The Program Committee for the 63rd annual meeting of the American Association for Laboratory Science (AALAS), chaired by Sonja Chou, chose trauma recovery research as a spotlight topic. This theme was reflected in the keynote address by Major General James K. Gilman during the Opening General Session on Sunday, November 4. Major General Gilman discussed recent advances in battlefield medicine and patient care and the role of lab animals in contributing to these advances. The spotlight topic was also highlighted in presentations throughout the conference that focused on working animals (such as dogs trained for military and other service); lab models of radiation syndrome and traumatic injury; and in vitro adjuncts to animal-based trauma research.

Sunday’s Opening General Session also featured the presentation of several annual AALAS awards. The Charles A. Griffin Award—the oldest AALAS award, first presented in 1954—recognizes ethical scientific or technological advancements in humane experimentation or improved animal care practices and was given to Marilyn Brown. The Nathan R. Brewer Lifetime Achievement Award for outstanding lifelong contributions to improving the care, quality and environment of animals used in biologic and medical research was given to Craig Franklin. Craig Fisk received the Joseph J. Garvey Management Award in recognition of his outstanding accomplishments in the administration of programs relating to the care, quality or humane treatment of animals used in biomedical research. The Pravin N. Bhatt Scientific Investigator Award for outstanding scientific accomplishments, established in 1994, was given to Joseph Garner. The George R. Collins Education and Training Award recognizing outstanding contributions to the field of laboratory animal training and education was presented to Denise Ostmeyer. Xiomara Santiago was recognized as Technician of the Year for her contributions to the promotion of laboratory animal care.

Each year, the AALAS national meeting features several special lectures. The first of these took place on Monday morning, November 5. The Charles C. Hunter Lecture pays tribute to the late Dr. Hunter, a former AALAS president known for his dedication to continuing education for laboratory animal technicians. This year’s Hunter Lecturer, Peggy Callahan, spoke about her research with captive wolves. The Charles River Ethics and Animal Welfare Lecture, sponsored in part by the Charles River Commitment to Humane Animal Research through Excellence and Responsibility Program, was given on Tuesday morning, November 6, by Bernard Rollin, who discussed the ethics of animal research. Also on Tuesday morning, the Wallace P Rowe Lecture, named after the first scientist to undertake systemic studies of viral infections of lab mice, was a presentation by Axel Kornerup Hansen titled “The impact of the gut microbiota on rodent models of human diseases.”

AALAS held its General Membership Meeting on Monday, November 5, which included a ceremony introducing the new President. AALAS leadership is a four-year commitment, beginning at the close of each annual meeting. During the first year, officers serve as Vice-President Elect, advancing to Vice President in their second year of service, to President in their third year and finally to Past-President in their last year. In Minneapolis, 2012 AALAS President Kathy Laber passed the gavel to Kim Saunders, 2013 AALAS President. Laber becomes the new Past-President, as Robert Dysko exits the office. Scott Mischler replaces Saunders as Vice President for 2013, and earlier in the year, Cindy Buckmaster was chosen as the Vice President-Elect. Nominations for the 2014 Vice President-Elect were due February 1, 2013.

On Wednesday, November 7, poster awards were given in three topic categories: clinical, husbandry/management and laboratory investigations. First place in the clinic category was awarded to Doreen Kohlert for her poster, “Unanaestheticized sublingual blood collection in rats.” Second place went to Kathryn Mullen’s poster, “A novel method of oral drug administration for rabbits,” and Erica Sheldon’s poster, “Rehabilitation technique after finger fracture in a baboon (Papio anubis).” In the husbandry/management category, “Creation and use of environmental enrichment checklists” by Denise Molk earned first place and “Pooled fecal floats from colony cages detect Aspicularia tetraperta and fur mites” by Julie Watson was awarded second place. Third place went to Michelle Wallace-Fields for her poster, “A novel approach to a mapping system to reduce labor and product costs and decrease chemical usage.” Finally, in the laboratory investigations area, “Impact of mouse age on fur pluck surveillance of Mycoplasma musculinus” by Kelly Rice took first place. The second-place poster was Amanda Leber’s work, “Mucosal cheek pouch tattoos allow repeat assessment of experimentally induced oral tumor development in Syrian hamsters (Mesocricetus auratus).” Shannon Stutler won third place with her poster, “Use of novel telemetry devices to collect individually discernible data sets from socially housed rhesus macaques (Macaca mulatta).”
Delay between adaptation and experimentation

Gradual adaptation of her rats to a restraint device seemed a logical and obvious strategy to Dr. Julia Marshall, a neurophysiologist at Great Eastern University. Her research focused on ocular responses to external stimuli, and her methodology required that the head of each rat that she used be immobile, although the remainder of the torso did not require full restraint. Her IACUC-approved adaptation protocol had three steps: first, a rat was placed into an empty plastic restraint tube once a day for three days; second, the rat was anesthetized and allowed to awaken in the tube once a day for three days; finally, the rat was lightly anesthetized, its head placed in a special restrainer within the plastic tube, and again allowed to awaken in the restrained position once a day for three days. The rat would remain in the tube for 30 minutes during the first session, then 45 minutes for the second session and finally for 60 minutes at the last session. After the conditioning was completed, the study, which lasted five consecutive days, would begin. A total of 15 rats would be tested, all requiring head restraint.

Marshall had used the same basic protocol for many years without a problem. The occasional rat that did not adapt to the restraint device was excluded from her study. But just before the most recent testing session, Marshall’s long-time research associate took ill, and the testing had to be delayed for a little over a week. The delay was quite obvious to the vivarium staff because the testing room was ready but unused. The attending veterinarian asked Marshall about her plans to ‘readapt’ the animals before the testing started, but Marshall said that wasn’t necessary because the rats had already been adapted to the restraint procedure. The veterinarian could not find any literature about the length of time a rat could remain adapted to a restraint procedure after a break in a testing protocol. When Marshall also could not produce any documentation relative to her model, the issue was quickly given to the IACUC. Unfortunately, the IACUC could not locate an expert who could confirm or refute Marshall’s opinion, and so the issue seemed to be headed for a stalemate.

What steps do you think the IACUC could or should take to resolve this problem?

RESPONSE

Pilot study

Stephen I. Levin, DVM, PhD, DACLAM & Nicolette A. Zielinski Mozny, PhD, DVM, DACLAM

The IACUC is faced with a difficult decision. If the Committee allows the study to continue without ‘readaptation’ to the restraint device, there is the potential for the rats to experience unnecessary or increased distress. If the IACUC requires ‘readaptation’ of the rats, the study will be further delayed. At the onset, there is a deviation in the experimental design with regard to the time interval from the initial training event to the start of the study. Depending on the verbiage in the approved protocol, continuing the experiments could be considered non-compliance. If the IACUC determines that the currently approved protocol does not allow for an alteration in the interval between adaptation and initiating the experiment, and that this change constitutes a “significant change” (Public Health Service Policy on Humane Care and Use of Laboratory Animals (PHS Policy), section IV.C.1)1 owing to the potential for increased distress, then the IACUC should require Marshall to submit an addendum to her protocol. Another factor the IACUC needs to address is the protocol approval process timeline.

There is also the potential that the data collected from this group of rats won’t be valid due to the time variable introduced. Requiring ‘readaptation’ of the rats would also introduce another variable into the study. Depending on the length of time it takes for the addendum to be approved, the rats that have already been adapted may not be good research models. The IACUC also needs to take into consideration what will happen to this group of animals if Marshall determines that they cannot be used for these experiments.

In order to ensure compliance with the PHS Policy, the IACUC should require that an addendum be submitted to cover the change in schedule. If there is truly no literature to support Marshall’s argument that the rats do not need to be ‘readapted,’ then she could propose a pilot study with this group of rats to determine whether the delay in the beginning of data collection affects the outcome of the experiments or results in increased distress to the rats. The IACUC could approve starting with five of the fifteen rats and grant approval for continuing with the remaining rats if Marshall presents evidence that the rats have remained adapted to the restraint. Marshall will need to include criteria that can be used to determine that the rats do not show increased stress compared with those used in her previous experiments. Such a pilot study would allow the protocol to be further modified with flexibility in the time interval between adaptation and data collection so that delays in the future will not result in non-compliance.
Is the change significant?

Walter L. Horne, DVM, DACLAM & David C. Riccio, PhD

Because the IACUC-approved protocol describes immediate onset of the study after conditioning, the introduction of a delay between the adaptation paradigm and the actual study represents a protocol change. It is up to the IACUC to determine whether the change is significant and requires IACUC approval before implementation. From the description provided, it is not clear whether the IACUC met to discuss the matter. In our opinion, it is essential for a quorum of the IACUC to meet promptly, review any available information pertinent to the issue and render a decision so that the investigator can proceed with the research accordingly. Marshall should be invited to the meeting to offer her perspective.

The outcome of the meeting, as decided by a majority vote of the members present, would be a determination as to whether the change is significant and requires IACUC approval or whether it calls for simple notification to the Committee that the change is being implemented. One of the critical factors to be considered in reaching the decision would be whether or not rats remain adapted for the period of time in question. In the absence of literature documentation of the need for 'readaptation', the IACUC is faced with the unenviable task of making a decision based on the opinions of the members present.

In reaching their decision, the IACUC members may choose to require complete 'readaptation' of the rats; to require implementation of one or multiple 'reminder' episode(s) of adaptation; or to accept the investigator's word and allow the study to proceed without further conditioning. In any case, two or three members of the Committee, preferably including the attending veterinarian, should be designated to observe the procedure with different rats to assess the animals' responses to the restraint in light of the IACUC's decision. Any member wishing to participate in the observation should be given the opportunity to do so, and the members should report their observations to the IACUC.

It is well documented that rats remember fear conditioning for well over a week, and even for several weeks. Studies also support the notion that a tolerance to stressors in rats persists for weeks. Given that the initial response of a rat to restraint will likely involve a fear component and that restraint is a known stressor, it is not unreasonable to conclude that rats that have undergone the prescribed adaptation paradigm will easily recall it and adapt readily to the restraint. There is a wealth of literature on rat learning and memory, and it is hard to imagine that a reasonable search would not identify publications clarifying whether 'readaptation' is necessary.

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RESPONSE

IACUC observation team

Joan T. Richerson, MS, DVM, MS, DACLAM, CPIA

In this scenario, the age of the rats and the design of the special restraint device used to immobilize the rat's head are not provided. For the purpose of this response, I am assuming that the rats are young adults and that they have been previously implanted with some type of head post or head plate that locks into the restraint device. Marshall's IACUC-approved adaptation procedure has always been performed in sequence, so she presumably has no experience with the potential effects of a delay in testing. Nonetheless, rats are known to use their memory of previous experiences in decision-making. In fact, one study demonstrated that adult rats trained to avoid one side of a double-sided chamber remembered which chamber to avoid three weeks after training had stopped. Consequently, Marshall's rats that had completed the adaption training a week earlier probably would recall being in the head retractor. However, recall of a previous experience does not ensure that the rats are adequately adapted to the 60-minute experimental sessions.

Given the lack of an expert consultant or supporting literature on the retention of adaptation to a restraint device in rats, the IACUC has several options to consider. The first is to ask Marshall to repeat the entire adaption procedure; however, this option is burdensome and would seem to be overly cautious given the recall ability of rats. A second approach is to have a team of IACUC members observe the rats undergoing the 60-minute experimental sessions. If the team concludes that the rats tolerated the procedure well, and the approved protocol language is broad enough, then no protocol deviation has occurred (and no protocol amendment is required). If the IACUC team observed that the rats were variable in their tolerance to the testing, the IACUC may require Marshall to conduct a stepwise abbreviated version of the adaption procedure to assess the point at which training for each rat should be resumed. In this case, Marshall would need to submit a protocol amendment outlining, in the event of a delay, a modified adaptation procedure addressing re-training for rats. The IACUC observation option is preferable to the complete re-training approach because it will most likely be welcomed by Marshall and provides a clear and defensible basis for subsequent IACUC decisions.

Nonetheless, in the future, the IACUC may want to reevaluate Marshall's adaption procedure and consider a new approach based on positive reinforcement. A number of investigators have reported training rats to accept head restraint using rewards. The positive reinforcement approach is a refinement, which is consistent with the recommendations of the Guide for the Care and Use of Laboratory Animals regarding restraint, removes the potential confounding effect.
of anesthesia, decreases the likelihood of injury while in the restraint and ensures the rat is in a relaxed state.


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