COGNITIVE CHANGES RESULTING AFTER SHOCK WAVE EXPOSURE IN A RAT MODEL

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INTRODUCTION

Blast over pressure (BOP) injury is currently a major issue in many of the continuing conflicts around the world. Most blast related injury is the result of exposure to improvised explosive devices (IEDs). These devices are not well defined due to the variability inherent to each device. However, they have become common due to the cheapness of production and ease of delivery to the intended target. The resulting explosion produces an associated pressure, or primary blast wave, that rapidly expands as it approaches the target. The effects are varied depending on the targets location from the epicenter of the explosion.

The primary concern is the effect on the war fighters and civilians exposed. The advent of better protection against BOP for areas of injury such as the lungs, has shifted the focus of blast effects onto the central nervous system (CNS). Due to the shift in focus, there has been a greater number of reports of cognitive deficits such as mild traumatic brain injury (MTBI) that are caused by BOP among soldiers and terror victims. Cognitive changes have also been noted in soldiers without associated severe injuries; thus, it is important to identify those whom may be affected without any outward signs.

METHODS

Male Sprague-Dawley rats (Harlan Labs, San Diego), weighing approximately 275 grams were used in this study. Approval from the Wayne State University Animal Investigation Committee was obtained prior to testing. The rats were allowed to acclimate for a period of five days. They were handled by researchers to help diminish fear, and were given food and water *ad lib* while being cycled on a 12 hr light/ dark schedule.

A testing regimen of thirty groups, each containing five rats was designed. Each group's test consisted of a different combination of pressure and time to post-exposure neurocognitive testing (Table 1). The rats were anesthetized with 3% isoflourane / 100% oxygen. During anesthetization, the rat was moved approximately 109 cm inside the tube positioning the rat's head to face the shock directly. Following exposure, rats awoke on their own accord. Cognitive testing was achieved using the Morris water maze.

Table1 : Single Low Intensity Shock Exposure Test Matrix

	0 kPa	90 kPa	103 kPa	117kPa	159 kPa	193 kPa
3 Hours	5	5	5	5	5	5
6 Hours	5	5	5	5	5	5
24 Hours	5	5	5	5	5	5
48 Hours	5	5	5	5	5	5
72 Hours	5	5	5	5	5	5

METHODS

A custom built 12-inch diameter shock tube (ORA Inc.) located at Wayne State University in the Biomedical Engineering Department was used to produce the shock front and dynamic overpressure (Figure 1). Compressed helium and Mylar sheets of varying thickness, were used to obtain different peak pressures. A pressure sensor was placed on the platform holding the rat determine the level of pressure the rat was exposed to. Pressure data was collected at 250 kHz.

Figure 1: Shock Tube at Wayne State University Biomedical Engineering

RESULTS

The Morris water maze data was analyzed using repeated measures ANOVA, and between effects were calculated by T-test ($p < .05$). Each test was conducted at each time point independently. Additional trends were noted observationally. Groups tested at 117kPa exhibited the most substantial distance, latency, and velocity differences. The distance and latency indicated differences most notably at the 24 and 48 hour time points (Fig. 2). This indicates that the rats not only took longer to reach the target, but also swam around the pool for a greater total length. These results suggest that the 117kPa rats could not find the target as well as the other pressure groups.

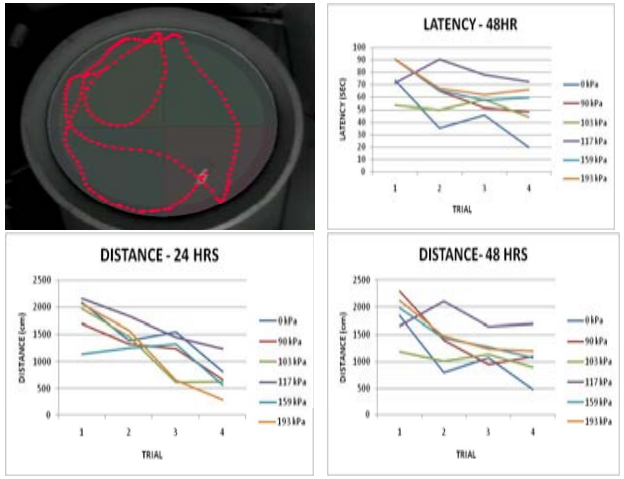

Figure 2. A graphic trace of an actual trial is shown above demonstrating the Morris water maze test. Latencies and distances are provided to demonstrate the large differences in the 117 kPa groups when compared to the other pressure intensities.

RESULTS

The results of velocity values were of the most interest. The 117 kPa exposed rats demonstrated the greatest differences amongst all of the rats. In comparison to rats in other test groups the 117 kPa groups were also not finding the target as efficiently. This may suggest that the rats were swimming at a high rate, unable to find the target. It is believed that these rats experienced greater levels of agitation and frustration. The most affected rats were unable to use spatial orientation skills to define and then locate the target in an efficient manner. The literature has indicated that this type of deficiency is associated with damage in the CA regions of the rat hippocampus.

The repeated measures indicate that the greatest contribution was related to the effect of time, meaning the negative slopes indicated that the rats were learning. Most effects were indistinguishable at 72 hours, where no major trends were evident.

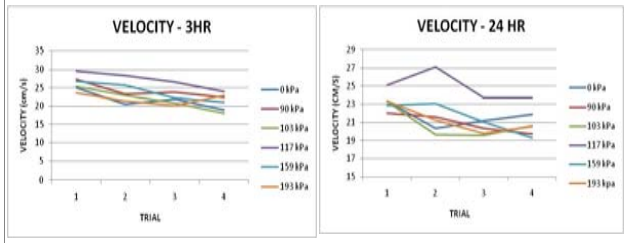

Figure 3. Values for the average velocity that the rats traveled during their trials are shown for the 3 and 24 hour time points. It is believed that the rats in the 117kPa group may have been the most stressed compared to the other groups.

CONCLUSIONS

The data demonstrated that the greatest changes, indicating cognitive damage, took place at the 117 kPa pressure range with the most notable changes during the 24 and 48 hour marks. Because pressures at greater and lesser intensities showed less of an effect, it is believed that there may be a range specific mechanism causing neurocognitive dysfunction within the rat. The unique combination of elevated velocity, distance, and latency indicate that these rats experienced a unique exposure.

It is important to determine what makes the 117 kPa pressure range so damaging. Of equal importance is to study the different combinations of peak pressure, impulse, duration, and rate of decay.

The possibility of a range specific mechanism is promising for further studies into the causes of blast induced mTBI.