RAT JUGULAR VEIN AND CAROTID ÅRTERY CATHETERIZATION FOR ACUTE SURVIVAL STUDIES

RAT JUGULAR VEIN AND CAROTID ARTERY CATHETERIZATION FOR ACUTE SURVIVAL STUDIES

A PRACTICAL GUIDE

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CATHETERIZATION

An implant procedure in which a small tube is inserted into a body cavity, duct, or vessel for the purpose of fluid administration or withdrawal ~ AALAS Reference Directory

Foreword

In biomedical teaching and research, catheterizations of the jugular vein and the carotid artery have been used to access the cardiovascular system in various animal species. Such surgical procedures are technically challenging in rodents because of the small scale involved. There are not many alternatives if the rodent's survival and easy post-operative handling are required. While rodents are becoming predominant research animals, reliable execution of these procedures is essential for many endeavors in pre-clinical research and product development. This practical guide should help scientists and technicians master the procedures in rats and thus confidently move forward to data collection.

For those who have been fortunate to work with Angela Heiser in the laboratory, we have long witnessed how dedicated to the profession a researcher can be. Angie enjoys her work immensely. Her laboratory records are always focused, highly organized, and simply deduced but with in-depth knowledge. In addition to the sciences, she can add stunning, artistic impression to the content. No wonder I have seen so many superb presentations by Angie. Publication of this practical guide certainly will be a milestone.

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INTRODUCTION

Jugular vein and carotid artery catheterizations are among the most widely used surgeries in research labs around the world. Typically, technicians teach these skills to incoming employees and move on to graduate studies or other fields. A resulting "oral history" of catheterization has been passed down from technician to technician. I have endeavored to capture these techniques on paper. Through the years, I have searched for and collected a number of training materials and guides for teaching purposes. This is my attempt to compile all the necessary information in one source.

These catheterizations are extremely important for confirmed intravenous delivery of test substances and arterial blood collection. Catheterization reduces the stress of multiple sampling as observed in association with tail vein or orbital sinus techniques (Ling, 2003; Flynn, 1988; Cocchetto, 1983). Very few adverse effects, including a possible rise of corticosterones and a decrease in platelets, are associated with indwelling catheters except under chronic conditions (Fagin, 1983; Richman, 1980). With practice and dedication to research and humane animal use, one may develop a high throughput paradigm generating predictable results with what is generally

thought to be a laborious, rate-limiting step in research. Counting thousands of catheterizations performed in my career, my survival and patency rate are 97%.

"We refer to the art of surgery, so why not make it an art and, like the artist, be engrossed in its handicraft." ~ S. Bunnell, Surgery of the Hand, 1944.

Some artists have argued that there is an element of science to their approach. I have discovered that surgery also involves an element of art. In fact, in 2004, UCLA organized an exhibit presenting "the world of nanoscience through a participatory aesthetic experience" (nano.arts.ucla.edu). From this basic guide, surgeons will evolve their own subtleties and personal preferences. My sincere hope is that this guide will secure knowledge for future generations of researchers in an original, undiluted format. Society demands a lot from science and this is my contribution.

~ Angie Heiser

PERIOPERATIVE CARE

Perioperative care includes pre-operative, intra-operative, and post-operative care of the patient. Careful attention to these areas is crucial to successful surgery. The goal of this section is to illuminate and define these often-overlooked components of the surgical process.

Pre-operative Care (prior to surgery)

- <u>Quarantine</u>: Acclimate incoming rats to their new environment and housing for a minimum of 24 hours. It is preferable to quarantine for 7 14 days. This "grace period" allows the animal to return to normal hormonal and metabolic parameters as evidenced by stable body weight following the stress of transport. The investigator can determine that the animals are free of latent or enzootic diseases. Regular handling promotes less stress to the animal and leads to a quicker recovery.
- <u>Pre-operative body weight</u>: Weigh pre-surgery since rats are likely to experience weight loss post-surgery.
- <u>Gross physical exam</u>: Observe the animal for nose or eye discharge, diarrhea, fur matting, and overall appearance and behavior. Palpate for any growths, tumors, or skin abnormalities.



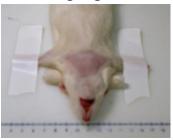
- <u>Antibiotic</u>: If antibiotics are preferred, it is most effective to administer prior to surgery in order to maximize blood levels during surgery and recovery.
- <u>Pre-analgesic</u>: Benefits of analgesics administered pre-surgery are many fold. Rats are less likely to exhibit depression in food intake or experience pain post-surgery and require lower injectable anesthetic doses during surgery. These combined factors contribute to a

quicker recovery and fewer side effects. Single doses are recommended of one of the following; (1) IM or SC flunixin (flunixamine, banamine) @ 1.1 – 3.3 mg/Kg (Stewart, 2003), (2) SC or IV buprenorphine @ 0.01 – 0.05 mg/Kg (Hayes, 1998; Colletti, personal experience).

• <u>Fasting</u>: Do not withhold food prior to surgery unless absolutely necessary because the rat is not likely to consume much post-surgery. An empty stomach prior to surgery is not required since rats are a non-vomiting species (Takeda, 1993).

Intra-operative Care (during surgery)

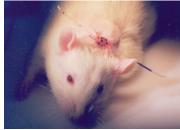
- <u>Mucous membranes</u>: Check the color of the eyes and tongue as an oxygen indicator. A blue color indicates possible hypoxia.
- <u>Body temperature</u>: Body temperature can be monitored. It is important to maintain body heat using a heating pad, heat lamp, or isothermic pad.
- <u>Total blood volume</u>: Avoid hypovolemic shock by controlling blood loss through good hemostasis during surgery.
- <u>Body position</u>: Use care to position the animal in the best possible way to protect cardiac and respiratory function.
- <u>Respiration rate</u>: Watch the animal's breathing by observing the rise and fall of the chest. Observe the pattern and depth of breathing. During surgery, it is possible to monitor by noting the pulse in the carotid artery and the color of the blood in the artery through the scope.



• <u>Tissue handling</u>: Take care to handle tissues gently causing as little disruption as possible. Using a retractor instead of clamped hemostats reduces trauma to skin. • <u>Wound closure</u>: The use of wound clips or subcuticular suturing may reduce self-mutilation during recovery.

Post-operative Care (after surgery)

- <u>Atropine:</u> Atropine sulphate (parasympatholytic) is often used to counteract decreased heart rate due to increased vagal tone. In addition, atropine is used to decrease salivation; allowing the airway to stay open. The surgeon may prefer to administer atropine immediately <u>after</u> surgery to avoid bleeding complications from atropine's effect of increased heart rate. The accepted dose is 0.05 mg/ kg IP. Check expiration date and make fresh.
- <u>Anesthetic recovery</u>: Before the animal is fully awake, emergencies can occur quickly and unexpectedly. This period of recovery requires the most frequent observation. The animal should be rotated every 30 minutes to avoid edema and irregular breathing. Keep the animal warm. Be careful to avoid heating pad burns from a high heat setting. Regulated heat sources are commercially available such as the ThermoCare ICU unit. Check the wound site for any bleeding.



- <u>Acute recovery</u>: This is a period during which the animal has resumed food and water intake and is approaching normal physiological parameters. The animal should have easy access to food and water. Transgel® or HydroGel[™] are effective water sources and can be left on the floor of the homecage with rat chow or Nutra-Gel (food & water source).
- <u>Individual housing</u>: Rats should be housed one to each cage post-surgery. Catheters are better protected from cage mate curiosity and chewing. Some facilities may require this

justification for individual housing because it is normally a more stressful housing condition. Rats prefer group housing (Gentsch, 1982).

Long-term recovery: During this last stage of recovery, the animal is exhibiting normal
physical and behavioral parameters. Rats may be more susceptible to corneal injury
following injectable anesthetics (Turner, 2005). Observe the wound site for bleeding,
infection, edema, unraveled sutures, and self-mutilation. Sutures can be removed at 7 – 10
days post-surgery. Observations should include motor function and the quantity/quality of
urine/feces. Monitor weight gain/loss.

Signs of Pain

Clinical observations of pain and stress in rats can include:

- guarding the wound site
- licking/biting/scratching wound
- vocalization
- rough hair coat/ decreased grooming
- red staining around eyes and nose (porphyrin)
- self-mutilation of wound
- immobility
- decrease in food/water intake
- decreased exploring and grooming
- restlessness
- reluctance to move
- increased respiration
- hunched posture