

Effects of the Early Repair of Traumatic Craniocerebral Injury on Neural Functions and the Extraction and Exploration of Medical Information

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Zheng *et al.*: Effects of the Early Repair of Traumatic Craniocerebral Injury on Neural Functions

The objective of the present study was to explore the effects of early repair of traumatic craniocerebral injury on neural functions, as well as the optimal extraction of medical information from craniocerebral injury images. Therefore, a total of 60 patients with traumatic craniocerebral injury were submitted to decompressive craniectomy and then cranioplasty. Afterward, all the patients were divided into the early group and the routine group. The changes in indicators of both groups after the patients underwent decompressive craniectomy were compared and retrospectively analysed. The National Institutes of Health stroke scale, Karnofsky performance status, and the Glasgow outcome scale scores in the 1st, 3rd, and 12th months after decompressive craniectomy of patients were observed. In terms of medical image information extraction, based on the active contour models of global region, the information was extracted from segmentation weak boundary images to quickly, completely, and clearly obtain the images of the cerebral region of patients with a traumatic craniocerebral injury. The results showed that the Glasgow outcome scale, Karnofsky performance status, and National Institutes of Health stroke scale scores of the early group were 3.23 ± 0.67 , 52.23 ± 7.54 , and 6.75 ± 0.23 , respectively. The Glasgow outcome scale, Karnofsky performance status and National Institutes of Health stroke scale scores of the routine group were 2.94 ± 0.37 , 51.42 ± 4.68 , and 6.32 ± 0.24 , respectively. The data of both groups were compared and the differences were not statistically significant. In the early group, the Glasgow outcome scale and National Institutes of Health stroke scores in the 6th month after trauma were 3.67 ± 0.682 and 13.84 ± 4.789 , respectively, while in the routine group, these were 3.29 ± 0.714 and 17.02 ± 6.453 , respectively and the differences were significant. It can be seen from the experimental results of extracting the target segmentation information that although the algorithm adds noise to the original image, it could accurately segment and extract the target region with little noise. It was not necessary to consider the selection of the initialization target, and the iteration could improve the segmentation efficiency of the algorithm. Also, it was found that given the condition of well-handled preoperative and preoperative indications, the early repair can promote the repair of neural functions of patients. Moreover, a contour model algorithm was proposed, which could effectively extract the medical information of the craniocerebral injury images, providing powerful theoretical guidance for the development of craniocerebral medical image information technology.

Key words: Craniocerebral injury, early repair, neural function, medical information, image algorithm

In recent years, with the development of social economy and science and technology, automobile technology has become increasingly advanced, and the automobiles have become much popular^[1]. The popularity of automobiles has increased the incidence rate of car accidents annually; subsequently, the incidence rate of craniocerebral injury has also increased^[2]. The defect of the skull is a common sequela after trauma and operations in patients with a craniocerebral injury. It is very common in clinical neurosurgery, which seriously affects the quality of life

and physical and mental health of people^[3]. Traumatic craniocerebral injury can be divided into 3 types, the scalp injury, the skull injury, and the intracranial injury. However, these types of injuries often appear together. Once the defect of skull occurs, with the changes in the difference of intracranial pressure and extracranial pressure, the cutaneous flap of skull defect is relaxed, the brain tissue enters and exits the defect area, and the atmospheric pressure can directly act on the functional areas and positions of the defect brain surface^[4]. If the skull defect is close to the venous sinus, it will affect

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the blood circulation in the venous sinus, destroy the stable state of the intracranial pressure, and cause the brain to lose its normal functions, which will lead to a series of clinical manifestations such as headache, dizziness, fatigue, and irritability^[5]. Severe traumatic craniocerebral injury, because of its own gravity and the atmospheric pressure, the brain tissue and cerebrospinal fluid in the cranial cavity will be compressed to the side that is under stress, resulting in lower pressure in the cranial cavity; the scalp can move back and forth at the skull defect site. If the patient stands upright, the intracranial pressure becomes much deeper and invagination occurs. If the patient lies down, the intracranial pressure rises and localizes, which inevitably causes the normal cerebral cortical vessels to stretch and deform, resulting in insufficient blood supply to the local brain tissue^[6]. With the passage of time, due to the insufficient blood supply, local brain tissue begins to shrink, leading to secondary brain injury^[7].

In recent years, medical image information extraction has attracted increasing attention of the public, especially the extraction of clinical medical information. Medical image information extraction is also the research direction of computer image processing^[8]. Medical image segmentation technology refers to dividing an image into a plurality of disjoint regions according to the sharpness, colour, and image texture of the extracted medical images, so that different regions have different features, and the features in the same region should be similar^[9]. Image segmentation is the basis of image information processing technology, which affects the results of other important steps such as image feature segmentation and target detection. The most common image segmentation methods are threshold segmentation, region segmentation, edge segmentation, and histogram method^[10]. Among these methods, the gray threshold segmentation method is one of the most commonly used parallel region technologies, and it is the most widely used type of image segmentation^[11].

The comprehensive changes in each indicator and score of both groups after the patients with craniocerebral injury underwent decompressive craniectomy are compared and retrospectively analysed to explore the effects of early repair of traumatic skull defect on the recovery of neural functions. Then, based on the fuzzy adaptive weight mixed active contour model algorithm, the image information of the brain injury

area of patients with craniocerebral injury is extracted, which provides powerful theoretical guidance for the development of cranial medical image information technology.

Patients between 16 and 70 y of age with no other serious diseases were included; the coalescence of the scalp after decompressive craniectomy was satisfied, without any infections or complications. When the patient was admitted to the hospital due to trauma, the Glasgow outcome scale (GOS) score was measured, and the National Institutes of Health stroke scale score must be greater than or equal to 7 points^[12]. A patient whose intracranial pressure is abnormal after decompressive craniectomy, with subcutaneous hydrops and infections were excluded from the study. Patient with serious organ diseases, medical history of diabetes mellitus, and intracranial hematoma and cerebral oedema were excluded and a patient whose history of the disease is vague or incomplete; a patient who suffers from severe complications after decompressive craniectomy were excluded.

A retrospective analysis was performed on 60 patients with traumatic craniocerebral injury. After various tests to confirm the compliance with the criteria, the patients were divided into two groups, i.e. the early group and the routine group. There were 30 patients in the early group, 17 females and 13 males, aged between 16 and 70 y, with an average age of 38 ± 9.4 y; the area of craniocerebral defects was 45-73, with an average of 61.53 ± 4.86 ; in the group, 12 patients underwent bilateral decompressive craniectomy and the remaining 18 patients underwent unilateral decompressive craniectomy. There were 30 patients in the routine group, 12 females and 18 males, aged between 16 and 70 y, with an average age of 35 ± 10.5 y; the area of craniocerebral defects was 49-76, with an average of 64.73 ± 5.68 ; in the group, 22 patients underwent unilateral decompressive craniectomy and the remaining 8 patients underwent bilateral decompressive craniectomy. The early group and the routine group were comparable in terms of gender, age, physical condition, physical fitness index, degree of craniocerebral defect, and postoperative recovery, and the differences were not statistically significant ($p > 0.05$).

Along the brain defect site of the patient, the skin was cut from the subcutaneous and galea aponeurotica with a scalpel. The cutaneous flaps and muscles of the

defect site were separated, and the inverted cutaneous flaps were fixed with threads to fully expose the skull defect. At the edge of the skull defect, the cerebral dura mater was gently cut open. If the incision is too large, it should be immediately repaired with a cerebral dura mater patch to prevent leakage of cerebrospinal fluid. Electric coagulation was used during the whole operation to prevent postoperative hematoma. The prepared titanium mesh was trimmed according to the size and shape of the skull defect; after being trimmed, it was disinfected. Next, the titanium mesh was placed in the large brain defect site for complete coverage repair. The titanium plate was firmly fixed to the skull with a titanium nail. If the area of the defect is large, in order to prevent postoperative subcutaneous fluid accumulation and infection, the cerebral dura mater should be fixed at the defect centre of the titanium mesh. The muscle layer was sutured, the galea aponeurotica, the scalp, and the subcutaneous drainage tube were sutured; then, the incision was dressed, and the subcutaneous drainage tube was connected to the vacuum suction device. At this point, the operation was completed, and the patient was taken to the ward for rest after the operation was completed^[13].

After the operation, close attention should be paid to the indicators and physical conditions of patients in both groups; the head CT scans were re-examined; the absence or presence of complications should be noticed; the respiratory tracts of patients should be smooth, infections should be prevented, and patients should stay in good moods^[14]. Next, 2 w after the physical indicators of patients were stabilized, the NIHSS and GOS scores were performed on patients in both groups; 6 mo after the trauma, the NIHSS scores were performed on patients in both groups. Then, respectively in the 1st, 3rd, and 12th mo after operations, the GOS, Karnofsky performance status (KPS) and the NIHSS scores were performed on patients in both groups to analyse and evaluate the effects of early repair on the neural functions of patients in both groups^[15].

The recent treatment effects of patients undergoing cranioplasty were compared first and then the treatment effects of patients undergoing cranioplasty were compared and analyzed respectively in the 1st, 3rd, and 12th mo after operations. The GOS and NIHSS scores were performed 2 w after decompressive craniectomy, and GOS and NIHSS scores were performed 6 mo after the trauma. The GOS, KPS, and NIHSS scores were performed respectively in the 1st, 3rd, and 12th mo

after decompressive craniectomy, and the therapeutic effects of the early group and the routine group were evaluated.

The contours in the parametric active contour model can be represented by a parametric curve composed of a series of discrete points. The parametric active contour model needs to minimize the internal energy function, which is the deformation of the contour curve and constantly approaching the target contour. The contour curve of the parametric active contour model could be expressed through the following Eqn. 1, $X(s) = [x(s), y(s)]$, where $X(s)$ is the coordinate function on the contour curve and $s \in [0, 1]$ is the normalized arc length parameter.

Therefore, the total energy function of the parametric active contour model can be expressed as Eqn. 2, $E_{\text{snake}} = \int E_{\text{in}}(X(S)) + E_{\text{ext}}(X(s)) ds$, where $E_{\text{in}}(X(S)) = \frac{1}{2}[\alpha |X'(S)|^2 + \beta |X''(s)|^2]$ is the internal function, and this energy internal function can maintain the smoothness of the contour curve. $X'(s)$ is the curvature of the contour curve and $X'(S)$ is the slope of the contour curve. The slope of the contour curve can reflect the smoothness and continuity of the function curve well, and the curvature of the contour curve can reflect the degree of tension of the function curve. E_{ext} is the external energy function of the contour curve, which is defined according to the data of the image. This function makes the contour curve close to the target area, which can make the curve in the image deform and continuously approach the target contour so that the curve reaches the minimum value at the boundary. α can reflect the shrinkage rate of the contour curve. As can be inferred from Eqn. 2, α is proportional to the shrinkage rate of the contour curve. The larger α is, the faster the curve contracts and the smaller α is, the slower the curve contracts. β is used to represent the weight coefficient of the curvature term, which can reflect the speed at which the contour curve approaches the target contour. When β is larger, the contour curve is less likely to be deformed. When β is smaller, the contour curve is more flexible, and the shape is more likely to change. In the process of curve evolution, the correct selection of these 2 parameters has a significant impact on the segmentation results.

In order to solve the problem of relying on the evolution curve parameters in the contour model, a method of geometric active contour model has been proposed. This method can be implemented by using the level set method and has good stability in numerical calculation.

Moreover, the geometric active contour model can adaptively process the changes of the curve topology to achieve multi-objective image segmentation. This makes the geometric active contour model widely used in the field of medical image information extraction. The basic Eqns. for the contour curve motion of an evolved geometric active contour model is Eqn. 3, $\frac{\partial c}{\partial t} = v(K, I)N$, in which, t represents time, c represents the contour curve of the evolution of the energy function, $v(K, I)$ represents the change curve and the velocity curve of the value, and N represents the unit vector. The above equation can reflect the changes in the evolution curve along the direction of the unit normal at the velocity v . K represents the internal force of the energy function in the model, which can keep the contour curve smooth.

According to the different energy functions, the geometric active contour model was divided into 2 types, one is the active contour model based on the region, and the other is the active contour model based on the boundary. The region-based active contour model was mainly discussed in the study. The region-based active contour model uses the internal and external statistical information of the evolution curve as the energy functions of the model. It can control the segmentation effect of the evolution curve on the weak boundary very well so that it can correctly extract the image information of the target area. Compared with the region-based active contour model, the principle of the boundary-based active contour model is that the evolution of the curve can ultimately stop at the target boundary based on the gradient flow of the image. In terms of images with weak boundaries, the boundary-based active contour model is difficult to properly stop the evolution curve at the target boundary. Due to the frequent occurrence of weak boundaries in medical images, the boundary-based active contour model is not the ideal model to segment and extract target regions in medical images.

The data in both groups were classified by using statistical methods. The clinical data of both groups were expressed as the mean number \pm the standard deviation (SD). The group-designed t-test was used to compare the averages of both samples. The χ^2 test was used to calculate and compare the ratios of both groups. The SPSS 19.0 statistics software was used to process the obtained data, the test level is $\alpha=0.05$, and $p<0.05$ indicates statistical significance.

The GOS scores of the early group and the routine group 2 w after decompressive craniectomy and 6 mo after trauma are shown in the following Table 1. It can be seen from Table 1 that the GOS score of the early group 2 w after decompressive craniectomy was 3.24 ± 0.457 , and the GOS score of the routine group 2 w after decompressive craniectomy was 3.05 ± 0.573 . The difference was not statistically significant ($p>0.05$). The GOS score of the early group 6 mo after trauma was 3.67 ± 0.682 , and the GOS score of the routine group 6 mo after trauma was 3.29 ± 0.714 . The difference was statistically significant ($p<0.05$).

The NIHSS scores of 2 w after decompressive craniectomy and 6 mo after trauma in the early group and the routine group are shown in the Table 1. It can be seen from Table 1 that the NIHSS score of the early group 2 w after decompressive craniectomy was 22.43 ± 5.231 , while that of the routine group was 23.57 ± 4.896 . The difference between the routine group and the early group was not statistically significant. The NIHSS score of the early group 6 mo after trauma was 13.84 ± 4.789 , and that of the routine group was 17.02 ± 6.453 . The difference between the routine group and the early group was statistically significant ($p<0.05$).

The comparisons of GOS, KPS, and NIHSS scores between patients in both groups in the 1st mo after operations are shown in the Table 2. As can be seen from Table 2, in the early group, the GOS, KPS, and

TABLE 1: COMPARISON OF GOS, NIHSS SCORES BETWEEN 2 WEEKS AFTER DECOMPRESSIVE CRANIECTOMY AND 6 MONTHS AFTER TRAUMA

	GOS scores of 2 w after decompressive craniectomy	GOS scores of 6 mo after the trauma
The early group	3.24 ± 0.457	3.67 ± 0.682
The routine group	3.05 ± 0.573	3.29 ± 0.714
pvalue	$p>0.05$	$p<0.05$
	NIHSS scores of 2 w after decompressive craniectomy	NIHSS scores of 6 mo after the trauma
The early group	22.43 ± 5.231	13.84 ± 4.789
The routine group	23.57 ± 4.896	17.02 ± 6.453
P Value	$P>0.05$	$P<0.05$

Mean number \pm standard deviation

NIHSS score were respectively 3.23 ± 0.67 , 52.23 ± 7.54 , and 6.75 ± 0.23 in the 1st mo after operation. The differences were not statistically significant ($p>0.05$). In the routine group, the GOS, KPS, and NIHSS score were respectively 2.94 ± 0.37 , 51.42 ± 4.68 , and 6.32 ± 0.24 . The differences between these data were not statistically significant ($p>0.05$).

The comparisons of GOS, KPS, and NIHSS scores between patients in both groups in the 3rd mo after operations are shown in the Table 2. As can be seen from Table 2, in the early group, the GOS, KPS, and NIHSS score were respectively 4.03 ± 0.32 , 63.15 ± 6.43 , and 4.35 ± 0.19 in the 3rd mo after operations. The differences between these data were not statistically significant ($p<0.05$). In the routine group, the GOS, KPS, and NIHSS score were respectively 3.46 ± 0.37 , 53.24 ± 6.28 , and 6.03 ± 0.41 in the 3rd mo after operations. The differences between these data were statistically significant ($p<0.05$).

The comparisons of GOS, KPS, and NIHSS scores between patients in both groups in the 12th mo after operations are shown in the Table 2. As can be seen from Table 2, in the early group, the GOS, KPS, and NIHSS score were respectively 4.76 ± 1.025 , 72.17 ± 2.989 , and 12.03 ± 5.156 in the 12th mo after operations. The differences between these data were statistically significant ($p<0.05$). In the routine group, the GOS, KPS, and NIHSS score were respectively

3.24 ± 0.953 , 63.48 ± 4.017 , and 15.23 ± 4.963 . The differences between these data were statistically significant ($p<0.05$).

In the early group, no hydrops under the cerebral dura mater have occurred to patients underwent early repair of traumatic craniocerebral injury; in the routine group, 5 cases of sub-cerebral dura mater hydrops have occurred. Thus, it can be seen that the ratio of the early group was significantly lower than that of the routine group, and the difference was statistically significant ($p<0.05$). In the early group, complications have occurred to 5 patients; in the routine group, complications have occurred to 8 patients. After statistical analysis, the difference was not statistically significant ($p>0.05$).

In the early group, after decompressive craniectomy, 2 patients have developed subcutaneous hydrops; in the routine group, 2 patients have developed subcutaneous hydrops. After the treatments of compression and dressing of the subcutaneous incision, the incision has recovered well. In the early group, 2 patients have developed complications; in the routine group, 1 patient has developed complications. The local TDP lamp irradiation and dressing treatment are performed on the suture incision again. It was found that the incision has recovered well. In the early group, there is still 1 case of intracranial infection. In the routine group, there are no cases of intracranial infection. The cerebrospinal fluid in the intracranial wound was continuously drained and the combined treatment with antiinflammatory drugs was given. Afterward, the incision has recovered well, and neither complications nor infections were observed through long-term observation.

In order to better prove that the experiment algorithm has good operability for medical image information extraction in the brain, the craniocerebral injury images of 20 patients were extracted and analysed, and the number of iterations, the convergence, and the accuracy of the results are counted. As can be seen from the following Table 3, the number of iterations and time spent by the proposed algorithm is less than that of the CV model and the LRBAC algorithm. Moreover, the image accuracy of the experiment algorithm is higher than that of the CV model and the LRBAC algorithm. Compared with the Jaccard coefficients of the CV model and the LRCC algorithm, the Jaccard coefficient of the experiment algorithm was significantly higher than the other 2 algorithms.

TABLE 2: GOS, KPS AND NIHSS SCORES IN THE 1ST, 3RD, 12TH MONTH AFTER OPERATION

1st month after operations in both groups			
Groups	GOS scores	KPS scores	NIHSS scores
The early group	3.23 ± 0.67	52.23 ± 7.54	6.75 ± 0.23
The routine group	2.94 ± 0.37	51.42 ± 4.68	6.32 ± 0.24
t	0.415	0.743	0.537
p value	$p>0.05$	$p>0.05$	$p>0.05$
3rd month after operations in both groups			
The early group	4.03 ± 0.32	63.15 ± 6.43	4.35 ± 0.19
The routine group	3.46 ± 0.37	53.24 ± 6.28	6.03 ± 0.41
t	3.357	4.149	3.742
P Value	$p<0.05$	$p<0.05$	$p<0.05$
12th month after operations in both groups			
The early group	4.76 ± 1.025	12.03 ± 5.156	72.17 ± 2.989
The routine group	3.24 ± 0.953	15.23 ± 4.963	63.48 ± 4.017
P Value	$p<0.05$	$p<0.05$	$p<0.05$

TABLE 3: COMPARISON BETWEEN EXTRACTION RESULTS OF MEDICAL INFORMATION FROM IMAGES OF 20 PATIENTS WITH CRANIOCEREBRAL INJURY

	Iterations	Time consumption (s)	Jaccard coefficient	Dice coefficient
CV model	114.5	7.886	0.736478	0.9326746
LRBAC algorithm	92.3	5.89642	0.7489563	0.9541237
Experiment algorithm	77.48	5.35864	0.89653868	0.89478695

The complications of patients with craniocerebral injury after decompressive craniectomy were mainly observed and counted. In the early group, there was no sub-cerebral dura mater hydrops; in the routine group, there were 5 cases of sub-cerebral dura mater hydrops. The ratio of the routine group was significantly higher than that of the early group. After statistical analysis, the difference was statistically significant ($p < 0.05$). A total of 5 patients in the early group have developed complications such as sub-cerebral dura mater hydrops, and 8 patients in the routine group have developed complications. However, there was no significant difference in the overall complication rate between the early group and the routine group ($p > 0.05$). In terms of medical image information extraction, 2 different algorithms of the active contour model were studied, and a hybrid active contour model algorithm was proposed based on adaptive weights. The improvement of the proposed algorithm could effectively segment the gray-scale image; in addition, the improved method has higher definition and precision for medical image information extraction. In summary, the following conclusions were drawn: the early repair of traumatic craniocerebral injury could effectively improve the recovery of neural functions and the quality of life of patients, which has high value in clinical application. The general traumatic craniocerebral injury has no complications after primary operation; under the condition of normal recovery of intracranial pressure, early repair operation should be performed as soon as possible, since it could not only improve the recovery time and recovery effects of patients but also reduce secondary damages to brain tissues. Target library initialization based on the adaptive weighted hybrid active contour model algorithm can effectively improve the convergence speed of the total energy function of the model, as well as improving the segmentation and extraction accuracy of the algorithm and the accuracy of medical image information.

REFERENCES

1. McMahon P, Hricik A, Yue JK, Puccio AM, Inoue T, Lingsma HF, *et al.* Symptomatology and functional outcome in mild traumatic brain injury: results from the prospective TRACK-TBI study. *J Neurotrauma* 2014;31(1):26-33.
2. Abbas K, Shenk TE, Poole VN, Breedlove EL, Leverenz LJ, Nauman EA, *et al.* Alteration of default mode network in high school football athletes due to repetitive subconcussive mild traumatic brain injury: a resting-state functional magnetic resonance imaging study. *Brain Connect* 2015;5(2):91-101.
3. Corps KN, Roth TL, McGavern DB. Inflammation and neuroprotection in traumatic brain injury. *JAMA Neurol* 2015;72(3):355-62.
4. Setiawan E, Wilson AA, Mizrahi R, Rusjan PM, Miler L, Rajkowska G, *et al.* Role of translocator protein density, a marker of neuroinflammation, in the brain during major depressive episodes. *JAMA Psychiatry* 2015;72(3):268-75.
5. Diaz-Arrastia R, Wang KK, Papa L, Sorani MD, Yue JK, Puccio AM, *et al.* Acute biomarkers of traumatic brain injury: relationship between plasma levels of ubiquitin C-terminal hydrolase-L1 and glial fibrillary acidic protein. *J Neurotrauma* 2014;31(1):19-25.
6. Hawryluk G, Whetstone W, Saigal R, Ferguson A, Talbot J, Bresnahan J, *et al.* Mean arterial blood pressure correlates with neurological recovery after human spinal cord injury: analysis of high frequency physiologic data. *J Neurotrauma* 2015;32(24):1958-67.
7. Vasquez BP, Tomaszczyk JC, Sharma B, Colella B, Green REA. Longitudinal recovery of executive control functions after moderate-severe traumatic brain injury: examining trajectories of variability and ex-Gaussian parameters. *Neurorehabil Neural Repair* 2018;32(3):191-9.
8. Perry SB, Billek-Sawhney B, Woollard J, Little S, Szalinski A. Balance and mobility improvements during inpatient rehabilitation are similar in young-old, mid-old, and old-old adults with traumatic brain injury. *J Head Trauma Rehabil* 2019;34(2):E66-E73.
9. Grool AM, Aglipay M, Momoli F, Meehan WP, Freedman SB, Yeates KO, *et al.* Association between early participation in physical activity following acute concussion and persistent postconcussive symptoms in children and adolescents. *JAMA* 2016;316(23):2504-14.
10. Shively SB, Horkayne-Szakaly I, Jones RV, Kelly JP, Armstrong RC, Perl DP. Characterisation of interface astroglial scarring in the human brain after blast exposure: a post-mortem case series. *Lancet Neurol* 2016;15(9):944-53.
11. Colonna M, Butovsky O. Microglia function in the central nervous system during health and neurodegeneration. *Annu Rev Immunol* 2017;35:441-68.
12. Failla MD, Conley YP, Wagner AK. Brain-Derived Neurotrophic Factor (BDNF) in traumatic brain injury-related mortality: interrelationships between genetics and acute systemic and central nervous system BDNF profiles. *Neurorehabil Neural Repair* 2016;30(1):83-93.

13. Barnes DE, Byers AL, Gardner RC, Seal KH, Boscardin WJ, Yaffe K. Association of mild traumatic brain injury with and without loss of consciousness with dementia in US military veterans. *JAMA Neurol* 2018;75(9):1055-61.
14. Jullienne A, Obenaus A, Ichkova A, Savona-Baron C, Pearce WJ, Badaut J. Chronic cerebrovascular dysfunction after traumatic brain injury. *J Neurosci Res* 2016;94(7):609-22.
15. Hayes JP, Bigler ED, Verfaellie M. Traumatic brain injury as a disorder of brain connectivity. *J Int Neuropsychol Soc* 2016;22 (2):120-37.

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This article was originally published in a special issue, "Clinical and Experimental Studies on Drug and Intervention Repurposing in China" *Indian J Pharm Sci* 2019;81(4)spl issue1;169-175