Reduced sensorimotor coordination and reactivity following traumatic brain injury in mice

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Introduction

Traumatic brain injury (TBI) sets off a complex cascade of events, which are not well understood, but can cause devastating impairments in both cognitive and sensorimotor functions. TBI rat models have been established; a mouse survival model of TBI with neurological deficits would allow use of genetic engineering tools to elucidate the fundamental processes that underlie the long-term effects of TBI. We sought to establish the level of fluid perfusion injury necessary to produce a TBI mouse model with reproducible neurological deficits, measured as sensorimotor coordination and sensorimotor reactivity.

Methods

Model

We utilized a lateral fluid percussion injury administered through craniotomy, with dura incised. We titrated the injury (pressure wave delivered) to a level that produced consistent neurological impairment with a high frequency of survival; injury was confirmed using magnetic resonance imaging (MRI). TBI animals were compared to a sham group of animals, which underwent anesthesia and scalp incision without burrhole or fluid percussion injury.

Sensorimotor testing

Sensorimotor coordination was tested by measuring is latency to fall on a rotating rod task, to which the animals had been acclimated prior surgery.

Acoustic Startle testing

Acoustic startle measurements were obtained using a stabilimeter chamber as previously described in mice (Fox, 2008) and rats (Hammack, 2009). Startle amplitude was defined as the maximal peak-to-trough voltage during the first 200 ms after the stimulus onset. The response to 30 noise bursts that varied in intensity (95, 100, or 105 dB) with a 30 s inter-trial interval was then determined.

Results

Survival

We established an optimal pressure of 37 PSI to deliver a consistent and survivable injury. (Fig 1)

Figure 1. Survival

Pressure (PSI)	20	30	40	50	35	40
Survival	3/3	3/3	1/3	0/3	3/3	1/3

Figure 2: Sensorimotor testing

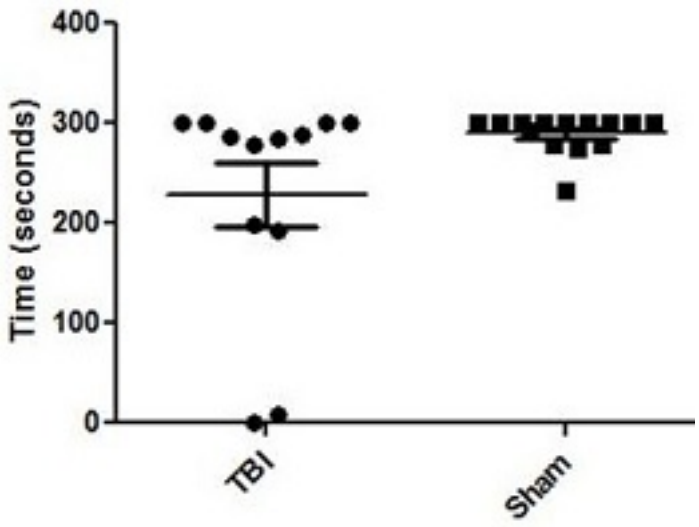
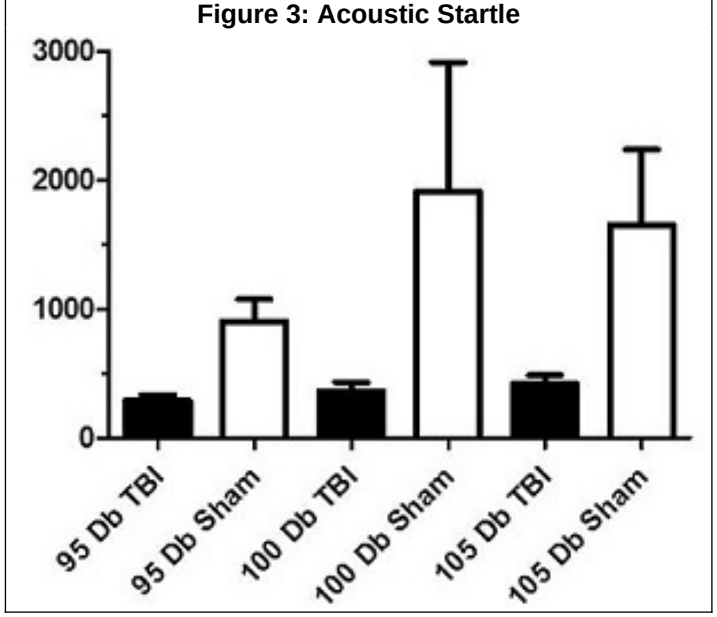


Figure 3: Acoustic Startle



Sensorimotor testing

Rotorod scores were 228 +/- 32 in the TBI group and 290 +/- 5 ($P<0.05$) in the sham injury group. (fig 2)

Acoustic Startle

With regards to acoustic startle reflex TBI animals had decreased startle amplitudes overall. Furthermore TBI animals showed a 65% decrease response compared to baseline versus sham animals which showed a 15% decrease compared to baseline (fig 3)

Conclusions

We established a mouse model of TBI, which affected motor behavior and sensorimotor function of mice. We determined the optimal pressure wave intensity to be 37 PSI to produce survivable defecits in sensorimotor function. Animals that were exposed to this level of lateral fluid percussion had significantly impaired sensorimotor function compared to sham animals as determined by rotorod and acoustic startle testing. This model will provide opportunities to study the effects of TBI in genetically engineered mice. The use of geenetically engineered mouse will allow further ellucidation of the pathways involved in the pathogenesis of cerebral dysfunction following TBI. Once the dysfunctional pathways are identified it is then possible to focus on target therapies to address these.

References

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Learning Objectives

Review the mouse TBI model.

Review the effects of the TBI injury on study animals.

Discuss Future directions of research.