Abstract  A model of asphyxial cardiac arrest in 17-day old rats is described. This clinically relevant model includes a period of hypoxemia followed by ischemia and resuscitation. Continuous physiologic monitoring is performed before, during, and after the insult. Graded insults produce consistent and dose-dependent brain injury with histological damage and behavioral impairment. The details of the procedures, along with outcome assessments and applications, are discussed.

Keywords:  Asphyxia, Cardiac arrest, Cerebral blood flow, Neurodegeneration, Sprague-Dawley rat

1  Model Selection

Cardiac arrest (CA) in infants and children is secondary to asphyxia in most cases. This differs from adults where CA is typically caused by cardiac arrhythmias such as ventricular fibrillation (VF) or ventricular tachycardia (VT). Asphyxial CA differs in physiology from VF- or potassium chloride-induced cardiac arrest because a period of hypoxemia, hypercarbia, and hypotension precedes cardiovascular collapse and circulatory arrest. Regardless of the underlying etiology, all CAs have a period of total body ischemia that can cause impaired and inter-related post-ischemic organ dysfunction. This multisystem organ dysfunction is reproduced in animal models of CA (VF or asphyxial), but not in models of isolated brain ischemia, mimicking the clinical condition.

To model pediatric asphyxial CA, our laboratory modified an established protocol of CA in adult rats and applied it to immature, postnatal day (PND) 17 rats. PND 17 rats resemble a 1-to-4-year-old human child in terms of a number of developmental parameters. The model of pediatric asphyxial CA described in this chapter is therefore especially relevant to scientists whose research interest involves CA in children.
2 Materials

2.1 Animal Selection

The use of all photographs has been preapproved by the Institutional Animal Care and Use Committee at the University of Pittsburgh.

We use Sprague-Dawley rat pups, PND 16–18. Pups are breastfed at this age and are therefore housed with a post-partum female rat, allowing them full access to nutrition prior to the experiment. Litters of one mother with eight pups are ordered to obtain rats with similar weights. It is our experience that pups below 30 g have lower survival rates post-resuscitation. Therefore, we typically use PND 16–18 rats weighing 30–40 g on the day of the experiment. Normal cardiovascular physiologic parameters of PND 17 rats under anesthesia with fentanyl or isoflurane are a heart rate (HR) of 350–450 beats min\(^{-1}\) and a mean arterial pressure (MAP) or 65–80 mmHg.

2.2 Anesthesia

In this model, we anesthetize the animals with either isoflurane or fentanyl. The choice of anesthetic depends on the parameter studied. Isoflurane provides an excellent plane of anesthesia and stable HR and MAP. Anesthesia with isoflurane has the advantages of being easier to titrate and more predictable. The recovery of the animal is rapid after isoflurane anesthesia; however, isoflurane markedly increases cerebral blood flow (CBF) as compared with fentanyl.\(^5\) Therefore, in experiments where measurement of CBF is important, fentanyl is a more desirable anesthetic choice than isoflurane.

2.3 Equipment

2.3.1 Surgery

– Surgical instruments (Fig. 1a): Roboz by Dumont 45° angle forceps; straight Dumont forceps; Roboz RS-5602 iris scissors; Roboz RS-5137 forceps 45° angle; scissors; curved hemostat; straight forceps
– Dissecting microscope
– Femoral arterial and venous catheters: PE 10 and PE 50 polyethylene tubing (Becton Dickinson; Fig. 1b)
– Glue: 3M Scotch Weld Instant Adhesive CA 4OH
– Syringes
– 6.0 silk sutures
– Short blunted needle, 23G
– Heparinized saline 1 unit ml\(^{-1}\)
– Heating pad
– Cotton tip applicators
– Iodine
– Lidocaine solution

2.3.2 Anesthesia and Intubation

– Isoflurane
– Plexiglas chamber
– Laryngoscope with a modified Miller 0 blade, machine-filed from base to tip to reduce the width of the blade (Fig. 1c)