Intracranial Pressure Increases during Exposure to a Shock Wave

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Abstract
Traumatic brain injuries (TBI) caused by improvised explosive devices (IEDs) affect a significant percentage of surviving soldiers wounded in Iraq and Afghanistan. The extent of a blast TBI, especially initially, is difficult to diagnose, as internal injuries are frequently unrecognized and therefore underestimated, yet problems develop over time. Therefore it is paramount to resolve the physical mechanisms by which critical stresses are inflicted on brain tissue from blast wave encounters with the head. This study recorded direct pressure within the brains of male Sprague-Dawley rats during exposure to blast. The goal was to understand pressure wave dynamics through the brain. In addition, we optimized in vivo methods to ensure accurate measurement of intracranial pressure (ICP). Our results demonstrate that proper sealing techniques lead to a significant increase in ICP values, compared to the outside overpressure generated by the blast. Further, the values seem to have a direct relation to a rat’s size and age: heavier, older rats had the highest ICP readings. These findings suggest that a global flexure of the skull by the transient shockwave is an important mechanism of pressure transmission inside the brain.

Key words: blast; improvised explosive device; intracranial pressure; overpressure; traumatic brain injury

Introduction

Blast traumatic brain injuries (blast TBI) caused by improvised explosive devices (IEDs) affect a significant percentage of surviving soldiers wounded in Iraq and Afghanistan (Warden, 2006). There is a pressing need for a comprehensive explanation of the mechanism of injury of TBI after exposure to blast. Substantial resources have been spent on the IED problem with regard to methods to defeat this threat, deal with casualties, and develop countermeasures. Although little is known about the mechanism of trauma induced by blast waves, it is now known that blast TBI can occur without obvious external injuries, loss of consciousness, or visible findings on magnetic resonance imaging (Bhattacharjee, 2008; Cernak et al., 1999; Guy et al., 2000; Irwin et al., 1997). The extent of a blast TBI, especially initially, is difficult to diagnose, as internal injuries are frequently unrecognized and therefore underestimated, yet problems develop over time. It is essential to understand the physical mechanisms by which critical stresses are inflicted on brain tissue from blast wave encounters with the head. Only with a careful assessment of the physics of the blast/head interaction will it be possible to determine the modes by which injury is inflicted at the cellular level. Subsequently, effective treatments and protective technologies may be developed.

The precise mechanism of blast TBI is not well understood and several hypotheses have been suggested. Some have proposed that damage is due to transosteal propagation (Clemedson, 1956; Clemedson and Jonsson, 1961a), or the shockwave entering the brain by propagating directly through the skull. Others contend that blood vessels from the body can transmit the outside hydrostatic pressure to the brain, causing damage (Cernak et al., 2001; Courtney and Courtney, 2009; Young, 1945), or suggest that damage to the lungs can elicit a physiological response creating injury to the brain (Cernak et al., 1996). Still others propose that a pressure wave imparted to a different point in the body could have enough magnitude to be transmitted to the brain and cause histologically observable damage (Suneson et al., 1990). Recently, computational simulations using a finite-element model that has not yet been validated by experimental results, have shown that skull flexure, in the form of transverse waves, may be a mechanism of stress transfer and injury (Moss et al., 2009). Preliminary studies conducted by our group have led us to hypothesize that other modes of skull deformation, including “global” compression, may contribute

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to generating injurious stress waves within the head (Dal Cengio Leonardi et al., 2009).

Some animal tests have been designed and carried out in an attempt to learn more about the mechanism of shock-wave transmission to the brain, but only a few animal studies recorded direct pressure within the brain tissue during exposure to blast (Chavko et al., 2007; Clemedson, 1956; Clemedson and Jonsson, 1961b; Romba and Martin, 1961). Such experiments are challenging to conduct because the instrumentation technology, which measures the true in vivo pressure condition during shock exposure, has not yet been perfected and validated. These tests also carry the burden of the complex preparation of the animals, which must be carried out while adhering to strict guidelines for animal handling.

The objective of our research was to investigate shock-wave dynamics through the brain. In order to provide clues about the mechanism by which this pressure was being imparted, we set out to measure the transient intracranial pressure (ICP) in an animal model subjected to an air shockwave, in order to identify features of the pressure wave profile, such as wave shape, peak overpressure, and impulse and duration of the positive phase. In the process of performing this study some factors of the head anatomy and the measurement technique were explored that might affect the results.

Regarding head anatomy, the orbits provide a potential pathway for an external pressure wave to propagate into the brain. Thus, ICP measurements were compared with and without this pathway blocked. Since the thickness and stiffness of the skull increase with the age and size of the rat (Gefen et al., 2003), measurements were compared for rats of different ages. Regarding instrumentation, the effects of the location of the sensor in a fluid cavity (lateral ventricle) or tissue mass (frontal cortex) were compared. Since theory would suggest that any pressure leakage would diminish pressure developed within the skull, the sensitivity of the ICP measurement to sealing of the gauge at its penetration point of the skull was assessed. As these measurements are critical to understanding the processes by which the brain is stressed, it was important to devise experiments that reliably replicate those of actual blast injury. Certain requirements needed to be met in terms of generating the shock-wave pressure (both static and dynamic components), animal restraint, and sensor mounting.

## Methods

### Wayne State University shockwave generator

While we acknowledge that the mechanism of brain injury from an IED blast could involve several factors, which have traditionally been referred to as primary, secondary, and tertiary injuries, our goal was to focus on one of the hypotheses for primary brain injury due to blast: global skull flexure. In order to do this in a standard laboratory setting, a shock tube is the most practical instrument to generate the shockwave. To simulate a free-field blast wave, a shock tube actuated by compressed gas is commonly used. In this study, the simulated blast waves were generated by a helium-driven shock tube located at the Wayne State University Bioengineering Center. Our shock tube consists of two separate chambers: the driver section (30 inches long, 12 inches in diameter), which is filled with highly pressurized helium; this is separated by a Mylar membrane from the driven section (242 inches long, 12 inches in diameter), which is filled with ambient air, and where the specimen is placed (Celander and Clemedson, 1954). Upon rupture of the membrane, a shockwave is propagated into the driven section by the rapid expansion of gases from the driver section.

The air shockwave developed in the test section evolves as a combination of waves, and approximates that from a chemical explosion, if care is taken in the location of the specimen within the tube. When the membrane bursts, a uniform shock front quickly develops and propagates down the test section. Since the cross-section of the shock tube is constant, the shockwave moves at a constant speed unattenuated down the tube until the reflected rarefaction from the closed end of the driver overtakes it. Prior to this overtaking, the shock waveform will feature a flat section after the peak. Following the overtaking, the waveform for static pressure, also called the incident pressure wave, will have a decaying profile similar to a blast wave. In this phase, the dynamic pressure component of the shockwave is similar to that of a free-field blast. It is important to note that any zone within the shock tube that is appropriate for blast simulation will eventually be affected by the arrival of disturbances and gas dynamic features entirely atypical of blast waves. Examples of such anomalous disturbances include the arrival of the contact surface with expanding driver gas, and the arrival of the strong rarefaction created by the open end of the tube. At some locations within the tube, the effects of these anomalous flow features are exaggerated, and will corrupt the experimental conditions much earlier. These factors were taken into consideration, and the animals were placed inside the tube at such a distance from the open end to optimize the shock-wave pressure. Our specimens were placed inside the driven section, and the head was positioned 198 inches downstream from the bursting membrane (44 inches from the open end of the tube).

Extremely adverse effects will result from experiments staged with a specimen near the end of the tube, where the end-rarefaction will quickly cause imbalance of high dynamic pressures, yet reduced static pressure conditions. The specimen in this regime would in fact be subjected to a nearly pure jet-stream outflow, with exaggerated underpressures or vacuum, or a shock propagating upstream.

### Animal preparation

Approval from the Wayne State University Institutional Animal Care and Use Committee was obtained prior to testing. All animals were purchased from the same vendor and were kept under the same housing conditions at the WSU animal facilities. Twenty-five male Sprague-Dawley rats (245–395 g) were anesthetized with ketamine/xylazine (100/20 mg/mL IP), their heads were shaved, and they were placed in a stereotaxic frame. A longitudinal incision allowed visualization of the bregma and the lambda. A 1-mm hole was drilled in the skull for insertion of a guided cannula (18 gauge). Two sites were chosen for placement of the cannula: the ventricle (–1.3 AP, –1.8 ML, –3.2 DV), or the frontal cortex (+3 AP, –2 ML, –1 DV). The cannula was anchored to the skull by bone cement, and two screws were used to reinforce the anchoring site. A dummy-cannula (cap) was screwed onto the cannula to close the opening while the animal was recovering. The scalp was sutured around the cannula, covering the screws and the bone cement. Seven days after surgery, the animal was anesthetized with ketamine/xylazine (100/20 mg/mL IP) and placed in a soft holder before exposure to shockwaves (Fig. 1).
The holder was positioned so that the rat's head was 44 inches from the open end of the tube, facing the shockwave frontally. By means of a long rod, the holder was connected to a trolley positioned outside the tube. The purpose of this moveable trolley was to minimize mechanical stresses imparted to the specimen due to its restraint in the shockwave flow.

The rats were instrumented with a specially-adapted miniature optical ICP gauge and exposed to simulated blast waves of approximately 10 psi (68.95 kPa) in magnitude, and 7.5 msec in positive phase duration (Fig. 1). After exposure, all anesthetized animals were immediately sacrificed by perfusion with 4% paraformaldehyde; the brains were removed and collected for histological verification of sensor position.

**Pressure sensors**

Two PCB sensors (model 102A06; PCB Piezotronics, Inc., Depew, NY) were mounted on the inside wall of the shock tube at two separate locations to monitor the development of the shock front and measure its speed. The first wall sensor was placed 72 inches downstream from the bursting membrane, and the second wall sensor was 181 inches downstream from the membrane. A third PCB sensor (model 137A22; PCB Piezotronics, Inc.), commonly called “the pencil” because of its aerodynamic shape, was placed 1 inch in front of the animal’s head (thus meeting the shock front slightly before the specimen) to record the static pressure delivered. A fourth sensor was used to record the ICP in the animal (model FOP-MIV; FISO Technologies, Quebec City, Quebec, Canada).

Multiple sensors were used in this study because they differ on several levels. First, the mechanism of measuring pressure is distinctive. The PCB sensors utilize a quartz piezoelectric element to convert strain created by a sudden change in ambient pressure into a voltage output, compared to the FISO sensors, that measure pressure by converting wavelength-modulated light into a voltage value. Additionally, the PCB...
sensors are robust and designed to withstand the energy of the shockwave in open air. The FISO optic sensor, on the other hand, was designed for medical applications and is very fragile, weighing only 0.163 mg. The characteristics of these sensors are especially important when making \textit{in vivo} measurements in small animals, since the sensor should approximate the density of the tissue surrounding it, and ideally move with the cells. Otherwise, the inertia of the sensor may affect the reading of \textit{in vivo} pressure.

\textbf{Experimental set-up}

In order to obtain the most accurate ICP measurements, we investigated the effects of various sealing methods of the cannula. The rodents were divided into three groups: A, B, and C, according to the sealing method used during exposure to the simulated blast. In group A, the cannula opening was not sealed after insertion of the optic sensor. The sensor was simply held in place by duct tape that wrapped around the cannula and the head. In group B, modeling putty was placed around the optic cable, at the opening of the cannula, and taping was performed as for group A. Using a modeling compound was a rudimentary attempt to provide partial sealing of the system. In group C, an optic sensor was modified to provide complete sealing of the cannula during testing. The optic sensor fiber was glued onto the dummy-cannula with a two-part epoxy glue (drying time 5 min) after the stem had been removed. The optic sensor and fiber replaced the internal stem of the dummy-cannula, and this mount provided a durable and full mechanical seal once the dummy was screwed onto the cannula (Fig. 2). For group C, additional care was taken to ensure the removal of air bubbles. Saline solution was placed in the cannula through a syringe and petroleum jelly was added to the cap thread immediately prior to insertion of the optic sensor to ensure that no air was left in the cannula. Note that this procedure was not necessary for the other two groups because of the different types of installation. For group A, by design there was no seal, therefore ambient air was in contact with the fluid in the cannula. For group B, putty was applied at the cannula entrance, while care was taken to have CSF all the way to the cannula’s edge. Unlike a rigid dummy-cannula, the modeling compound easily adapts to the cannula’s contours, creating direct contact between the CSF and the putty.

Each anesthetized rat was subjected to a minimum of six shockwave tests with experimental conditions kept identical for three trials at a time. Group A was subjected to different incident overpressures to determine the optimal testing pressure. Groups B and C were exposed to only one incident overpressure, and in the first three trials the eyes were left exposed to the shockwave, while in the next three the eyes were protected by eyegear (to study the effects of the apertures in the skull on pressure transmission). A total of 129 exposures occurred at the chosen pressure of 10 psi (68.95 kPa). In all three groups two brain locations were randomly investigated. Each rat had the optic pressure sensor placed either in the frontal cortex or in the lateral ventricle (numbers in ventricle/cortex: group A 1/6; group B 3/2; group C 5/8). The lateral ventricle was chosen to compare with a previous study (Chavko et al., 2007), while the frontal cortex site was introduced to investigate if changes in depth with respect to the shockwave would have an effect on the measured pressure-wave profile results.

\textbf{Histological assessment of cannular position}

All animals survived testing and subsequently underwent transcardial perfusion with 4\% paraformaldehyde. The brains were removed, processed for post-fixation, and embedded in embedding compound. Sections were cut and stained with hematoxylin and eosin (H&E) to inspect the area of the brain in which the cannula was placed (Fig. 3).

\textbf{Statistical analysis}

Statistical analyses were performed using the statistical package SPSS ver.18 (SPSS Inc., Chicago, IL). First, a paired samples \textit{t}-test was run between the eyes-exposed and the eyes-protected means for both peak and impulse to determine the significant differences. Since differences were not significant and because they were measured from the same rats, those measures, either eye-protected or eye-exposed, were treated as homogeneous observations from the same subject. Therefore, all measures from each rat were used for the data analysis. A linear mixed model was run for the dependent variable “Impulse,” assuming that the repeated observations within each rat would cause correlated error terms. A first-order autoregressive covariance structure was chosen for the repeated time factor. The factors “Seal” (groups A, B, and C) and “Position” (Cortex versus Ventricle) were taken as fixed, and the “rat ID” was treated as a random factor. The analysis

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{fig2}
\caption{Placement of the intracranial pressure sensor for group C, which is the sealed group. (A) A piece of plastic tubing is glued on top of the dummy cannula to protect the optic cable at its exit from the head. (B) The dummy-cannula is screwed onto the guided cannula cemented onto the rat’s skull, and the rat is positioned inside the tube.}
\end{figure}
SHOCK WAVE CAUSES INCREASED ICP

Results

A total of 25 rats were tested: 7 for group A (unsealed); 5 for group B (partially sealed); and 13 for group C (fully sealed). Table 1 shows an example of one rat from each group. Note the high consistency of the values extrapolated from the data collected from each individual rat during the six tests.

For each rat, we recorded 10 msec of pre-trigger data and 40 msec of post-trigger data: this allowed to log a brain pressure baseline (used later to zero each record) and to assure capture of the shockwave’s entire positive and negative phase. However, the time duration shown in two of the columns of Table 1 is that of the positive phase only. We documented the weight of the rat before the commencement of testing, and the location of the intracranial (IC) optic pressure sensor. From the data collected, the area under the positive phase (impulse) for both the incident pressure wave recording (pencil sensor), and the intracranial pressure wave recording (optic sensor) was calculated. All IC pressure and impulse values were normalized to their associated value of incident pressure. This normalization is necessary to compare the relative differences in IC pressure to the incident blast, and it is shown in the last two columns of Table 1. The normalized impulse values were obtained by dividing each IC impulse (Impulse Optic) value by the respective incident impulse value (Impulse Pencil). The normalized IC peak pressure values were obtained by dividing each IC peak pressure value (Max Optic Pressure) by the respective incident first peak pressure (Pencil First Peak Pressure). Note that since normalization requires one to ratio two values that are expressed in the same units (psi/psi in the case of pressure, for example), the result is simply a number without unit. As it is not possible to produce an identical shockwave for each test, the significance of such normalized numbers are relative to the pressure and impulse that were provided for that particular test by the shock tube and measured by the pencil gauge. For each test, the first peak of the “pencil profile” (the plot that chronologically recorded the value of static overpressure in the air next to the specimen) was chosen as the representative value for the incident wave peak pressure. It should be noted that the record from the pencil probe shows a higher sharp peak within a millisecond following the shock front, which is a reflection from the specimen and its holder (Fig. 1). Therefore the pencil first peak more truly represents the peak value of the incident wave. Since the maximum value of the pencil profile is reached later on, and is due to a reflection wave coming from the opposite direction of the shock front, that maximum value on the plot can be considered an artifact, and it is not the actual pressure that will hit the specimen.

Statistical analysis showed a significant difference \[F(2,16.89) = 9.586, \ p = 0.002\] in normalized impulse values when examining group A versus group B versus group C, respectively (Fig. 4). This difference is attributable to the different sealing methods used. The mean normalized impulse values were 0.92 for group A, 1.06 for group B, and 1.21 for group C (Fig. 4). It is important to note that to compare the effects seen among the different groups we used the normalized impulse values. The normalized impulse, by representing an integration of the positive-phase pressure profile over time, better tells the story of what is happening to
the seal, especially in the case of group B, for which there was a sudden pressure variation (Fig. 5). Figure 5 shows an example of three ICP profiles, one from each group, plotted against the incident wave profile at the specimen location. Comparing each ICP profile to the incident overpressure, we note that the curve from group A follows quite closely the overpressure measured near the animal. On the other hand, the curves from the other two groups greatly differentiate them from the incident overpressure, especially in the first 3 msec from the inception of the shock front. Group B (partially sealed) shows a sharp rise in pressure and a seemingly sharp decrease in pressure that goes even below the incident over-pressure, which we attribute to failure of the seal. Likewise group C initially presents with a sharp rise in pressure, but contrary to group B, as the seal continues to hold, the IC pressure remains above the incident overpressure until near the end of the positive phase. Overall we found that proper sealing technique caused an average 30% increase in impulse value for fully sealed versus unsealed.

After we determined the appropriate sealing method (group C), we further investigated how age and weight affected ICP measurements in this group. The weight of group C ranged from 245 to 395 g, and the age ranged from 61 to 95 days. Figure 6 demonstrates the consequence of animal age when measuring ICP. There was a significant increase $F(2,6.92) = 15.770, p = 0.003$ in ICP values in the

<table>
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<th>Location</th>
<th>Test type</th>
<th>Pencil first peak pressure (psi)</th>
<th>Max optic pressure (psi)</th>
<th>Duration pencil (msec)</th>
<th>Duration optic (msec)</th>
<th>Impulse pencil (psi*msec)</th>
<th>Impulse optic (psi*msec)</th>
<th>Normalized IC peak pressure</th>
<th>Normalized IC impulse</th>
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<td></td>
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For groups C and B (rats 28 and 25, respectively), there were three tests performed with eyes exposed (EE), and three tests performed with eyes protected (EP). For group A, rat 223, three tests were conducted at one overpressure and three at another; the eyes were always exposed. For rat 223, the only tests presented are the ones at the same overpressure as for groups C and B. The duration in milliseconds for both the pencil and optic sensor refers to the positive phase only. The normalized columns were obtained by dividing the optic sensor value by the respective pencil value.

psi, pounds per square inch; IC, intracranial; NA, not available.

FIG. 4. Mean normalized impulse values with standard error for group A (unsealed), B (partially sealed), and C (completely sealed; *p = 0.028; **p = 0.005 for pair-wise comparisons).
older animals. Mean normalized IC peak pressure values were found to be 1.40 for the 61-day-old rats, 1.54 for the 67-day-old rats, and 1.68 for the 95-day-old rats. The mean weights for the 61-, 67-, and 95-day-old rats were 269, 280, and 365 g, respectively.

When evaluating sensor placement within the brains of the rats in the sealed group, we observed that ventricle placement provided readings that were slightly more consistent than those from the cortex. When comparing the results from the position of the ICP sensor, we found that the difference in positions was significant \( F(1,6.92) = 9.784, p = 0.017 \), regardless of age (the interaction term between days and position was not significant). When comparing results for rats of the same age and weight, we observed that the results from the cortex had higher starting values than those from the ventricle, but that they decreased more with successive trials (Figs. 7 and 8). We hypothesize that this shift in the cortex measurements was due to a “well” of fluid developed at the sensor tip, such that the results eventually approached those for the fluid-filled ventricle. Placement of the optic sensor in the fluid of the ventricle appears to cause less interference between the liquid material surrounding the sensor and the device itself, explaining the more consistent results compared to the cortex. Also, when comparing rats having similar age and weight (within 6 g), and different sensor placement, 94% of the tests showed that cortex placement produced higher normalized peak pressure values than ventricle placement. Note that only tests without eyegear were used in this comparison. Since the sensor in the ventricle was positioned deeper in the brain, we hypothesize that the lower peak pressure value could be due to a pressure decrease caused by transmission via a longer path. Additional investigations are needed to examine this hypothesis.

To study the effects that orbits may have on pressure transmission within the brain, we protected the eyes with a custom-made device. This eyegear was a simple strip of
1-mm-thick copper encased in fabric. Copper was chosen because it is lightweight, which added less mass to the rat’s skull; it is also pliable, which helped adjust the fit to the rat’s contours; and most significantly, it is able to reduce transmission of incident stress waves (Cooper et al., 1991), which we hypothesized would decrease the measured ICP value. Analyses of the transmission of the shockwaves when the orbits were protected found that 69% of the rats had higher ICP values when wearing the eyegear than when the eyes were exposed. Therefore protection of the eyes offered no mitigation of pressure transference to the brain in the sealed rat model. Ultimately, the changes in ICP values between eyes-exposed and eyes-protected animals were not statistically significant. However, the rise in ICP peak value between eyes-exposed and eyes-protected was consistent enough to be noted, and an example of this effect is shown in Figure 9. To explain this effect we suggest that the added mass of the eyegear probably caused an increase in energy transfer to the

![FIG. 7. Example of intracranial pressure (ICP) measures for three trials when the optic sensor was in the cortex. Notice the decrease in peak value from the first to the third trial.](image1)

![FIG. 8. Example of intracranial pressure (ICP) measures for three trials when the optic sensor was in the ventricle. Notice the decrease in peak value from the first to the third trial.](image2)
skull-brain system. This finding may be useful for the future development of protective headgear.

**Discussion**

Understanding the exact means by which stress is imparted to brain tissue from blast exposure to the head, and carefully resolving the spatial and temporal nature of these stress conditions, are fundamental to resolving the blast TBI problem. There is a pressing need for a comprehensive explanation of the mechanism of TBI after exposure to blast, and the testing of animals instrumented with pressure sensors in the brain is one step toward fulfilling this need. The results of the current study highlight two major findings, which will have a major impact on understanding the pressure wave dynamics seen during blast. First, we discovered that with proper sealing methods, there is a significant increase in ICP when the brain is exposed to a shockwave. Second, the physical maturity of the animals themselves has a considerable effect on the ICP measured within the brain.

The present study shows that the degree to which a test aperture is sealed can significantly affect ICP measurements. This is important because apertures must be created to obtain ICP readings with current sensor technologies. These findings demonstrate that without proper sealing of the skull, accurate measurements of ICP may not be obtained. Furthermore, when the cannula was left unsealed, the ICP values closely followed the incident shock-wave overpressure. This was not the case when the seal was engaged. When comparing the ICP profiles for the partially sealed group, the variations in the shapes of the ICP profiles were greater than those in the other two groups. This is probably because of the intrinsic variability of the partially sealed set-up. Finally, when looking more closely at the ICP profiles for the sealed group, there is an oscillation, which appears in the initial 2 msec from inception of the pressure front. We hypothesize that this oscillation is due to the specific material response of the rat skull that reveals itself at the ICP sensor. Because the sensor is anchored to the skull, it is impossible to avoid mapping skull motion if it occurs. Thus, global flexure of the skull, caused by the pressure-wave dynamics with the head, could translate into pressure oscillation within the tissues.

Additionally, the present study confirms that the weight and age of the animals are the most influential factors on pressure-wave transmission. The rat’s weight and age directly determine the skull's overall size and maturity (Gefen et al., 2003), with older rats presumably possessing thicker, more rigid skulls. Transosteal propagation should cause the thicker skulls to have lower ICP values; therefore the higher pressures should be seen in the younger rats. Instead, global flexure may explain why the younger rats had lower ICP values. When pressure is exerted on the skull of a young rat, the more flexible, pliant structure is capable of deforming more easily than an older, more rigid skull. Since pressure is a force applied to a surface, the ability to increase even slightly the surface value due to a more flexible material (e.g., bones and suture lines), allows the younger rat to keep the ICP at a lower value. Thus, the deformation allows dissipation of some of the pressure that otherwise would build inside. Our results demonstrate a strong correlation between the ICP values and the rat’s maturity, and such findings seem to suggest that global flexure of the skull by the transient shockwave is an important mechanism of pressure transmission inside the brain. Ongoing investigations are exploring these effects in more detail.

**FIG. 9.** Example of intracranial pressure (ICP) measures for the same rat with the eyes exposed and the eyes protected; 69% of the rats in group C had higher ICP values when wearing the eyegear; however, this change was not significant. To minimize variation between trials, we compared only the two trials next to each other (third and fourth trials) when determining these percentages. The added mass of the eyegear may have caused the difference in peak pressures seen with the eyes exposed and the eyes protected.
In conclusion, in this study we demonstrated that there are significant factors of paramount importance when investigating pressure-wave dynamics in an animal model of blast TBI. The results suggest that to obtain reliable and accurate measurements of intracranial pressurization, proper sealing of the skull needs to be achieved. When a seal is achieved, the results demonstrate that ICP values have a direct association to a rat’s size and age, and are significantly higher compared to the overpressure outside the head. Consequently one must be aware that in order to translate the results of shockwave transmission in the rodent brain to a human model, one needs to take into consideration the animal’s physical maturity for the type of shockwave study that they are performing. Overall, these results suggest that global flexure of the skull may contribute to the mechanism behind how the brain is injured during primary blast exposure.

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