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Fluid percussion injury device for the precise control of injury parameters

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HIGHLIGHTS

- A novel fluid percussion injury (FPI) system was designed and built.
- The system generated fluid percussions with independently adjustable peak pressures, rise times and impulses.
- Immediate post-injury behavior was similar between the custom FPI system and the commonly used FPI system.
- Fluoro-Jade labeling in the hilus and CA2-3 and granule cell population spike amplitude were consistent between systems.
- Slow fluid percussion rise times increased mortality and reduced motor function in a subset of adult rats.

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ABSTRACT

Background: Injury to the brain can occur from a variety of physical insults and the degree of disability can greatly vary from person to person. It is likely that injury outcome is related to the biomechanical parameters of the traumatic event such as magnitude, direction and speed of the forces acting on the head.

New method: To model variations in the biomechanical injury parameters, a voice coil driven fluid percussion injury (FPI) system was designed and built to generate fluid percussion waveforms with adjustable rise times, peak pressures, and durations. Using this system, pathophysiological outcomes in the rat were investigated and compared to animals injured with the same biomechanical parameters using the pendulum based FPI system.

Results in comparison with existing methods: Immediate post-injury behavior shows similar rates of seizures and mortality in adolescent rats and similar righting times, toe pinch responses and mortality rates in adult rats. Interestingly, post injury mortality in adult rats was sensitive to changes in injury rate. Fluoro-Jade labeling of degenerating neurons in the hilus and CA2-3 hippocampus were consistent between injuries produced with the voice coil and pendulum operated systems. Granule cell population spike amplitude to afferent activation, a measure of dentate network excitability, also showed consistent enhancement 1 week after injury using either system.

Conclusions: Overall our results suggest that this new FPI device produces injury outcomes consistent with the commonly used pendulum FPI system and has the added capability to investigate pathophysiology associated with varying rates and durations of injury.

1. Introduction

Each year an estimated 1.7 million Americans and 10 million people worldwide sustain a traumatic brain injury (TBI). Worldwide, TBI is predominate in low to middle income countries which may relate to increased risk factors and availability of medical treatment (Faul et al., 2010; Hyder et al., 2007). Considering all cases of TBI, the degree of disability can vary greatly from person to person. TBI can occur from a variety of physical insults to the brain such as an automobile accident, sport collision or blast wave. Indeed, it is likely that the wide range of TBI outcomes may be due to the biomechanics of the traumatic event such as magnitude, direction and speed of the forces acting on the head. A majority of TBI

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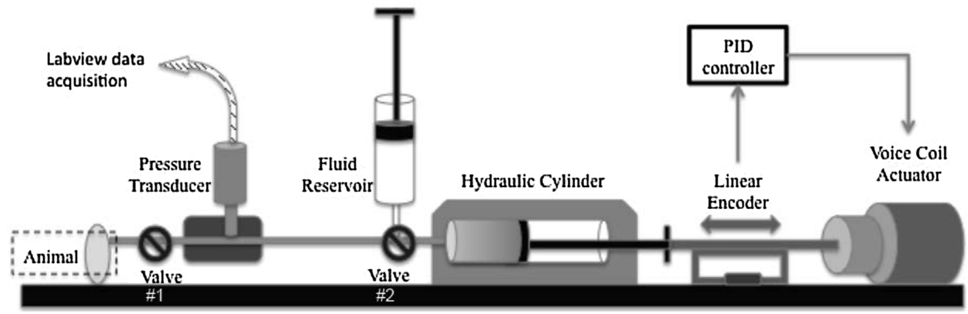

Fig. 1. Programmable fluid percussion injury system. A voice coil linear actuator drives a hydraulic cylinder to produce a fluid percussion. A PID closed loop control system uses encoder feedback to program specific movements that translate into definable fluid percussion waveforms. A pressure transducer is located near the animal connection to measure the fluid percussion applied.

studies link the magnitude of the primary injury (i.e. peak pressure in the fluid percussion model) to severity in terms of brain pathology and behavioral outcomes. The contributions that the temporal characteristics of the injury such as rise time and duration have on damage to the brain have just begun to be investigated (Cater et al., 2005; Magou et al., 2011; Ganpule et al., 2013; Sundaramurthy et al., 2012).

In closed head injury, damage to axons is thought to be induced by deformation of the brain tissues in response to an insult (Smith and Meaney, 2000; Meaney et al., 1995). Lateral fluid percussion brain injury (FPI) is one of the most commonly used and well-characterized experimental models of TBI. It is used to deform the brain of rodents to produce both focal and diffuse injury characteristics (Cortez et al., 1989; Dixon et al., 1987; Graham et al., 2000; Hicks et al., 1996; Morales et al., 2005; Thompson et al., 2005). Potentially, one of the biggest contributors to differences in TBI outcome could be the rate at which pressure changes in addition to magnitude of pressure that deforms the brain (Magou et al., 2011; Ganpule et al., 2013; Sundaramurthy et al., 2012). The term “rate” is defined as the rise time to peak pressure. Because brain tissue is viscoelastic, both rate and magnitude of the pressure will affect how the tissue responds mechanically and thus could lead to unique pathophysiologies (Magou et al., 2011; Shuck and Advani, 1972; Arbogast et al., 1997). Greatly contrasting examples would be a head impact from a fall vs. a blast wave; the latter being several order of magnitude higher in rate.

The contribution of the rate of injury was recognized in early head injury physical models (Sundaramurthy et al., 2012; Shuck and Advani, 1972; Arbogast et al., 1997; Smith et al., 1997; Liu et al., 1975; Adams et al., 1983; King et al., 2003), where injury was correlated with rotational acceleration of the head. Currently, there are no animal models directly examining whether the pathophysiological outcome of injury depends on the rate of the delivered injury. This is likely due to the limitations of the available animal models to only adjust for injury magnitude. For instance, FPI and weight drop injury vary either by height adjustment of the pendulum in FPI (Dixon et al., 1987; McIntosh et al., 1989) or by height or mass adjustment of the dropped weight (Dail et al., 1981; Feeney et al., 1981; Marmarou et al., 1994; Sawauchi et al., 2003). A notable exception, the miniature pig injury model, can adjust rotational acceleration. In this model the device rapidly rotates the animal’s head over the designated angular excursion at specific angular accelerations, which correlated with severity of diffuse brain trauma (Smith et al., 1997). The model, however, is difficult to replicate and not widely used.

In this study we have developed a computer controlled FPI device based off the widely used animal model. Using a voice coil actuator to drive the fluid percussion, this system can generate a desired pressure waveform including independent control of injury rise time and duration. Here we characterized the system capabilities and verified it against a commonly used FPI device.

2. Methods

2.1. Computer controlled fluid percussion device

A voice coil actuator driven fluid percussion injury system (vcFPI) was developed to precisely control the characteristics of the pressure waveform including rise time and peak pressure. Fluid percussions were generated by moving a rigidly connected hydraulic cylinder with a linear voice coil actuator (LA2-42-000A, BEI Kimco) (Fig. 1). Accordingly, the controlled motion of the voice coil and hydraulic cylinder translates into a controlled rise in fluid pressure. A flat-faced pressure transducer (px61v0-100gv, Omegadyne) was mounted at the output of the hydraulic cylinder to measure the applied fluid percussion. A 2.6 mm-ID female Luer-loc fitting connected the injury device to a male Luer-loc connector cemented to the rat skull. LabView (National Instruments) was used to acquire the fluid percussion pressure waveform for analysis.

The movement of the voice coil actuator was controlled by a proportional-integral-derivative (PID) controller (Pfister et al., 2003) (S100, Automation Modules) (Fig. 1). A linear optical encoder (Zeiss, LEI 5, 1 μm resolution) was used to close the PID control loop. Voice coil hydraulic cylinder motion was programmed to make a desired, target displacement using a triangular motion scheme. A triangular motion refers to the velocity profile of the motion at a constant acceleration. The desired or target motion is determined by the equation of motion and the programmed velocity and acceleration. The optimum values for displacement and velocity leading to the desired pressure pulse were determined experimentally. Displacement was varied to control the desired peak pressure. Velocity was chosen to achieve the desired rate of rise. A constant acceleration was specified at the maximum value for a linear rise in the pressure.

2.2. Characterization of pressure waveform generation

Motion control is affected by the physics of the system including the mass and friction of the moving parts and the compliance of the load attached to the hydraulic cylinder (i.e. a rat head). To characterize the motion control of the mechanical system without the presence of a load, valve #1 was closed creating a non-compliant system (Fig. 1). A span of displacements was executed and the resulting pressure was recorded. Pressure pulse data was analyzed to determine peak pressure, rise time, and impulse. Rise time was calculated as the pressure rise from 10% increase to 90% of the peak representing the rate at which the injury was delivered. The impulse of the pressure waveform is a representation of the total energy transferred to the brain tissues and was calculated as the