Journal of the Neurological Sciences 294 (2010) 23–28

Contents lists available at ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

Development of a rat model for studying blast-induced traumatic brain injury

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ARTICLE INFO

Article history:
Received 31 August 2009
Received in revised form 22 March 2010
Accepted 20 April 2010
Available online 16 May 2010

Keywords:
Blast
Traumatic brain injury
Animal model

ABSTRACT

Blast-induced traumatic brain injury (TBI) has been the predominant cause of neurotrauma in current military conflicts, and it is also emerging as a potential threat in civilian terrorism. The etiology of TBI, however, is poorly understood. Further study on the mechanisms and treatment of blast injury is urgently needed. We developed a unique rat model to simulate blast effects that commonly occur on the battlefield. An electric detonator with the equivalent of 400 mg TNT was developed as the explosive source. The detonator's peak overpressure and impulse of explosion shock determined the explosion intensity in a distance-dependent manner. Ninety-six male adult Sprague–Dawley rats were randomly divided into four groups: 5-cm, 7.5-cm, 10-cm, and control groups. The rat was fixed in a specially designed cabin with an adjustable aperture showing the frontal, parietal, and occipital parts of the head exposed to explosion; the eyes, ears, mouth, and nose were protected by the cabin. After each explosion, we assessed the physiologic, neuropathologic, and neurobehavioral consequences of blast injury. Changes of brain tissue water content and neuron-specific enolase (NSE) expression were detected. The results in the 7.5-cm group show that 87% rats developed apnea, limb seizure, poor appetite, and limpness. Diffuse subarachnoid hemorrhage and edema could be seen within the brain parenchyma, which showed a loss of integrity. Capillary damage and enlarged intercellular and vascular space in the cortex, along with a tattered nerve fiber were observed. These findings demonstrate that we have provided a reliable and reproducible blast-induced TBI model in rats.

1. Introduction

In modern wars such as those in Iraq and Afghanistan, blast-induced TBI has become a major cause of mortality and morbidity [1–3]. This has become the case in domestic terrorist acts as well [4,5]. Most of previous studies on blast injuries focused on damage to thoracic and abdominal organs [6]; much less is known about blast injury to the brain.

Injury can occur through several complicated mechanisms: primary blast injury, secondary injury, tertiary injury, and quaternary injury [7–9]. Primary blast injury refers to effects from the blast overpressure wave itself. During explosion, blast waves generate extreme pressure changes that can cause stress and shear injuries. In addition, the blast wave that follows the overpressure wave can propel with considerable force objects such as shrapnel contained within improvised explosive devices, causing secondary injury. The blast wave may also cause the individual to be knocked down or blown into solid objects, resulting in tertiary injury. Finally, the heat produced by improvised explosive devices may cause burns, or injuries may result from the inhalation of noxious gases, which is known as quaternary injury.

Primary blast injury has become the most-studied area with new emphasis on blast injury to the brain. Nakagawa et al. [10] developed a shock wave-induced brain injury model by focusing a microexplosion-generated shock wave in the rat brain. Long et al. [11] studied TBI in rats by using a shock tube-generated airblast. We found there were some limitations in their models. Most important of all, we found that the wave pattern of the shock wave generated by the shock tube is quite different with that generated by improvised explosive devices at battlefields. The most difficult problems in establishing an animal model for studying blast injury are finding a stable, reliable explosion source, and then how to delineate primary injury from secondary, tertiary, and quaternary injury. Pressure generators allow the effects of the primary blast wave itself to be studied and offer

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doi:10.1016/j.jns.2010.04.010

more experimental control. Under appropriate shielding, it is also possible to isolate the effects of blast injury to the body from those to the brain.

To address these issues, we have developed reliable experimental apparatus for studying cerebral blast injury in a rat model. It represented an improvement over existing models. Firstly, we used explosive materials — detonator to produce shock waves that mimic explosive weapons widely used on the battlefield, it shared the same chemical compound with commonly used weapons so that shock waves could be generated with the best possible accuracy. Secondly, we designed a cabin to separate the brain from eyes, ears, nose, and mouth, avoiding to confound the analysis of brain injury. By the application of appropriate shielding, it was also possible to isolate the effects of blast injury to the body from injury to the brain. The way in which the rat was fixed in the cabin also allowed us to separate primary injury from secondary, tertiary, and quaternary injury. Furthermore, the distance between the rat and source of explosion could be set at will to expose the rats to different impacts from the explosion, allowing effects of the primary blast wave itself to be studied and to offer more experimental control.

2. Materials and methods

The explosion source was a blast wave generated by an electric detonator with the explosive equivalent of 400 mg TNT (Changjiang Electric-Technical Co., Chongqing, P.R. China), consisting of 100 mg dinonyl ortho-phthalate and 250 mg trimethylene trinitroamine. All detonators were consistently made using the following parameters: density, 1.816 g/cm^3; and detonation velocity, 4000 m/s. A Wavebook/516A data acquisition system (Quatronix Inc., Akron, Ohio) and piezoelectricity potentiometric transducer (113A31, GuangZhou Compass Sensor Instrument Co., Ltd., GuangZhou, P.R. China) were used to detect the peak overpressure and other parameters of the explosion blast wave, and the specially designed cabin and diagram of explosive scenario (Fig. 1).

Ninety-six male adult Sprague–Dawley rats weighting between 250 g and 300 g (Experimental Animal Center of Sichuan University, Chengdu City, Sichuan Province, P.R. China) were randomly divided into four groups including a 5-cm group (30 rats), 7.5-cm group (30 rats), 10-cm group (30 rats), and control group (6 rats). The first three groups were randomly divided based on days from injury into five subgroups containing six rats each: 1 d, 2 d, 3 d, 5 d, and 7 d. Animal procedures were approved by the Institutional Animal Care and Use Committee of the Sichuan University. Before explosion, the rats were anesthetized by an intraperitoneal injection of 1.5 mg (1.5%, 1 ml) of pentobarbital sodium. Then the anesthetized rat was fixed with a flexible string on the inner side of the cabin with the occipital portion of the head facing the aperture (Fig. 1A). After fixation, the entire head was exposed through the window; the portions below the foramen magnum and above inner canthus were protected from explosion (Fig. 1B).

After explosion, the physiologic and neurobehavioral indices were recorded, including appetite, behavior, and survival time. Animals in each subgroup were studied on the same day. The brain

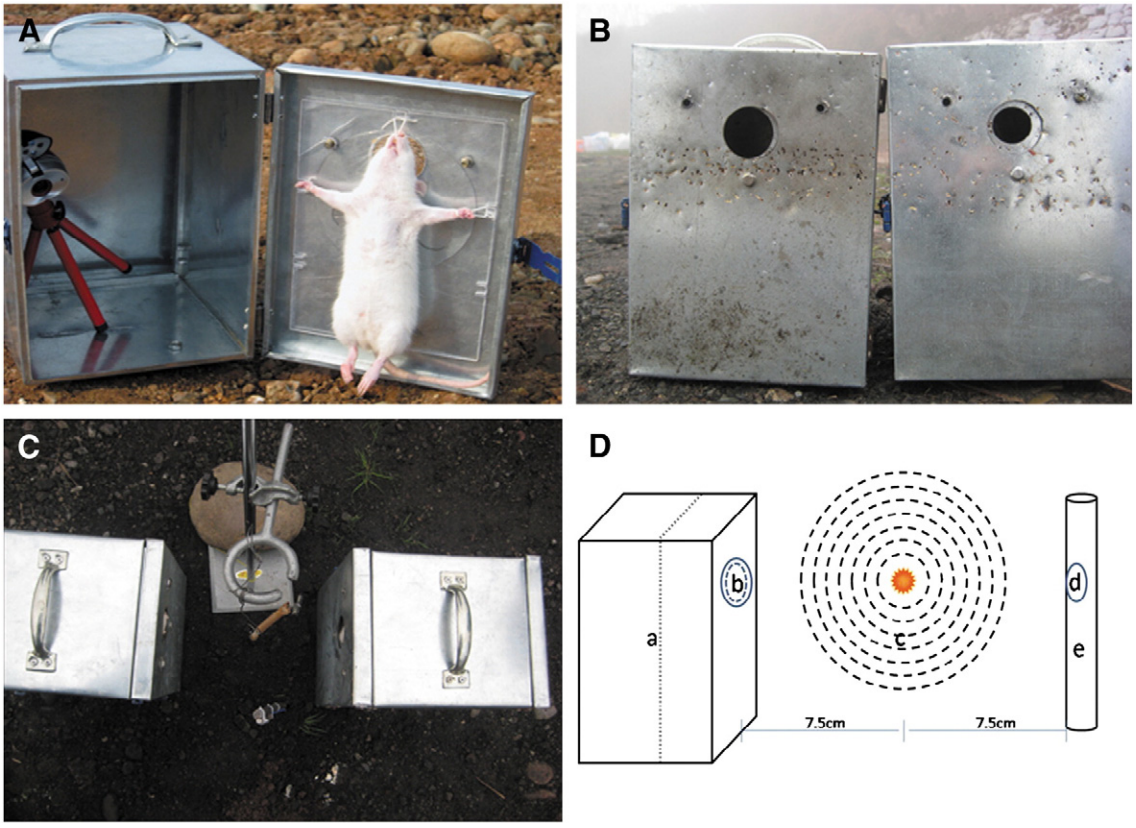

Fig. 1. (A) The specially designed cabin in which rat and monitor were fixed was made with aluminium, was 30 cm high, 20 cm wide, and 20 cm long, and weighed 5.0 kg. The monitor recorded the behaviors of the injured rats. (B) A 2–5-cm diameter round, adjustable aperture was placed in the lateral wall of the cabin. Through the aperture, the blast wave released by the electric detonator in the outer portion of the cabin damage the fixed rat. (C) The piezoelectricity potentiometric transducer fixed on a steel column with the same height as rat head was placed outside the cabin, and its distance from the detonator and rat head was equal. After the explosion, the overpressure signal of shock was transmitted to the Wavebook/516A data acquisition system. All the signals were recorded and analyzed using 7.0 software. (D) Diagram of explosive scenario: a: explosive cabin; b: adjustable aperture; c: explosive source; d: piezoelectricity potentiometric transducer; and e: steel column for fixing piezoelectricity potentiometric transducer. b and d have the same height, and the same distance from the detonator.

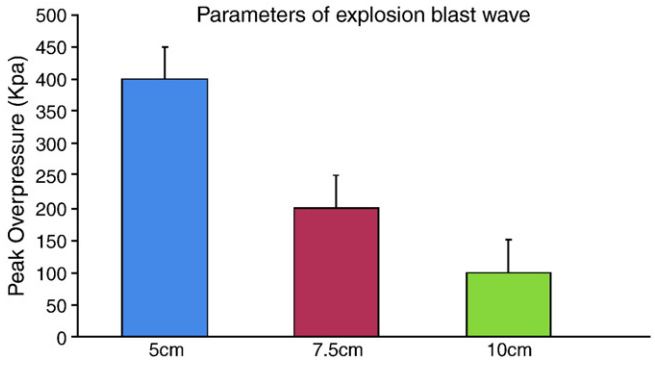

Fig. 2. Peak overpressure ranged from 103 to 396 kPa, showed obviously different ($p<0.01$) when compared with each other.

tissues and blood samples were obtained and the following were studied: (1) histopathologic changes; (2) neuron-specific enolase (NSE) expression changes; and (3) tissue water content changes. The detection kit for serum NSE and primary rabbit antirat antibody were purchased from a commercial vendor (0700409, Lengton Bioscience Co., Shanghai, P.R. China).

Two milliliters of blood was drawn from the rats postexplosion by stabbing the heart directly to detect the serum NSE concentration. After centrifuging for 5 min at 3000 rpm, the supernatant was separated and stored in a −70 °C refrigerator for later use. The NSE concentration was detected with an enzyme-linked immunosorbent assay method.

2.1. Histopathological examination

Rats in every subgroup were killed on the same day by cervical dislocation and they underwent craniotomy immediately. Brain tissue was harvested from the following injured areas: temporal, parietal, and occipital lobes and the cerebellum and brain stem. The tissues were initially fixed with 10% formalin, dehydrated by graded ethanol, and then embedded in paraffin. 0.5 mm-thick slices were cut and stained with hematoxylin and eosin. All the slices were observed by two independent neuropathologists.

2.2. Immunohistochemical detection of NSE in cortex neurons

For immunohistochemistry, 5-μm-thick serial sections were cut from paraffin-embedded rat brain specimens. The sections were routinely deparaffinized and rehydrated; detections were performed according to the manufacturer's instructions (SABC detection kit).

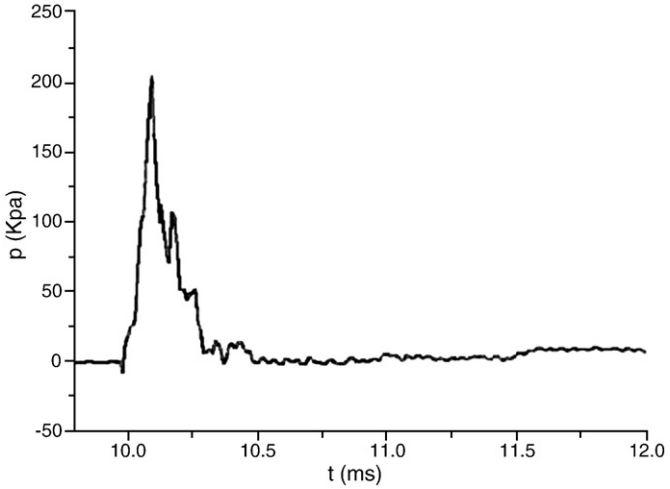

Fig. 3. Components and wave pattern of the blast pressure wave. Peak overpressure in the 7.5-cm group was 204 kPa.

2.3. Measurement of brain water content

Approximately 0.6 g brain tissue was obtained and the wet weight was accurately obtained using an electronic balance. It was baked in a 100 °C-oven for 24 h and the dry weight was obtained. The percentage of change in water content was calculated using the following formula: water content changing percentage (%) = (wet weight − dry weight) / wet weight × 100%.

2.4. Data analysis

All statistical analyses were performed using a commercially available software package (SPSS11.0, Chicago IL). The blast

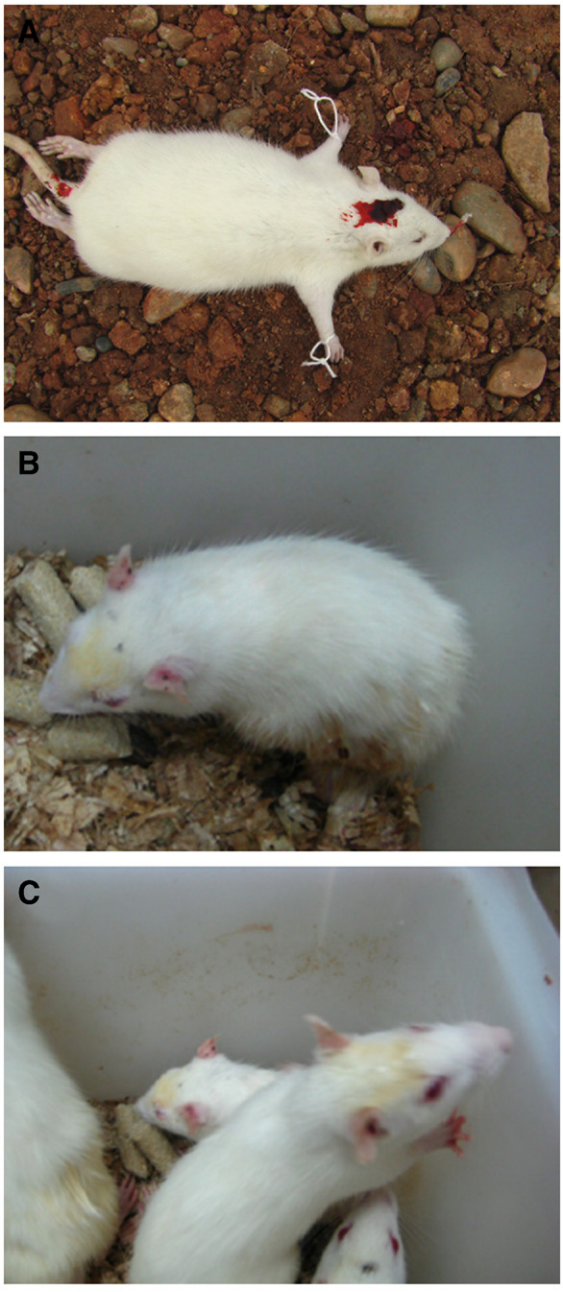

Fig. 4. (A) After the explosion, the rats in the 5-cm group died immediately. (B) The rats in the 7.5-cm group showed poor mental status. (C) The 10-cm group was still active.

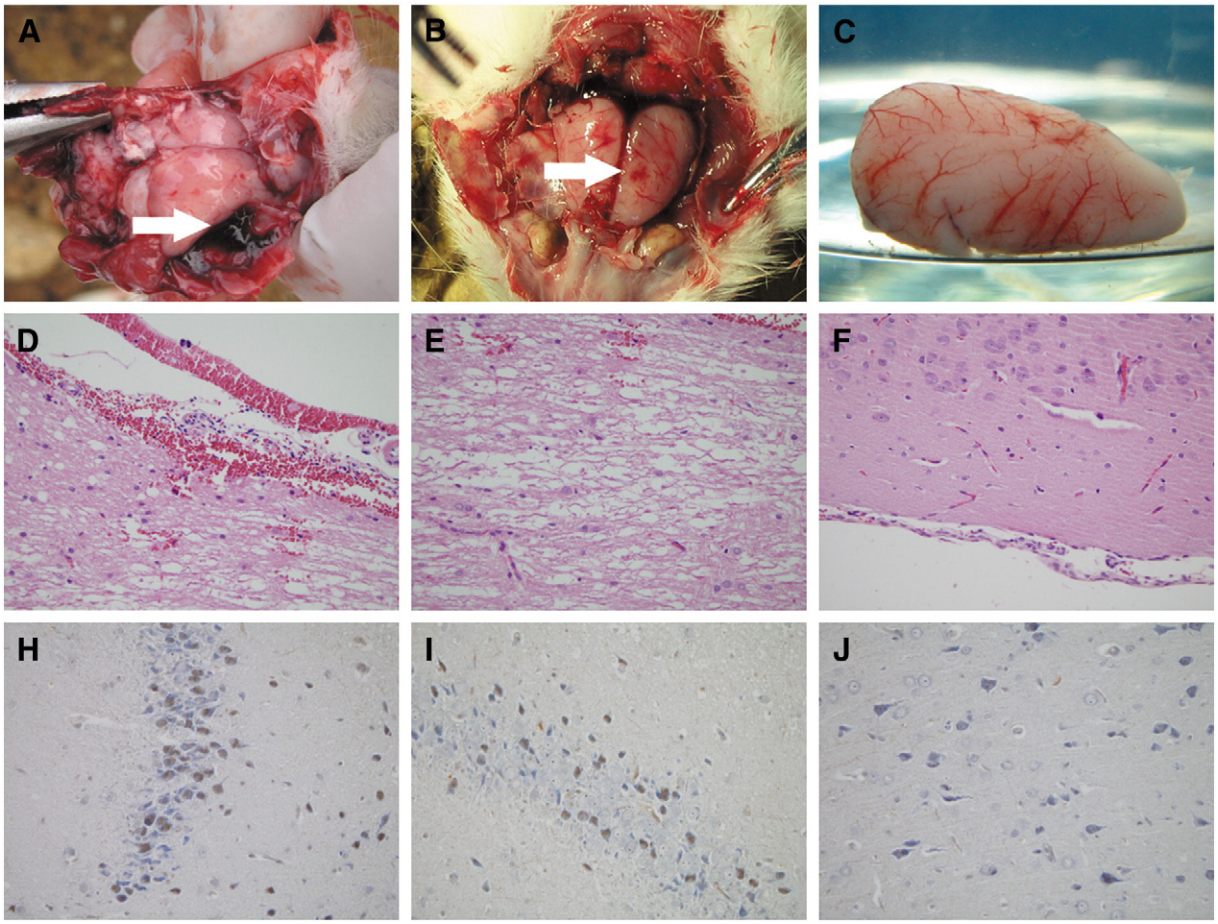

Fig. 5. Gross observation and histopathological examination of rat brain tissues. (A) In the 5-cm group, serious brain contusion, laceration, and hematoma were found (white arrow). (B) In the 7.5-cm group, the brain cortex was diffusively engorged with blood and loss of continuity was observed. Obvious contusion could be seen in frontal and parietal lobes (white arrow). (C) Diffuse subarachnoid hemorrhage and edema could be seen within the brain parenchyma. (D) In the 7.5-cm group, capillary damage, intercellular and vascular spaces were enlarged in the cortex. (H & E, 400×). (E) In the 7.5-cm group, tattered nerve fiber was observed. (H & E, 400×). (F) In the 10-cm group, cortex injury was slighter, and structures were intact (H & E, 400×). (H–J) Immunohistochemical staining for NSE in the control group, the 10-cm group (H), and the 7.5-cm group (I,J).

overpressure value, duration of apnea, level of serum NSE, and the number of positive NSE cells in the cortex as well as the water content for each group of specimens were expressed as mean ± standard deviation and analyzed by two-way analysis of variance, adjusting for multiple comparisons or two-sample *t* test. Apnea and seizures were analyzed by chi-square test. All reported *p* values were two sided, and $p<0.05$ was considered statistically significant.

3. Results

3.1. Peak overpressure of the explosion blast wave

The average peak overpressure ranged from 100 kPa to 400 kPa (Figs. 2 and 3); therefore, we adopted three distances 5.0 cm, 7.5 cm, and 10 cm by which to divide the rats into different groups.

3.2. Physiologic and neurobehavioral observation

Nine rats (30%) in the 5-cm group died in the explosion (Fig. 4A); all survivors in this group died in the next 3 d so further study of the brain water content and histopathologic examination could not be carried out (Fig. 5A). All rats in the 7.5-cm and 10-cm groups survived the explosion. Breathing rhythm changed in all groups after the explosion. The clinical manifestations included apnea, followed by partial recovery of respiration, which was slow and deep and then accelerated gradually; and seizure for 3–12 s. After the explosion the rats appeared limp and sluggish and they had poor appetites when awake (Table 1). The rats in the 7.5-cm group displayed inactive (Fig. 4B), but rats in the 10-cm group were active in 10 cm (Fig. 4C).

3.3. Serum NSE concentration

At 1 d after the explosion, the NSE concentration in the 7.5-cm group peaked and was three times that in the control group ($p<0.01$). Thereafter the NSE concentration decreased continuously but was still higher compared with control groups at 3 d; by 5 d it was near normal. The NSE concentration in the 10-cm group increased early after the explosion, but decreased rapidly, and went back to normal at 2 d ($p<0.01$) (Table 2).

Table 1
Observation of physiology and neurobehavioral.

Group	Cases of apnea* (%)	Duration of apnea	Cases of seizure** (%)	Survival time (d)
5.0-cm	29 (96.7)	28.6 ± 5.8	27 (90.0)	$2.1^{\triangle\triangle}$
7.5-cm	22 (73.3)	$25.3 \pm 3.2^{\triangle}$	25 (83.3)	7
10.0-cm	11 (36.7)	12.5 ± 3.6	14 (46.7)	7

Immediate apnea and seizure were seen in all the three groups ($^{*}p<0.05$, $x^2=25.61$; $^{**}p<0.01$, $x^2=16.7$). Duration of apnea and survival times were obviously different ($^{\triangle}p<0.01$ when compared with the 10-cm group; $^{\triangle\triangle}p<0.01$when compared with the 7.5-cm and 10-cm groups).

Table 2
NSE concentration in serum.

Group	No.	NSE concentration in serum (ng/L)				
		1 d	2 d	3 d	5 d	7 d
Control	6	3.41 ± 0.13				
5.0-cm	30	–	–	–	–	–
7.5-cm	30	10.27 ± 1.18*	7.08 ± 0.83*	6.27 ± 1.18*	4.28 ± 0.86	3.87 ± 0.63
10-cm	30	5.77 ± 0.18*△	4.24 ± 0.96△	4.08 ± 0.82△	3.90 ± 0.65	3.68 ± 0.55

*$p<0.05$ when compared with the control group; △$p<0.05$ when compared with the 7.5-cm group.

3.4. Histopathological examination

In the 7.5-cm group, the brain cortex was engorged and showed a loss of integrity by gross observation; obvious contusion could be seen in frontal and parietal lobes (white arrow) (Fig. 5B). Diffuse subarachnoid hemorrhage and edema could be seen within the brain parenchyma (Fig. 5C). Light microscopy revealed capillary damage, enlarged intercellular and vascular spaces in cortex, and tattered nerve fiber (Fig. 5D,E). In the 10-cm group, injury to the cortex was minor; structures were intact and no contusion was evident (Fig. 5F).

3.5. Immunohistochemical detection of NSE in cortex neuron

The NSE staining intensity of the brain cortex in the 7.5-cm and 10-cm groups was lower than that in the control group (Fig. 5H,I,J). In the 7.5-cm group, the number of positive NSE cells at 2 d postexplosion was the lowest among all the time points. In the 10-cm group, that number at 1 d postinjury was the lowest (Table 3).

3.6. Measurement of brain water content

Brain water content in the 7.5-cm and 10-cm groups was significantly higher than that in the control group. After the explosion, the water content of the brain in the 7.5-cm group continually increased, reaching its peak at 3 d, and went back to normal in 5–7 d. In the 10-cm group, the water content of brain tissue reached peak in 1 d postexplosion, showing no significant differences with the 7.5-cm group at this time point, but it was significantly lower than that of the 7.5-cm group at each time point thereafter ($p<0.05$), and returned normal rapidly (Table 4).

4. Discussion

After the explosion of the electric detonator, blast waves accelerate at high pressure and high speed through the air and generate extreme pressure changes that can produce shearing damage to the brain because of the different traveling velocities [7,8]. Furthermore, the cavity is the effect when blast waves enter the brain because it is an inhomogeneous medium. Shifting and resetting of brain tissue could be another cause of injury [7,12]. We believe that primary blast injury is the major cause of neurotrauma. There were lots of factors influencing blast injuries, including blast wave velocity, peak overpressure, increased pressure duration, and ambient pressure. The peak overpressure was the major factor determining the level of blast injury, and it was distance dependent [13,14]. Measurement of the explosion shock showed that the blast waves produced by electric detonators in this study were stable. This study demonstrated that the application of blast waves generated by an electric detonator resulted in cerebral contusion and hemorrhage in the brain parenchyma in repeatable manner, which is similar to the findings in other organs, such as kidney, liver, and lung, in which the injury is considered to be due to small vessel rupture [15,16].

In this study, nine rats (30%) in the 5-cm group died in the explosion, and the rest died 3 d later. The distance between the rats' heads and the detonator was so close that the peak overpressure and impulse were high enough to kill the animals. Neither the 5-cm group nor the 10-cm group agreed with the standard model which kept alive and hurt moderately after the explosion.

Comparison among groups showed that a shorter distance between the detonator and the rat's head was related to a more serious brain injury. Blast waves were transmitted through the cerebrospinal fluid to the medulla oblongata and affected the respiration center,

Table 3
The number of positive NSE cells in the cortex.

Group	No.	Number of positive NSE cells in the cortex				
		1 d	2 d	3 d	5 d	7 d
Control	6	66.03 ± 6.90				
5.0-cm	30	–	–	–	–	–
7.5-cm	30	45.36 ± 7.23*	41.36 ± 7.23*	44.89 ± 5.49*	48.97 ± 4.44*	50.28 ± 4.86*
10-cm	30	49.53 ± 7.39*	52.08 ± 6.80*△	54.08 ± 5.10*△	57.50 ± 7.41△	59.97 ± 7.17

*$p<0.05$ when compared with the control group; △$p<0.05$ when compared with the 7.5-cm group.

Table 4
Water content of brain.

Group	No.	Brain water content (%)				
		1 d	2 d	3 d	5 d	7 d
Control	6	74.68 ± 1.67				
5.0-cm	30	–	–	–	–	–
7.5-cm	30	78.97 ± 1.34*	80.27 ± 2.95*	82.59 ± 1.39*	77.37 ± 0.88	74.76 ± 1.05
10-cm	30	78.83 ± 1.09*	77.13 ± 1.41△	76.62 ± 1.08△	75.24 ± 1.27△	74.33 ± 0.99

*$p<0.05$ when compared with the control group; △$p<0.05$ when compared with the 7.5-cm group.

leading to apnea. The closer the distance, the more serious was the injury to the medulla oblongata, causing more serious the clinical manifestations. The incidence of apnea in the 5-cm group was significantly higher than that in the 7.5-cm and 10-cm groups, and recovery time of spontaneous breathing was much longer.

Studies suggested that the serum NSE concentration is a sensitive biomarker for the degree of brain injury [17]. In this study, the NSE concentration increased early postexplosion in the 7.5-cm group, reaching a peak at 1 d, which may imply the early leakage of intracellular NSE into the blood. Moreover, with worsening secondary damages and breakup of neurons, this leakage may have aggravated [18]. Serum NSE levels gradually decreased due to its degradation in the blood, which facilitated the recovery from brain injury as well as the improvement in the damaged blood–brain barrier. Based on the opinion of Hatfield and Mckernan, that the increasing amount of serum is closely related to the number of damaged neurons [19], we supposed that the brain damage was worse at 1 d postexplosion. The number of NSE-positive cells was significantly lower in the 7.5-cm group when compared with the normal control, with its low value appearing at 2 d postexplosion, demonstrating a delay in serum NSE peak. We suppose that the NSE-positive cell number is a better surrogate marker for injury because a balance between NSE released from cytoplasm and blood degradation was achieved at 1 d post-explosion, halting the serum NSE rise despite the neurons continuing to die and release NSE into the blood after this time point.

After the explosion, the water content of rats' brains in the 7.5-cm group continually increased, reaching a peak at 3 d, and returning to normal in 5–7 d. During transmission inside the head, blast wave may cause cerebrovascular injury as well [20]. Injured vessels cause cerebral edema. Inflammatory mediators released from contusions and intraparenchymal hemorrhage may cause hypoxia and ischemia of neurons and result in swelling and necrosis of neurons [21]. After that, cerebral edema worsens in scale and extent and water contents increased accordingly. It is considered that the degree of brain injury is proportionate to the extent of cerebral edema. Cerebral edema, which begins to emerge soon after the explosive blast wave hits the brain, may cause incremental increased intracranial pressure and aggravate brain injury.

Although Nakagawa et al. [10] developed a shock wave-induced brain injury model by focusing microexplosion-generated shock wave in the rat brain and Long et al. [11] studied TBI in rats by using a shock tube-generated airblast, we found that there were some limitations in their models. First, the source of explosion was problematic. Previous studies have not used explosive materials to produce shock waves that mimic explosive weapons widely used on the battlefield. In the present study, the electric detonators used shared the same chemical compound with commonly used weapons so that shock waves could be generated with the best possible accuracy. Moreover, repeated measurement ensured its stability as a reliable explosion source. Second, previous studies did not separate the brain from eyes, ears, nose, and mouth: damage to these organs during explosion can confound the analysis of brain injury. In the present study, the rats' other organs were protected by a specially designed cabin: only the head was exposed to explosion through the window, through which the blast wave was released in the outer portion of the cabin. By the application of appropriate shielding, it was also possible to isolate the effects of blast injury to the body from injury to the brain. The way in which the rat was fixed in the cabin also allowed us to separate primary injury from secondary, tertiary, and quaternary injury. Furthermore, the distance between the rat and source of explosion could be set at will to expose the rats to different impacts from the explosion, allowing the effects of the primary blast wave itself to be studied and to offer more experimental control.

Findings of the present study were consistent with the clinical manifestations of injuries seen on the battlefield, so this model may offer some advantage for the research into the mechanism of blast-induced TBI and its treatment. There are, however, many factors influencing blast injuries; this model still needs to be improved and optimized.

Author disclosure statement

No conflicting financial interests exist.

Acknowledgments

This work was supported in part by Key Medical Grant of 11th five years' plan from Chengdu Army Region (No. Z07002).

We thank Shi Yu-jun, Bao Ji, Li Xia, and Lu Min for the technical assistance.

References

[1] Tanielian T, Jaycox LH. Invisible wounds of war: psychological and cognitive injuries, their consequences, and services to assist recovery. Santa Monica, CA: Rand Corp; 2008.
[2] Shanker T. Iraqi bombers thwart efforts to shield G.I.s. New York Times; June 2 2007. p. 1.
[3] Warden D. Military TBI during the Iraq and Afghanistan wars. J Head Trauma Rehabil 2006;21:398–402.
[4] Frykberg ER. Medical management of disasters and mass casualties from terrorist bombings: how can we cope? J Trauma 2002;53:201–12.
[5] de Ceballos JP, Turegano-Fuentes F, Perez-Diaz D, Sanz-Sanchez M, Martin-Llorente C, Guerrero-Sanz JE. The terrorist bomb explosions in Madrid, Spain—an analysis of the logistics, injuries sustained and clinical management of casualties treated at the closest hospital. Crit Care 2005;9:104–11.
[6] Chavko M, Prusaczyk WK, McCarron RM. Lung injury and recovery after exposure to blast overpressure. J Trauma 2006;61:933–42.
[7] DePalma RG, Burris DG, Champion HR, Hodgson MJ. Blast injuries. N Engl J Med 2005;352:1335–42.
[8] Taber KH, Warden DL, Hurley RA. Blast-related traumatic brain injury: what is known? J Neuropsychiatry Clin Neurosci 2006;18:141–5.
[9] Kluger Y, Nimrod A, Biderman P. The quinary pattern of blast injury. Am J Disaster Med 2007;2:21–5.
[10] Nakagawa A, Fujimura M, Kato K, Okuyama H, Hashimoto T, Takayama K, et al. Shock wave-induced brain injury in rat: novel traumatic brain injury animal model, in Intracranial Pressure and Brain Monitoring XIII: mechanisms and treatment. Acta Neurochir Suppl 2008;102:421–4.
[11] Long JB, Bentley TL, Wessner KA, Cerone C, Sweeney S, Bauman RA. Blast over-pressure in rats: recreating a battlefield injury in the laboratory. J Neurotrauma 2009;26:1–14.
[12] Eastridge BJ, Blackbourne L, Wade CE. Radiologic diagnosis of explosion casualties. Am J Disaster Med 2008;3:301–5.
[13] Finkel MF. The neurological consequences of explosives. J Neurol Sci 2006;249: 63–7.
[14] Bochicchio GV, Lumpkins K, O'Connor J. Blast injury in a civilian trauma setting is associated with a delay in diagnosis of traumatic brain injury. Am Surg 2008;74: 267–70.
[15] Bell MK. Standardized model is needed to study the neurological effects of primary blast wave exposure. Mil Med 2008;173:5–8.
[16] Durak D, Fedakar R, Turkmen N. Blast injury: lessons learned from an autopsy. Hong Kong Med J 2008;14:489–91.
[17] Celtik C, Acunas B, Oner N, Pala O. Neuron-specific enolase as a marker of the severity and outcome of hypoxic ischemic encephalopathy. Brain Dev 2004;26: 398–402.
[18] Hatfield RH, Mckernan RM. CSF neuron-specific enolase as a quantitative marker of neuronal damage in a rat stroke model. Brain Res 1992;577:249–52.
[19] Swartz KR, K.Z., Liu F, Sewell D, Schochet T, Campbell I, et al. Interleukin-6 promotes post-traumatic healing in the central nervous system. Brain Res 2001;896:86–95.
[20] Ramasamy A, Harrisson SE, Clasper JC. Injuries from roadside improvised explosive devices. J Trauma 2008;65(4):910–4.
[21] Vink R, Young A, Bennett CJ. Neuropeptide release influences brain edema formation after diffuse traumatic brain injury. Acta Neurochir Suppl 2003;86: 257–60.