Survival and Functional Outcomes at Discharge After Traumatic Brain Injury in Children versus Adults in Resource-Poor Setting

Laura N. Purcell[1], Rachel Reiss[3], Jessica Eaton[4], Ken-Kellar Kumwenda[5], Carolyn Quinsey[2], Anthony Charles[1,5]

■ BACKGROUND: More than 90% of trauma mortality occurs in low- and middle-income countries, especially in sub-Saharan Africa. Head injury is the primary driver of trauma mortality in the prehospital and in-hospital setting.

■ METHODS: An observational study was performed on patients presenting with traumatic brain injury (TBI) from October 2016 through May 2017 at Kamuzu Central Hospital, Malawi. Bivariate analysis and logistic regression were performed to determine the odds of favorable functional outcomes and mortality after controlling for significant covariates.

■ RESULTS: Of the 356 patients with TBI, 72 (20.2%) were children <18 years of age. Males comprised 202 (87.1%) and 46 (63.9%) of the adult and pediatric cohorts, respectively. Motor vehicle crash was the leading etiology in adults and children. There was no significant difference between adult and pediatric Glasgow Coma Scale score on admission, 10.8 ± 3.9 versus 10.9 ± 3.5, respectively ($P = 0.8$). More adult ($n = 76$, 32.3%) than pediatric ($n = 13$, 18.1%) patients died. On multivariable analysis, pediatric patients were more likely to have a favorable outcome defined by a Glasgow Outcome Scale of good recovery or moderate disability (odds ratio 3.70, 95% confidence interval 1.22–11.17, $P = 0.02$) and were less likely to die after TBI (odds ratio 0.29, 95% confidence interval 0.09–0.93, $P = 0.04$).

■ CONCLUSIONS: We show a survival advantage and better functional outcomes in children following TBI. This may be attributable to increased resiliency to TBI in children or the prioritization of children in a resource-poor environment. Investments in neurosurgical care following TBI are needed to improve outcomes.

INTRODUCTION

Globally, traumatic brain injury (TBI) is the primary driver of trauma mortality.[1] An estimated 69 million people, at least 3 million of whom are children, experience TBI each year.[2,3] Beyond mortality in the acute postinjury period, TBI is associated with up to 7× increased risk of death for up to 13 years after injury and an overall reduced life expectancy.[4,5] Even those who survive TBI may suffer development of neuroendocrine and neuropsychiatric sequelae or lifelong impairments in physical, cognitive, social, and vocational function.[6-8] TBI is now recognized by the medical community as a chronic disease, given the progressively evolving compensatory responses in the injured brain.[9,10] This "silent epidemic" engenders enormous economic and social strain worldwide as it impacts not only patients but also their caregivers and the larger community.[11-13]

There is a significantly disproportionate burden of TBIs in low- and middle-income countries (LMICs), which accounts for 73% of TBI incidence.[2] The asymmetry in disease burden extends to outcomes, as severe TBIs are twice as likely to result in death in LMIC than their high-income country (HIC) counterparts.[14] Although incidences vary widely by country, TBIs in sub-Saharan Africa (SSA) are currently estimated to have an

Key words
- Head injury
- Traumatic brain injury
- Traumatic brain injury in adults and children

Abbreviations and Acronyms
CI: Confidence interval
GCS: Glasgow Coma Scale
HIC: High-income countries
KCH: Kamuzu Central Hospital
LMIC: Low- and middle-income country
MVC: Motor vehicle crash
OR: Odds ratio
SSA: Sub-Saharan Africa
TBI: Traumatic brain injury

incidence of 801 per 100,000 (95% confidence interval 732—871).[2] This represents a substantial increase from prior estimates of only 150—170 per 100,000 in 2007.[12] This rise is driven by increasing motorization, population growth, unchecked modernization, and regional conflict.[8,15-17] In SSA, there are few enforced traffic safety regulations and there is limited safety-promoting infrastructure. As a result, 34% of road traffic injuries are associated with TBI.[2,15,18]

Despite the global importance of TBI, it is far from well characterized. Epidemiologic understandings of this disease process are obscured by poor surveillance.[8] The SSA estimations of the TBI burden may be inappropriately low given the dearth of data available from this setting.[2] Difficulties in determining the true extent of disease are compounded by the lack of worldwide consensus regarding TBI diagnosis and classification.[2,8] Further, most reports regarding outcomes after TBI only report mortality and not morbidity. We, therefore, sought to bridge this gap and determine TBI mortality and functional outcomes within the pediatric and adult trauma population in central Malawi.

METHODS

We performed a retrospective analysis of the prospectively collected head trauma database at Malawi's Kamuzu Central Hospital from October 2016 through May 2017. Patients were included in the database if they had a history of head trauma, altered consciousness, and/or radiographic evidence of TBI. Patients were excluded from the database if they were brought in dead or treated and discharged from the emergency department. Also, patients were excluded if they had head trauma but no loss of consciousness, a decrease in their Glasgow Coma Scale (GCS) score, or radiographic evidence of TBI. Patients were excluded from the retrospective analysis if they were missing outcomes data. Pediatric patients were defined as ≤18 years of age.

Malawi is a small, landlocked country in Southeast Africa. Its health care system is stratified into 3 tiers: primary health care centers at the local level, district hospitals located in each of the 28 districts, and 4 central hospitals that provide surgical care to the country, 1 of which is Kamuzu Central Hospital (KCH), a 900-bed referral hospital in the capital of Lilongwe, Malawi. KCH is the tertiary hospital for 8 district hospitals serving 6 million people in the central region of Malawi. The emergency department has 4 beds, with 2 additional rooms available for mass casualties. The emergency department is staffed by 2 rotating interns, 3 nurses including a charge nurse, 2 clinical officers, and an on-call surgical resident and consultant. There is also a 5-bed intensive care unit and a 5-bed high-dependency unit for both medical and surgical patients. There was one consultant neurosurgeon on staff during the study period.

The study population was analyzed using descriptive statistics in the overall sample. Univariate analysis was used to determine data distribution and missing values. Less than 5% of missing data were seen in the database. Bivariate analysis was performed by stratifying over adult and pediatric cohorts. The central tendency in univariate and bivariate analyses was reported as means (± standard deviation) or medians (interquartile range) if the covariates were not normally distributed. To compare the distribution across demographic variables in bivariate analysis, χ^2 for categorical variables, Student's t-test for normally distributed continuous variables, and Kruskal-Wallis for not normally distributed continuous variables were used.

To determine which predictors were associated with favorable outcome after TBI, we performed a multivariate logistic regression predictive model. A favorable outcome was defined as a Glasgow Outcome Scale of good recovery or moderate disability, and poor outcome was defined as severe disability, vegetative state, or death. Glasgow Outcome Scale was determined at the time of patient discharge from KCH. A priori, the variables included were time from injury to presentation; the presence of another chest, abdomen, pelvis or extremity injury; shock index; undergoing a neurosurgical procedure; and head injury severity. Head injury severity was categorized into mild (GCS >13), moderate (GCS = 9—13), and severe (GCS ≤8). Variables significant at P < 0.05 in bivariate analysis for functional outcome were also included in the multivariate model. The fully adjusted model included time from injury to presentation; the presence of a chest, abdomen, pelvis, or extremity injury; shock index; undergoing a neurosurgical procedure; injury etiology; sex; and head injury severity. A backward elimination approach was performed to reduce error in both models. Variables were removed on the basis of P value (>0.05). Precision was maintained, and a reduction of bias was seen as there was a narrowing of the confidence intervals and a <10% change in coefficients, respectively. On the basis of these criteria, injury etiology was removed from the final model as its inclusion was not statistically significant in the multivariate logistic regression.

To determine which predictors were associated with mortality after TBI, we performed a multivariate logistic regression predictive model. A priori, time from injury to presentation, the presence of another chest, abdomen, pelvis or extremity injury; shock index, undergoing a neurosurgical procedure, and head injury severity were added to the model. Other variables significant at P < 0.05 on bivariate analysis for mortality were also included with the fully adjusted model including sex; time from injury to presentation; the presence of a chest, abdomen, pelvis, or extremity injury; shock index; undergoing a neurosurgical procedure; injury etiology; and head injury severity. A backward elimination approach was performed to reduce error, as previously described. Injury etiology was removed from the final models as its inclusion was not statistically significant in the multiple logistic regression. Removal resulted in minimal change in the coefficients with narrowing of the confidence intervals.

This analysis was performed using StataCorp v14.2 (College Station, Texas, USA). For this study, confidence intervals are reported at 95%, and alpha was set at 0.05. The institutional review boards approved this study.

RESULTS

Of the 356 patients with TBI included in this study, 72 (20.2%) were children. In the overall cohort, the average age was 29.5 ± 16.4 years with a male predominance (n = 248, 81.6%). The majority of TBIs were from motor vehicle crashes (MVCs) (n = 184,

Table 1. Patient Demographics Stratified by Adult and Pediatric (≤18 years) Cohorts

	Total (n = 356)	Adults (n = 284)	Pediatric (n = 72)	P Value
Age (years): μ ± SD	29.5 ± 16.4	35.8 ± 13.8	9.2 ± 5.3	<0.001
Male: number (%)	248 (81.6)	202 (87.1)	46 (63.9)	<0.001
Time to presentation: μ ± SD	0 (0—1)	0 (0—1)	0 (0—1)	0.06
Injury mechanism: number (%)				0.007
Blunt	281 (92.7)	210 (90.5)	71 (100.0)	
Penetrating	22 (7.3)	22 (9.5)	0 (0.0)	
Injury etiology: number (%)				<0.001
Motor vehicle crash	184 (60.5)	144 (62.1)	40 (55.6)	
Assault	76 (25.0)	67 (28.8)	9 (12.5)	
Fall	31 (10.2)	15 (6.5)	16 (22.2)	
Other	13 (4.3)	6 (2.6)	7 (9.7)	
Total admission GCS: μ ± SD	10.8 ± 3.8	10.8 ± 3.9	10.9 ± 3.5	0.8
Neurologic symptoms: number (%)				
Ataxia	13 (4.3)	10 (4.3)	3 (4.2)	1.0
Amnesia	19 (6.3)	16 (6.9)	3 (4.2)	0.4
Aphasia	22 (7.2)	17 (7.3)	5 (6.9)	0.9
Weakness	31 (10.2)	23 (11.3)	5 (6.9)	0.3
Numbness	7 (2.3)	6 (2.6)	1 (1.4)	0.6
Seizures	29 (9.5)	20 (8.6)	9 (12.5)	0.3
Total 24-hour GCS: μ ± SD	11.6 ± 4.0	11.5 ± 4.0	11.8 ± 3.9	0.6
Other injury: number (%)				0.4
None	178 (58.5)	133 (57.3)	45 (62.5)	
Chest, abdomen/pelvis, or extremity	126 (41.5)	99 (42.7)	27 (37.5)	
Neurosurgical operative intervention: number (%)	35 (11.5)	28 (12.1)	7 (9.7)	0.6
Outcome: number (%)				0.09
Death	88 (29.0)	75 (32.3)	13 (18.1)	
Discharge	204 (67.1)	148 (63.8)	56 (77.8)	
Transferred	7 (2.3)	6 (2.6)	1 (1.4)	
AMA	5 (1.6)	3 (1.3)	2 (2.8)	
Glasgow Outcome Scale: number (%)				0.05
Death	89 (29.4)	76 (32.9)	13 (18.1)	
Vegetative state	2 (0.7)	2 (0.9)	0 (0.0)	
Severe disability	9 (3.0)	7 (3.5)	1 (1.4)	
Moderate disability	29 (9.6)	18 (7.8)	11 (15.3)	
Good recovery	174 (57.4)	127 (55.0)	72 (65.3)	
Time from presentation to outcome: median (IQR)	5 (2—10)	5 (2—10)	5 (2—11.5)	0.5

SD, standard deviation; GCS, Glasgow Coma Scale; AMA, discharged against medical advice; Glasgow Outcome Scale; IQR, interquartile range.

60.5%), followed by assaults (n = 76, 25%). There was 29.4% (n = 89) mortality in the overall cohort (Table 1).

The average age in the adult and pediatric cohorts was 35.8 ± 13.8 and 9.2 ± 5.3 years, respectively. Both cohorts were primarily male, 202 (87.1%) in the adult and 46 (63.9%) in the pediatric cohort, P < 0.001. In adults, the leading mechanisms of injury were MVC (n = 144, 62.1%) and assaults (n = 67, 28.8%) in contrast to the pediatrics cohort, which were MVC (n = 40, 55.6%)

Table 2. Logistic Regression Predicting Favorable Outcome After Traumatic Brain Injury

	Odds Ratio	95% Confidence Interval	P Value
Pediatric patients	3.70	1.22–11.17	0.02
Female sex	1.49	0.54–4.06	0.4
Time to presentation	0.98	0.93–1.03	0.5
Other injury	0.80	0.40–1.63	0.5
Shock index	0.58	0.13–2.54	0.4
Neurosurgery Intervention	2.03	0.63–6.55	0.2
Head injury severity			
Mild	Ref	Ref	Ref
Moderate	0.20	0.08–0.50	0.001
Severe	0.05	0.02–0.12	<0.001

Ref, a reference to "Mild" to which moderate and severe is compared with.

Table 3. Multivariate Logistic Regression Predicting Mortality After Traumatic Brain Injury

	Odds Ratio	95% Confidence Interval	P Value
Pediatric patients	0.29	0.09–0.93	0.04
Female sex	0.65	0.23–1.82	0.4
Time to presentation	0.96	0.89–1.04	0.3
Other injury	0.91	0.43–1.92	0.8
Shock index	1.57	0.35–6.93	0.6
Neurosurgery intervention	2.03	0.08–1.25	0.1
Head injury severity			
Mild	Ref	Ref	Ref
Moderate	5.12	1.89–13.85	0.001
Severe	18.71	7.26–48.19	<0.001

Ref, a reference to "Mild" to which moderate and severe is compared with.

and falls (n = 16, 22.2%), P < 0.001. There was no difference in the total admission GCS (10.8 ± 3.9 vs. 10.9 ± 3.5, P = 0.8), neurologic symptoms, GCS at 24 hours after admission (11.5 ± 4.0 vs. 11.8 ± 3.9, P = 0.6), and neurosurgical intervention between the adult and pediatric cohorts. The adult cohort had higher mortality than the pediatric cohort (n = 76, 32.9% vs. n = 13, 18.1%) and was less likely to have a good functional outcome (n = 145, 62.8% vs. n = 83, 80.6%; see Table 1).

In the logistic regression model predicting functional outcomes, pediatric patients (odds ratio [OR] 3.70, 95% confidence interval [CI] 1.22–11.17, P = 0.02) compared with adults had greater odds of favorable functional outcomes when controlled for pertinent covariates. Patients with moderate (OR 0.20, 95% CI 0.08–0.50, P = 0.001) and severe (OR 0.05, 95% CI 0.02–0.12, P < 0.001) head injury were more likely to have poor functional outcome after TBI (Table 2).

In the logistic regression model predicting mortality, pediatric patients (OR 0.29, 95% CI 0.09–0.92, P = 0.04) had lower odds of mortality. Patients with moderate (OR 5.12, 95% CI 1.89, P = 0.001) and severe (OR 18.71, 95% CI 7.26–48.19, P < 0.001) head injury had higher odds of mortality than those with mild head injury (Table 3).

DISCUSSION

The World Health Organization classifies TBI as the leading cause of death and disability among children and young adults globally, and TBI is the greatest driver of injury-related mortality worldwide.[19] The burden of TBI is greatest in LMIC, where 85% of the world's population lives.[20] In this comparative study between adults and children with TBI, we demonstrate reduced mortality in children compared with adults following TBI and 3× higher odds of good functional outcome at the time of discharge.

Our findings are similar to other studies in the literature, suggesting improved functional outcomes in the pediatric population following TBI.[21-23] However, most of these studies are from HIC. A 2012 retrospective study by Zonfrillo et al[24] of 13,798 children aged 7–18 years with TBI and a 2015 study by Jimenez et al[25] on 10,141 children aged 6 months to 18 years found significant improvement in functional outcomes at discharge with further improvement after discharge. Though there is a paucity of data in LMICs, in an analysis of adult patient outcomes after TBI in HIC and LMIC, De Silva et al[14] showed the overall TBI-related mortality is similar in high and low-income countries at 27% and 26%, respectively. The most significant disparity in mortality outcome is in severe TBI, where the mortality is 30% and 51%, respectively.[14]

There is currently no consensus as to why children have a survival and functional outcome advantage over adults after TBI. Several theories have been proposed. First, the greater flexibility of cranial bones in young children, as a function of suture patency, may enhance the capacity of the skull to absorb traumatic forces, thereby reducing focal brain injury.[26] Second, for long-term outcomes, the central nervous system retains the ability to recover and adapt secondary compensatory mechanisms after injury.[27] The basis of recovery stems from neuroplasticity, defined as the ability for neuronal circuits to make structural and functional adaptive changes. These changes range from molecular, synaptic, and cellular changes to more global network changes.[28] Compared with the pediatric brain, the adult brain is thought to have less physiologic and neuroanatomic reorganization after injury.[29,30]

Though children may have better functional outcomes at the time of discharge, their ability to sustain this functional advantage over time has been called into question as it is now recognized that after severe TBI, children may be at risk of "neurocognitive stall."[31] Various TBI functional outcomes results in children and young adults have emerged that showed initial recovery curves followed by function plateaus.[32] There is evidence that children sustaining generalized brain trauma are more vulnerable to long-term cognitive deficits and, in some

cases, further declines in functioning when compared with typically developing peers.[33]

Although TBI prevention strategies, such as road traffic safety in HIC, have been remarkably successful, these achievements are not replicated in LMIC. Increased use of motor vehicles, coupled with inadequate infrastructure and insufficient adoption of safety measures, has resulted in substantial increases in the burden of TBI in LMIC.[34] The immense economic burden of TBI worldwide necessitates improved prevention and treatment strategies from a health-economic perspective. This is particularly important in resource-poor settings where the per-capita health care expenditure is already low. Furthermore, the spectrum of clinical care for TBI extending from prehospital care, immediate access to emergency care, availability of surgeons, critical care capabilities, and neuroimaging to long-term postacute care in LMIC must be available to reduce TBI morbidity and mortality.

This study has several limitations. We did not obtain postdischarge follow-up, and hence long-term functional outcomes could not be determined. The head trauma database at KCH did not include pediatric and adult patients who died before arrival to the hospital or present only to the district hospitals. Lastly, we may not have controlled for unrecognized confounding variables in our logistic regression models.

CONCLUSION

Given the better functional outcomes and mortality, a more aggressive management approach should be pursued in children with TBI despite head injury severity. Developing individualized TBI management strategies, based on age, clinical presentation, and evidence of raised ICP, may improve TBI management even in a resource-poor setting. In addition, injury prevention strategies should be instituted as part of a public health strategy for all.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Laura N. Purcell: Conceptualization, Methodology, Writing - original draft. **Rachel Reiss:** Data curation, Writing - original draft. **Jessica Eaton:** Data curation. **Ken-Kellar Kumwenda:** Supervision. **Carolyn Quinsey:** Supervision. **Anthony Charles:** Writing - review & editing.

REFERENCES

1. Roozenbeek B, Maas AI, Menon DK. Changing patterns in the epidemiology of traumatic brain injury. *Nat Rev Neurol.* 2013;9:231.

2. Dewan MC, Rattani A, Gupta S, et al. Estimating the global incidence of traumatic brain injury. *J Neurosurg.* 2018;1:1-8.

3. Dewan MC, Mummareddy N, Wellons JC III, Bonfield CM. Epidemiology of global pediatric traumatic brain injury: qualitative review. *World Neurosurg.* 2016;91:497-509.

4. McMillan TM, Teasdale GM, Weir CJ, Stewart E. Death after head injury: the 13 year outcome of a case control study. *J Neurol Neurosurg Psychiatry.* 2011;82:931-935.

5. Ventura T, Harrison-Felix C, Carlson N, et al. Mortality after discharge from acute care hospitalization with traumatic brain injury: a population-based study. *Arch Phys Med Rehab.* 2010; 91:20-29.

6. Areas FZ, Schwarzbold M, Diaz AP, et al. Predictors of hospital mortality and the related burden of disease in severe traumatic brain injury: a prospective multicentric study in Brazil. *Front Neurol.* 2019;10:432.

7. Fleminger S. Why do some patients after head injury deteriorate over the long term? *J Neurol Neurosurg Psychiatry.* 2012;83:1036.

8. Nguyen R, Fiest KM, McChesney J, et al. The international incidence of traumatic brain injury: a systematic review and meta-analysis. *Can J Neurol Sci.* 2016;43:774-785.

9. Wilson L, Stewart W, Dams-O'Connor K, et al. The chronic and evolving neurological consequences of traumatic brain injury. *Lancet Neurol.* 2017;16:813-825.

10. Maas A. Traumatic brain injury: changing concepts and approaches. *Chin J Traumatol.* 2016;19: 3-6.

11. Coburn K. Traumatic brain injury: the silent epidemic. *AACN Adv Crit Care.* 1992;3:9-18.

12. Hyder AA, Wunderlich CA, Puvanachandra P, Gururaj G, Kobusingye OC. The impact of traumatic brain injuries: a global perspective. *NeuroRehabilitation.* 2007;22:341-353.

13. Langlois JA, Rutland-Brown W, Wald MM. The epidemiology and impact of traumatic brain injury: a brief overview. *J Head Trauma Rehab.* 2006; 21:375-378.

14. De Silva MJ, Roberts I, Perel P, et al. Patient outcome after traumatic brain injury in high-, middle-and low-income countries: analysis of data on 8927 patients in 46 countries. *Int J Epidemiol.* 2008;38:452-458.

15. Mehmood A, Zia N, Kobusingye O, et al. Determinants of emergency department disposition of patients with traumatic brain injury in Uganda: results from a registry. *Trauma Surg Acute Care Open.* 2018;3:e000253.

16. Zia N, Mehmood A, Namaganda RH, Ssenyonjo H, Kobusingye O, Hyder AA. Causes and outcomes of traumatic brain injuries in Uganda: analysis from a pilot hospital registry. *Trauma Surg Acute Care Open.* 2019;4:e000259.

17. James SL, Theadom A, Ellenbogen RG, et al. Global, regional, and national burden of traumatic brain injury and spinal cord injury, 1990−2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol.* 2019;18:56-87.

18. Udoh DO, Adeyemo AA. Traumatic brain injuries in children: a hospital-based study in Nigeria. *Afr J Paediatr Surg.* 2013;10:154.

19. World Health Organization. *Neurological disorders: public health challenges.* Geneva, Switzerland: World Health Organization; 2006.

20. Murray CJ, Lopez AD, World Health Organization. The global burden of disease: a comprehensive assessment of mortality and disability from diseases, injuries, and risk factors in 1990 and projected to 2020: summary. p 23-30. https://apps. who.int/iris/bitstream/handle/10665/41864/0965546608_eng.pdf

21. Alberico AM, Ward JD, Choi SC, Marmarou A, Young HF. Outcome after severe head injury: relationship to mass lesions, diffuse injury, and ICP course in pediatric and adult patients. *J Neurosurg.* 1987;67:648-656.

22. Luerssen TG, Klauber MR, Marshall LF. Outcome from head injury related to patient'age: a longitudinal prospective study of adult and pediatric head injury. *J Neurosurg.* 1988;68:409-416.

23. Emami P, Czorlich P, Fritzsche FS, et al. Impact of Glasgow Coma Scale score and pupil parameters on mortality rate and outcome in pediatric and adult severe traumatic brain injury: a retrospective, multicenter cohort study. *J Neurosurg.* 2017; 126:760-767.

24. Zonfrillo MR, Durbin DR, Winston FK, Zhao H, Stineman MG. Physical disability after injury-related inpatient rehabilitation in children. *Pediatrics.* 2013;131:e206-e213.

25. Jimenez N, Osorio M, Ramos JL, Apkon S, Ebel BE, Rivara FP. Functional independence after inpatient rehabilitation for traumatic brain injury among minority children and adolescents. *Arch Phys Med Rehabil.* 2015;96:1255-1261.

26. Ghajar J, Hariri RJ. Management of pediatric head injury. *Pediatr Clin North Am.* 1992;39:1093-1125.

27. Nudo RJ. Recovery after brain injury: mechanisms and principles. *Front Hum Neurosci.* 2013;7:887.

28. Sophie Su YR, Veeravagu A, Grant G. Neuroplasticity after traumatic brain injury. In: Laskowitz D, Grant G, eds. *Translational Research in Traumatic Brain Injury.* Boca Raton, FL: CRC Press/ Taylor and Francis Group; 2016.

29. Burda JE, Sofroniew MV. Reactive gliosis and the multicellular response to CNS damage and disease. *Neuron*. 2014;81:229-248.

30. Nahmani M, Turrigiano GG. Adult cortical plasticity following injury: recapitulation of critical period mechanisms? *Neuroscience*. 2014;283:4-16.

31. Chapman SB. Neurocognitive stall, a paradox in long term recovery from pediatric brain injury. *Brain Inj Profess*. 2006;3:10-13.

32. Savage RC. The developing brain after TBI: predicting long term deficits and services for children, adolescents, and young adults. *Int Brain Inj Assoc*. 2009;4.

33. Finnanger TG, Olsen A, Skandsen T, et al. Life after adolescent and adult moderate and severe traumatic brain injury: self-reported executive, emotional, and behavioural function 2−5 years after injury. *Behav Neurol*. 2015;2015.

34. Maas AI, Stocchetti N, Bullock R. Moderate and severe traumatic brain injury in adults. *Lancet Neurol*. 2008;7:728-741.