Abstract  Hallmarks of traumatic brain injury in man can be faithfully reproduced in the laboratory using fluid percussion injury. Variations in the surgical procedure provide the ability to induce focal diffuse or mixed focal and diffuse brain injury in various laboratory species. Being fully scalable, fluid percussion can induce mild, moderate, or severe brain injury in subjects of any age. This chapter outlines the procedures for midline (diffuse) fluid percussion brain injury in adult male Sprague-Dawley rats and lateral (mixed) fluid percussion brain injury in adult male mice. With these procedures, it becomes possible to generate brain-injured laboratory animals for studies of injury-induced pathophysiology and behavioral deficits, for which rational therapeutic interventions can be implemented.

Keywords: Fluid percussion, Rat, Mouse, Brain injury, Trauma

1 Model Selection

Fluid percussion permits the study of experimental traumatic brain injury (TBI) in a model that is reproducible, clinically relevant, and scalable between species and injury severities. Brain injury is induced by a rapid (~20 ms) fluid pulse through a craniotomy onto the intact dura that follows the inner curvature of the skull and creates an elastic decompression of the brain.1,2 The mechanical forces disrupt cell membranes, blood vessels, and neuronal processes. By increasing the angle from which the pendulum hammer falls, greater pressures can be generated to travel through the fluid-filled cylinder and impact the brain. At a moderate level of injury, 20–25% of animals die as a result of the injury within the acute posttraumatic period (15 min), generally from respiratory failure and pulmonary edema. This is a normal and desired feature of TBI models, as it reflects human TBI.

In laboratories worldwide, subtle variations in surgical and injury procedures reproduce the spectrum of brain injuries found in the human population. Primarily, the location of the injury site determines the major features of the injury, where a midline location induces a diffuse injury...
and a lateral location induces a focal injury with a diffuse component.\textsuperscript{3–5} Fluid percussion injury reproduces the acute reflex suppression, functional deficits, and histopathology evident after TBI in man.\textsuperscript{6} The model continues to be implemented to evaluate pathophysiological mechanisms underlying posttraumatic degeneration, behavioral deficits, and therapeutic interventions to mitigate the degeneration and promote recovery of function.\textsuperscript{7}

This chapter focuses on the streamlined procedures employed in the author’s laboratory, which are a result of years training in several different laboratories in these techniques. In either rats or mice, the cranial surgery is performed under inhaled isoflurane anesthesia, allowing a rapid recovery from the surgery. Injury is induced later the same day under light isoflurane anesthesia to mimic, as close as possible, the human condition at the time of injury.

2 Materials

2.1 Animals

Fluid percussion brain injury has been successfully performed on various species, including cats, rabbits, pigs, rats, and mice. The adaptation of fluid percussion to rats\textsuperscript{8–10} was followed by its implementation in mice.\textsuperscript{11} The procedures outlined in this chapter focus on adult male Sprague-Dawley rats (~400 g) and 8-week-old adult male C57Bl/6 mice (~25 g). To maximize the success of the brain injury, examine all animals for any signs of ill health (e.g., rough coat, bleeding or dirty eyes, runny or bleeding nose, and scratches around eyes or nose area). Weigh all animals prior to surgery to follow injury-induced weight loss.

2.2 Equipment

2.2.1 Anesthesia

Rodent nose cone for inhaled anesthesia

2.2.2 Surgery

Microwave heating pads (BrainTree Scientific, #39DP)

Stereotactic head holder

Scalpel

Delicate bone scraper (Fine Science Tools, #10075–16)

Bulldogs (Fine Science Tools, #18050–28, #18051–28)

Chisels Wedelstaedt 3/4 DE (Henry Schein, #600–4972)

2.2.2.1 Rat Surgery

Dremel tool with engraving cutter #106

Trephine (4.7 mm) (Miltex, #26–140)

Fingernail drill with 5/64” drill bit (Miltex, #33–232)

Stainless steel skull screws (2–56 × 3/16”) (Small Parts Inc., #MX-0256–03B-25)

2.2.2.2 Mouse Surgery

Custom trephine (3 mm)