L.K., Roberts, K.N., Sullivan, P.G., Miller, K., Scheff, S. 2009. Early mitochondrial dysfunction after cortical contusion injury. *J Neurotrauma*, 26:1271-80

Haddad SH, Arabi YM. 2012. Critical care management of severe traumatic brain injury in adults. *Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine*, 20:12

Hoch, F.L. 1992. Cardiolipins and biomembrane function. *Biochim Biophys Acta*., 1113:71-133

Jasper, U.S., Opara, M.C., Pyiki, E.B., Akinrolle, O. 2014. The epidemiology of hospital-referred head injury in northern Nigeria. *Journal of Scientific Research and Reports*, 3:2055-64

Jennet, B. 1974. Early traumatic epilepsy. Incidence and significance after nonmissile injuries. *Arch Neurol.,* 30:394-8

Katayama, Y., Becker, D.P., Tamura, T., Hovda, D.A. 1990. Massive increases in extracellular potassium and the indiscriminate release of glutamate following concussive brain injury. *J Neurosurg.,* 73:889-900

Labate, D., Inuso, G., Occhiuto, G., La Foresta, F., Morabito, F.C. 2013. Measures of brain connectivity through permutation entropy in epileptic disorders. Neural Nets and Surroundings: *Springer,* 19: 59-67

Lesnefsky, E.J., Hoppel, C.L. 2006. Oxidative phosphorylation and ageing. *Ageing Res Rev.,* 5:402-33

Lifshitz, J., Sullivan, P.G., Hovda, D.A., Wieloch, T., McIntosh, T.K. 2004. Mitochondrial damage and dysfunction in traumatic brain injury. *Mitochondrion,* 4:705-13

Majores, M., Elis, J., Wiestler, O.D., Becker, A.J. 2004. Molecular profiling of temporal lobe epilepsy: comparison of data from human tissue samples and animal models. *Epilepsy Res.,* 60:173-8

McCormic, D.A., Contreras, D. 2001. On the cellular and network basis of epileptic seizures. *Annu Rev Physiol.,* 63:815-46

Misra, M., Salazar, J.L., Bloom, D.M. 1996. Subdural-peritoneal shunt: treatment for bilateral chronic subdural hematoma. *Surg Neurol.,* 46:378-83

Nadler, J.V. 2003. The recurrent mossy fiber pathway of the epileptic brain. *Neurochem Res.,* 28:1649-58

Najafi MR, Tabesh H, Hosseni H, Akbari M, Najafi MA. 2015. Early and late posttraumatic seizures following traumatic brain injury: a five year follow-up survival study. *Advanced Biomedical Research*, 4:82

Ravizza T, Gagliardi B, Noe F, Boer K, Aronica E, Vezzani A. 2008. Innate and adaptive immunity during epileptogenesis and spontaneous seizures: evidence from experimental models and human temporal lobe epilepsy. *Neurobiol Dis*., 29:142-60

Richter C. 1995. Oxidative damage to mitochondria DNA and its relationship to ageing. *Int J Biochem Cell Biol*., 27:647-53

Singh RP, Jain M, Lakhar BN, Jain S. 2015. Head trauma and posttraumatic epilepsy ─ a radiologist study. *International Journal of Recent Advances in Multidisciplinary Research*, 2:371-3

Sullivan PG, Keller JN, Bussen WL, Scheff SW. 2002. Cytochrome c release and caspase activation after traumatic brain injury. *Brain Res*., 949:88-96

Sullivan PG, Keller JN, Mattson MP, Scheff SW. 1999b. Traumatic brain injury alters synaptic homeostasis: implications for impaired mitochondrial and transport function. *J Neurotrauma*, 15:789-98

Tani H, Bandrowski AE, Parada I, Wynn M, Huguenard JR, Price DA, *et al*. 2007. Modulation of epileptiform activity by glutamate and system A transport in a model of posttraumatic epilepsy. *Neurobiol Dis*., 25:230-8

Thapa A, Chandra SP, Sinha S, Sreenivas V, Sharma BS. 2010. Posttraumatic seizures ─ a prospective study from a tertiary level trauma center in a developing country. *Seizure*, 19:211-6

Treiman DM, Meyers PD, Walton NY, Collins JF, Colling C, Rowan AJ, *et al*. 1998. A comparison of four treatments for generalized convulsive status epilepticus. *N Engel J Med*., 339:792-8

Van Remmen H, Richardson A. 2001. Oxidative damage to mitochondria and ageing. *Exp Gerontol*., 36:957-68

Vespa PM, Miller C, McArthur D, Eliseo M, Etchepare M, Hirt D, *et al*. 2007. Nonconvulsive electrographic seizures after traumatic brain injury result in a delayed, prolonged increase in intracranial pressure and metabolic crisis. *Crit Care Med*., 35:2830-6

Wang HC, Chang WN, Chang HW, Ho JT, Yang TM, Lin WC, *et al*. 2008. Factors predictive of outcome in posttraumatic seizures. *J Trauma*, 64:883-8

****