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Association of Primate Veterinarians Guidelines for Nonhuman Primate Restraint

Purpose

The Association of Primate Veterinarians (APV) recognizes that several forms of restraint, including physical and chemical, are necessary for the safe handling of nonhuman primates (NHPs). The following guidelines aim to provide information to researchers, animal caregivers, veterinarians, and institutional animal care and use committees (IACUCs) on safe and humane restraint for primates.

Background

The purpose of physical or chemical restraint is to allow animal-related tasks (e.g. husbandry, veterinary care, experimental procedures, manipulation for data collection, etc.) to be conducted humanely and efficiently with both animal and human safety in mind, and while minimizing animal stress or distress.

Procedural Guidance

General Considerations. Whenever possible, nonhuman primates should be trained, using positive reinforcement principles, to cooperate with routine husbandry tasks, such as cage changing, as well as to participate voluntarily with routine experimental practices. Nonhuman primates have significant cognitive abilities and training for cooperation in husbandry and research tasks. This can significantly reduce human and animal stress and the likelihood for injury or accidents to occur. When it is not possible to train animals to cooperate because of time or other constraints, physical and chemical methods of restraint may need to be considered. The following are considerations when determining the most appropriate restraint equipment or method to use:

1. Time required for animal habituation and training to restraint method
2. Potential impact on the research;
3. Frequency of handling required;
4. Type of equipment available;
5. Duration of restraint;
6. Species-specific behavioral and postural differences; and
7. Other considerations (e.g. pregnancy, animals with preexisting conditions, animals with jackets or implants, etc.).

Positive Reinforcement Training. Training animals to cooperate without the need for restraint devices or drugs is strongly encouraged and convenience alone must not dictate the method used for restraint. Whenever possible, cooperation by nonstressed, conscious animals yields the most relevant data for studies. Ideally, the veterinarian and researcher should work with a behaviorist and the training plan should have reasonable, sequential steps and attainable goals. The plan also should take into consideration the unique personality traits of each animal and their capacity to learn and remember tasks to condition them to be a willing worker. The plan should be based on receiving rewards (e.g. treats, juice, and other rewards) for the tasks learned and reproduced, and receiving no rewards for the lack of progress (i.e. positive reinforcement). Clicker training is designed to obtain desired behaviors by giving food and treats immediately after the sound of a clicker and has been used with very good success in primates. (Wolf, 2012).

Habituation to Restraint. It is essential that NHPs be habituated to minimize stress when they must be restrained awake in a device for a prolonged period of time. Examples of situations that might require habituation include placement in a restraining device for >30 min on a regular basis in repeated sessions e.g., blood sampling, head restraint, reach/grasp motor tasks and visual tasks. The duration for which a primate must be restrained is dependent upon the duration of the procedure and individual behavioral traits and cognitive capacity of each animal. For example, aggressive, dominant animals may require different habituation strategies compared to more submissive animals. Appropriate habituation to restraint is achieved when the animal exhibits normal physiologic and behavioral characteristics and when they enter the restraint device voluntarily (NRC, 2002). In lieu of habituation some animals may be conditioned to using the restraint device with use of the positive reinforcement training.

Physical Restraint. Methods of physical restraint include hand restraint, pole and collar, transfer box, restraint chair, jacket, and portable squeeze unit. Animals hand caught or trained to a collar restraint should have lower body support provided directly by the restrainer or via a flat surface, such as the floor. Alternatively, after capture, the primate should be immediately transferred to a primate chair or other restraint device to minimize potential discomfort and distress. When a restraint device must be used it should be: clean, of an appropriate size, and maintained in proper working order to ensure the comfort and safety of the animal and human handler. The device should be inspected before each use to ensure that all mechanical parts are secure and functioning smoothly to avoid injury to the animal or the handler. Ideally, restraint chairs that allow primates free use of arms and legs should be equipped with a guard to protect handlers from exposures.

Chemical Restraint. Animals may be trained to voluntarily cooperate for many procedures and this should be considered for primates that will be maintained for extended periods of time or for long-term studies. Chemical restraint, for example, ketamine (alone or in combination, e.g., dexmedetomidine, midazolam) may be considered when immobility is required (e.g., electrocardiography) or when the planned procedure has the potential to cause more than slight or momentary distress or discomfort (e.g., removal of skin sutures, etc.). Another consideration for using chemical restraint in primates is to ensure safety for personnel. When the use of chemical restraint is elected, NHPs should be fasted prior to chemical immobilization to reduce the risk of aspiration. Care should be taken to ensure that procedures involving chemical restraint are scheduled with a maximal interval to avoid repeated fasting, inappetence, and associated weight loss; prolonged episodes of hypothermia, bloat, and other stressors associated with administration of sedative or anesthetic agents. Performing multiple experimental/clini-

cal procedures under a single chemical restraint event is often preferred to multiple anesthetic episodes over a short period of time. The lowest dose of drug should be used to achieve the desired effect to minimize potential side effects associated with the particular immobilizing agent.

The following are important considerations when using chemical restraint in primates:

1. Pain and/or distress expected with the procedure;
2. Safety of the animal and human handlers;
3. Size and maturity of the animal; and
4. Opportunity for positive reinforcement training or habituation to the procedure.

Selection of the appropriate sedative or anesthesia regimen should be made in consultation with the veterinary personnel. Specific pharmacologic reversal agents should be used whenever possible to reduce duration of immobility and counteract potential side effects (e.g., hypothermia, bradycardia or hypotension). Aspiration is always a risk, even in fasted animals. Primates must be monitored appropriately until they have completely recovered from immobilization. Ideally, animals recovering from anesthesia should be placed in a comfortable, warm, quiet area or space, preferably with restricted access to climbing apparatus, until they regain full physical coordination, to minimize potential associated injuries and trauma. Depending on the operational features of some housing facilities it may be possible to use pet carriers or transport boxes to facilitate separation between animals and offer a secure place and additional time for the reflexes to return. There are situations in which one or more of these criteria cannot be met due to facility limitations such as large compound, outdoor housing areas or emergencies. In these instances, proper precautions should be in place and professional judgment with a focus on animal welfare should be exercised. If NHPs are socially housed they should remain separated where possible until they have regained full physical coordination and mental awareness to minimize potential injuries. Animals living in large social outdoor groups may have to be recovered in indoor housing areas where other recovering animals may be present and removing access to climbing structures is not practical. In such cases, it is imperative to have appropriate supervision.

Duration of Restraint. Restraint should be minimized to the shortest duration possible. If the animal is to be physically restrained for > 30 min on a regular basis, it must be habituated. Other techniques should be investigated to avoid prolonged restraint, such as use of indwelling catheters and vascular access ports for repeated collection of blood samples, alternative study designs, etc. Prolonged restraint in chairs may lead to decubitus ulcer formation in addition to mental fatigue of the animal. In the U.S., the United States Department of Agriculture (USDA) Animal Welfare Regulations (AWR) state that "Maintenance under [physical restraint] must be for the shortest period possible." The AWR go on to state, "In instances where long-term (more than 12 hours) restraint is required, the nonhuman primate must be provided the opportunity daily for unrestrained activity for at least one continuous hour." (AWA & AWR, 2002).

Monitoring. Animals should be carefully observed during all types of restraint, and they should never be left unattended without some form of direct or indirect monitoring to ensure animal safety. Suitable forms of monitoring may include telemetry, vital sign (e.g. heart rate) monitors, a remote video system or monitoring output on computer tasks. Anesthetized animals should not be left unattended, even in closed cages, as ready access may be required for individuals that are entrapped or in respiratory distress. Some institutions, however, may have specific SOPs allowing deviation from such requirement, backed by historical and statistical data and approved by IACUC. Anesthetized animals should be monitored for respiratory/heart rates and body temperature where practical. Awake animals should be closely observed for evidence of pallor, and also vocalization, constant position shifting, and awkward posturing. Proximity to other restrained animals should be considered to minimize aggression and potential trauma.

Personnel Training. Personnel working with restrained primates must be familiar with normal behavior in healthy unrestrained animals. Such familiarity is vital to being able to recognize any departures from normal and, in particular, any evidence of discomfort and distress exhibited by animals under physical/manual restraint. Knowledge and experience in monitoring vital signs in animals under chemical restraint/sedation is paramount where medical or experimental intervention may be necessary. If any restraint equipment is used, personnel should be trained to operate the equipment and how to deal with equipment failure to minimize animal injury and preserve human safety.

Endpoint Considerations. Animals that fail to habituate to the planned restraint should be evaluated and considered for removal from study if alternative methods are not viable. Duration of the habituation trials should be discussed by and consensus reached between the veterinary clinician in charge, the principal investigator and IACUC.

Record Keeping. IACUCs should be aware of the various types of NHP restraint equipment and modalities and review them at least annually within the program description or through specific protocol review. All relevant information (e.g. the animal's response to the training/physical restraint, drug doses, recovery and complications etc.,) should be recorded in the medical records and research logs.

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