

UNITED STATES DEPARTMENT OF AGRICULTURE ANIMAL AND PLANT HEALTH INSPECTION SERVICE ANNUAL REPORT OF RESEARCH FACILITY (TYPE OF PRINT)	1. REGISTRATION NO. 57-R-0003 CUSTOMER NO. 896	FORM APPROVED OMB NO. 0579-0036
2. HEADQUARTERS RESEARCH FACILITY (Name and Address, as registered with USDA, include Zip Code) EMORY UNIVERSITY 1440 CLIFTON ROAD, NE ATLANTA, GA 30322 (404) 727-7428		
3. REPORTING FACILITY (List all locations where animals were housed and used in actual research, testing, teaching, or experimentation or held for these purposes. Attach additional sheets if necessary.)		

NOV 30 2006

October 1, 2005 - September 30, 2006 FACILITY LOCATIONS (Sites)

Emory University & Yerkes National Research Primate Center
See Attached List of Facilities

REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY (Attach additional sheets if necessary or use APHIS FORM 7023A)					
A. Animals Covered By The Animal Welfare Regulations	B. Number of animals being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not yet used for such purposes.	C. Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving no pain, distress, or use of pain-relieving drugs.	D. Number of animal upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic, or tranquilizing drugs were used.	E. Number of animals upon which teaching, experiments, research, surgery or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic, analgesic, or tranquilizing drugs would have adversely affected the procedures, results, or interpretation of the teaching, research, experiments, surgery, or tests. (An explanation of the procedures producing pain or distress in these animals and the reasons such drugs were not used must be attached to this report)	F. TOTAL NO. OF ANIMALS (Cols. C + D + E)
4. Dogs	0	6	71	0	77
5. Cats	0	5	43	0	48
6. Guinea Pigs	0	1	102	0	103
7. Hamsters	0	0	8	0	8
8. Rabbits	0	120	183	0	303
9. Non-Human Primates	1632	657	1510	26	2193
10. Sheep	0	0	46	15	61
11. Pigs	0	0	275	0	275
12. Other Farm Animals	0	0	0	0	0
13. Other Animals					
VOLES	0	798	192		990

- ASSURANCE STATEMENTS**
- 1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anesthetic, analgesic, and tranquilizing drugs, prior to, during, and following actual research, teaching, testing, surgery, or experimentation were followed by this research facility.
 - 2) Each principal investigator has considered alternatives to painful procedures.
 - 3) This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and approved by the Institutional Animal Care and Use Committee (IACUC). **A summary of all the exceptions is attached to this annual report.** In addition to identifying the IACUC-approved exceptions, this summary includes a brief explanation of the exceptions, as well as the species and number of animals affected.
 - 4) The attending veterinarian for this research facility has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL (Chief Executive Officer or Legally Responsible Institutional Official) I certify that the above is true, correct, and complete (7 U.S.C. Section 2143)	(Type or Print) DATE SIGNED 11/29/06
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Exceptions to Regulations and Standards

Physical Restraint and Exemptions from Social Enrichment for Nonhuman Primates: Single-housing In Sight and Sound of Conspecifics:

Included in this section are primates that were housed in any condition other than group or pair housing for any significant period of time. For example, study subjects discussed below include those that were housed continuously in protected-contact housing, and those housed in protected-contact and/or group or pair housing for a significant portion, but not the entirety, of the period covered in this report.

A. Some animals used under these conditions are in studies of normal control of movement or motion disorders induced by MPTP. Monkeys given MPTP may be kept in social isolation for periods of three days after drug administration and while MPTP and its toxic metabolites are excreted. Before and after MPTP administration, monkeys in these studies are trained to do simple motor tasks such as reaching, touching a target on a video screen, depressing a key to make a video target appear, and controlling a joystick to move a cursor to a target on a video screen. During these tasks, these monkeys are loosely restrained in a chair and typically spend 4-6 hours per daily session in the laboratory. During these periods, monkeys with head appliances may also undergo short-term fixed head restraint to access the appliances for neurophysiologic recording and microdialysis. Additionally, the administration of the neurotoxin MPTP to induce Parkinson’s Disease (PD) in macaques causes physical impairments that put such animals at risk of plummeting in the social order and wounding and fight injury from a cage mate. Consequently, animals given MPTP are generally housed singly, but in colony rooms within sight, sound and close physical proximity of other animals of the same species. Likewise, to prevent damage to expensive and sensitive surgically-implanted devices by a conspecific, monkeys may be housed singly, but otherwise within sight and sound of conspecifics.

• Analysis of the Neuronal Microcircuitry Basal Ganglia:	4 squirrel monkeys and 2 rhesus macaques
• Glutamate and GABA Related Therapies in Parkinson’s Disease	2 rhesus macaques
• Function of Dopamine in the Primate Substantia nigra; GABA-B Receptors and Parkinson’s Disease	8 rhesus macaques
• Influence of Subthalamic nucleus on Striatal Dopamine	4 rhesus macaques

B. In the study of Alzheimer-like disease, animal will be studied following injections of lentiviral constructs in the brain following craniotomy. The safety and efficacy of immunizations also will be evaluated. Single or protected contact housing is required after surgery for 6 to 16 weeks to evaluate behavior or other clinical complications.

• Lentiviral Mediate Expression of Trangenic Beta-APP and Presenilin in Squirrel Monkey: a New Model of Alzheimer’s Disease Pathogenesis	2 squirrel monkeys
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C. Infectious disease vaccine development studies may require single housing to prevent disease agent transmission. Some of the studies described here involve the development of a SIV/HIV vaccine, investigation of the role of host immune response in protecting against or contributing to the appearance of immune system damage following AIDS infection, evaluation of the function of the

thymus during infection with SIV, evaluation of the development and pathogenicity of mutant viruses that develop over time in chronically infected animals, the effect of opiate dependency on the progression of AIDS, and the testing of the immunogenicity and efficacy of different AIDS vaccines and treatment regimens. Single housing is required after exposure to the virus to prevent transmission of virus from animal to animal. In addition, the animals need to be accessed frequently for blood draws. The experimental design requires that the efficacy of vaccines will be assessed after a single exposure and without the possible confound of exposure to mutant viruses. Infected animals in an experimental group will be housed together after approximately one month. In some experiments, animals are singly housed one month prior to inoculation to allow sufficient time for acclimatization to the new housing arrangement so that the stress of separation doesn't influence susceptibility to or course of infection.

A study testing the effects of T cell depleting antibodies in SIV-infected mangabeys requires frequent antibody infusions and blood draws during the first 3 weeks of the treatment (animals are assessed up to 4 times per week), followed by weekly blood draws for the remainder of the study, which lasts 2 months. Because these animals will be frequently handled for testing, animals are housed in protected contact housing.

Malaria studies are being done to develop a vaccine and to provide antigens for serologic and molecular studies, genomic libraries, antibody production, and gametocytes for infection of mosquitoes. Chimpanzees infected with malaria are housed individually in metabolism cages. This is usually required for a period of 1-2 months. It is also necessary to house the animals indoors to prevent contact with the local mosquito population. Following blood collections and treatment of the malaria infection, the animals are returned to their normal housing environment. Protected-contact housing is utilized in other malaria vaccine studies in monkeys due to the requirement of daily heel or ear sticks (as well as blood collection and immunization), as well to avoid frequent reunions following stressful procedures. During the period to evaluate viral load and safety testing of gene therapy in a hepatitis C study, it is necessary to maintain the animals in metabolism cages. This is due to frequent blood collections and surgical interventions during the initial 4–6 weeks on study.

• Molecular Analysis of Plasmodium Vivax Surface Antigens	25 squirrel monkey
• Core A: Preclinical Trials and Pathology (Part of NCVDG Grant: DNA and Protein Immunogens for SIV/HIV Vaccines)	40 rhesus macaques
• Core A: Nonhuman Primates (Part of Program Project Grant "DNA/MVA Immunogens, Cross-Clade Immune Responses	30 rhesus macaques
• Cellular Immune Responses and AIDS Pathogenesis	13 rhesus macaques and 11 mangabeys
• Molecular Evolution of Multiply Deleted SIV in Vitro	26 rhesus macaques
• Core C: Primate Studies	32 rhesus macaques
• Mechanism of Oral SIV Transmission	16 rhesus macaques
• Infant Immunoprophylaxis Against a Primate Letivirus	24 rhesus macaques
• SHIV Transmission Through Oral Versus Other Mucosae	14 rhesus macaques
• Role of Virus Specific Immunity in Primate AIDS	9 mangabeys and 29 rhesus macaques
• Molecular Analysis of Antigenic Variation in Malaria	18 rhesus macaques

• Understanding Spontaneous Control of Pathogenic SIV Infection	1 rhesus macaques
• Immune Modulation of Neurotropin in SIV Infection	13 rhesus macaques
• Environmental Enrichment of Yerkes Primate Center Animal Colony	13 rhesus macaques
• Maintenance of Yerkes Primate Center Animal Colony	169 rhesus macaques
• Project 3: Attenuated Listeria Vectors as an AIDS Vaccine in Macaques	23 rhesus macaques
• Poxvirus Immunity and DNA/MVA HIV Vaccines	39 rhesus macaques
• Therapeutic Vaccine for HIV	7 rhesus macaques
• Cellular Immune Responses in SIV-Infected Sooty Mangabeys	2 sooty mangabeys
• Determinants of Vaccine-Induced Memory T-Cell Development	15 rhesus macaques
• Studies of the Natural Infectoin of Sooty Mangabeys	8 sooty mangabeys
• Immune Reconstruction in SIV-Infected Macaques-f/k/a Analysis of Thymic Function During SIV Infection	4 sooty mangabeys
• Generation of /P. Vivax/ And DNA and Chromosones	23 squirrel monkeys
• Genetics of Neuropathogenic SIV Infection	8 pigtailed macaques
• Development of a Low Inoculum SHIV Challenge Model	22 pigtailed macaques

D. Studies of dose and delivery vehicle in non-human primates have become a critical step to prepare for human clinical trials in lumbar fusion studies. Spine fusion surgery will be performed on animals followed by administration of different bone growth factors. Then animals will be in protected contact housing to prevent possible trauma to the surgical wound.

• Use of Osteoinductive Factors to Enhance Spine Fusion	15 rhesus macaques
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E. The integration of functional MRI (fMRI) technology with proven utility will significantly advance research efforts in biomedical and behavioral sciences. One proposal is directed towards brain activation studies during cocaine use. This may help to determine the brain structures and neural circuits that underlie the addictive properties of cocaine. In studies on cocaine and drug abuse, animals will be used for pharmacological and neurochemistry experiments involving the placement of an indwelling venous catheter for drug delivery during daily sessions lasting 1-2 hours. Some animals also have indwelling guide cannulae. The catheters and guide cannulae must be protected from contact by other animals. If contact is allowed, the preparations can be compromised with the risk of physical injury and infection. Protected contact housing reduces the risk since both animals can control proximity to others. The animals may require single housing if they persistently place themselves at risk to damage their indwelling venous catheters or guide cannulae, or that demonstrate a proclivity to damage another animal's catheter.

Determining the relationship between prefrontal cortical circuitry and components of dopaminergic neurotransmission is the focus of one research study that will enhance understanding of the cognitive processes subserved by the prefrontal cortex. This will hopefully shed light on human disease states, notably schizophrenia. In order to identify particular neural connections in the prefrontal cortex of macaques, axonal tracers will be injected intracerebrally. Following stereotaxic surgery,

craniotomies will be made over the prefrontal cortex. Subjects must be in protected contact housing to protect craniotomy sites and sutures.

Assessment of specific roles of separate neuronal structures are performed on monkeys to evaluate the brain's response to damage at different ages. Studies will provide detailed descriptions of loss of memory functions, and other developmental disorders that occur. Single cage housing will be required for post surgical events until healing has occurred. Implants may require single cage housing to prevent damage to implants in incompatible animals.

• Transition States of Drug Addiction in Nonhuman Primates	18 rhesus macaques
• Development of Functional Magnetic Resonance Imaging (MRI) for Behavioral Studies in Nonhuman Primates	8 Rhesus Macaques
• PET Neuroimaging and Cocaine Neuropharmacology in Monkeys	31 Rhesus macaques
• Cocaine use and Monoamine Function in Nonhuman Primates	50 squirrel monkeys
• Analysis of the Neuronal Microcircuitry Basal Ganglia	2 squirrel monkeys
• Orbitofrontal Limbic Ontogeny and Early Dysfunction	18 rhesus macaques
• Development of Reversible Inactivation Technique	2 rhesus macaques
• Development of Medial Temporal Lobe Function	6 rhesus macaques
• Development of Reversible Inactivation Technique for the study of Higher Cognitive Functions in Monkeys	2 rhesus macaques
• Brain Metabolic Effects of Deep Brain Stimulation	2 rhesus macaques
• Discrimination of Antipsychotics in Nonhuman Primates	8 rhesus macaques

F. Visual, vestibular and oculomotor systems must work together for normal visual function. Various disease processes or injuries can compromise the normal interaction of these systems. Research in this area will provide a basic science foundation for understanding eye movement control in humans. Primates are used since they exhibit the same set of eye movements as humans. To facilitate the research, scleral search-coils are implanted to precisely measure eye movement. In addition, head movements need to be restricted during visual testing to allow accurate tracking of visual targets. Therefore, a stainless-steel receptacle is implanted. It is sometimes necessary to house animals in protected housing when they have surgical implants. This is to protect the animal from any injury due to aggressive behavior of other animals. Animals also sometimes wear goggles which may be removed during paired housing.

• Neural Control of Visual Vestibular Behavior	8 rhesus macaques
• Visual Processing and Smooth Eye Movement	21 rhesus macaques
• Binocular Coordination of Eye Movements in Monkeys	10 rhesus macaques

G. Studies of pancreas, kidney, and bone marrow transplants as well as arterial grafts are investigating the ability of costimulation blockade to protect the organs from rejection. For experiments involving bone marrow transplantation, single housing is required for the first 75-100 days following the transplant due to the potential complications including immunosuppression, anemia, leukopenia and thrombocytopenia. After that time, the animals may be paired with same sex and age animals. In the pancreatic islet cell transplant model, daily monitoring of urine and stool output are necessary to diagnose steatorrhea, polyuria and ketoacidosis. In addition, pancreatic enzyme replacement and

Rapamycin are administered orally in a treat and it is essential that the amount consumed by each animal is recorded. Following renal transplantation, animals will require protected housing so that an accurate assessment of daily food/water intake and urine/feces production be accounted. Prior to surgery, animals may be pair-housed. With immunosuppressive therapy, healing can be delayed. A study using nonhuman (mouse) stem cells involves inoculation of the cells in the nonhuman primate model to evaluate survival of the cells and effects on the recipients.

• Nonhuman Primate Pancreatic Islet Cell Transplantation	2 rhesus macaques
• The Effect of Dosing Strategy for LEA29Y on Renal Allograft Survival in Rhesus Macaques	23 rhesus macaques
• Costimulation, Chimerism and Tolerance in Transplantation	45 rhesus macaques
• Injection of Immune Privileged Mouse Progenitor	2 rhesus macaques
• CD28 Blockade and anti-LFA-1 and Transplantation Tolerance	8 rhesus macaques

Physical Restraint, Exemptions from Social Housing, and Food or Water Restriction of Nonhuman Primates

Nonhuman primates used under these conditions are in motion disorder studies or studies of brain function. Most of the animals are used to research the cause and treatment of Parkinson’s Disease (PD) because of the great similarity of brain function and that Parkinson’s-like disease can be induced in them by giving the neurotoxic chemical – MPTP. Monkeys in these studies usually are given MPTP by intracarotid injection, so that only one side of the brain is affected. These monkeys have only slight deficits in precise control of movements on one side of the body and have no substantial movement problems. In general, isolation housing is only done for a 3 day period immediately after administration of MPTP during the time of excretion of the neurotoxin in the feces and urine. Otherwise, monkeys in these studies are housed within sight and sound of other animals of the species and permitting physical contact with a compatible conspecific.

Monkeys in studies requiring food or water restriction are provided *ad libitum* food and water on weekends according to standard husbandry practices. During weekdays, food or water is restricted overnight and in the morning (12-15 hours total) and then food or water is provided to satiety during morning or afternoon test sessions as an inducement to perform video-based tasks. Single housing is necessary to facilitate food or water restriction – otherwise a conspecific would be subjected to unnecessary restriction or food sharing might occur. Monkeys are trained using food or water as an inducement to perform simple motor tasks such as reaching, touching a target on a video screen, depressing a key to make a video target appear, and controlling a joystick to move a cursor to a target on a video screen. These monkeys, except as indicated, are loosely restrained in a chair and typically spend 4-6 hours per daily session in the laboratory. During these periods, the monkeys with head appliances may also undergo short-term fixed head restraint to access the appliances for neurophysiologic recording and microdialysis. Water or food is provided during and immediately after the testing session to meet the daily ration. The total intake of the restricted material, food or water, is recorded daily and the animal’s body weight is checked and recorded at least twice weekly to ensure that are being well maintained.

In eye movement studies, animals must be awake, alert and comfortably seated. The tasks involve following a smoothly moving or jumping target spot that is rear-projected on a tangent screen. First the animals are fitted with a collar that it will always wear. It is made of a soft nylon material. Animals are then adapted to pole handling and using a primate chair. It takes most animals 4 weeks to reach proficiency. Animals are trained 5 days per week for time periods of 15 minutes to 3 hours.

A study to develop a transgenic model of Huntington's Disease uses the primate chair during semen collections and, again, during cognitive testing procedures for offspring produced. In these tests, the monkeys are habituated to the use of a chair over a one to two week period before performing the task for preferential looking while sitting with free movement of arms and legs.

In cocaine abuse studies, cocaine is scheduled as the consequent event and is sufficiently reinforcing that food and water restrictions are not necessary. However, for self-administration experiments, subjects are trained to sit quietly in standard primate chairs over a 2-4 week period. The pole-and-collar system for handling and training nonhuman primates will facilitate immobilization. Initially, subjects will be immobilized for approximately 20-30 minutes per training session, but over the course of several weeks, the amount of time will increase to from 1 to 4 hours per session. Each subject will be immobilized at least twice per week for 6 weeks. In a related study, changes in sensitivity to the CNS effects of cocaine are assessed after the monoamine neurotransmitter is manipulated pharmacologically. The animals are trained to be seated in a loosely fitting chair during daily (Mon. – Fri.) sessions. The chair is designed to provide minimal skin contact with the animal, and is limited primarily to the waist and buttocks. Typically, experiments are conducted so as to require no more than one hour per day in the apparatus. This minimal restraint provides protection of indwelling catheters used for drug administration and contact with a localized area of the tail for electrical stimulation.

Startle reflex testing is done in one study after each monkey is habituated to chair restraint. The sessions are 2-3 times per week for 60 minutes each session. The tests continue for 2 weeks. These tests may be repeated every 3-4 months to monitor potential developmental changes in emotionality.

Some of the animals used under these conditions are in oculomotor, visual disorders, and visual cortex studies. Monkeys are used because they are capable of the same range of eye movements as humans. Infant monkeys are swaddled in a blanket. Older animals have a chair adjusted for comfort. The chair includes a standard design that allows the animal to sit in a natural position. The animal is allowed to sit in the chair for 5-15 minutes on the first occasion, during which time treats (apple slices, applesauce, etc) are offered to make the chair session a positive experience. Head movements in the animals during visual testing are restricted by an implanted stainless steel receptacle (SSR) on the head. In other studies, head movement is restricted with a custom-fit helmet.

In these studies with transiently-induced movement disorders or studies of midbrain function, monkeys are trained to do simple motor tasks such as reaching, touching a target on a video screen, depressing a key to make a video target appear, and controlling a joystick to move a cursor to a target on a video screen. During these tasks, these monkeys are loosely restrained in a chair and typically spend 4-6 hours per daily session in the laboratory. Animals assigned to studies to distinguish different types of cognition or memory may be tested in homecages, specifically designed rooms or using physical restraint.

To motivate the animals to work effectively, the first feeding of the day may be reduced or delayed. However, water or food is provided during and immediately after the testing session to meet the daily ration. The total intake of the restricted material, food or water, is recorded daily and the animal's body weight is checked and recorded at least twice weekly to ensure they are being well maintained.

1. Food and/or water restricted, but provided during and after laboratory testing sessions:

• Subcontract "Effects of Viewing Distance on Eye Growth and Refractive Development	4 rhesus macaques
• Binocular Coordination of Eye Movements	10 rhesus macaques
• Episodic Memory in Rhesus Monkeys: Spatial and Temporal Contexts	7 rhesus macaques
• Basal Ganglia Discharge Patterns in Parkinsonism	4 rhesus macaques
• Laminar Specific Neural Mechanisms for Memory in the Entorhinal Cortex	2 rhesus macaques
• Local Field Potentials in the Basal Ganglia	2 rhesus macaques
• Neural Control of Visual Vestibular Behavior	8 rhesus macaques
• Controlled and Automatic Cognition in Monkeys: Development of a New Model System	6 rhesus macaques
• Neurology of Memory in the Nonhuman Primate	15 cynomolgus macaques

2. Short-term physical restraint only:

• Binocular Coordination of Eye Movements	10 rhesus macaques
• Sugars as Novel Cyoprotectants for Primate Oocytes	2 rhesus macaques
• Function of Dopamine in the Primate Substantia Nigra: GABA-B Receptors and Parkinson's Disease	8 rhesus macaques
• Maintenance of Yerkes Primate Center Animal Colony	169 rhesus macaques
• Transition States of Drug Addiction in Nonhuman Primates	17 rhesus macaques
• Regulation of Motor Function in Parkinson's Disease	11 rhesus macaques
• Conte Primate Core	2 rhesus macaques
• Behavioral, Neural and Endocrine Covariates of Differential Rearing History in Juvenile Macaca Mulatta	58 rhesus macaques
• Behavioral Effects of Neonatal Amygdala Lesions in Monkeys Living in the Semi-Naturalistic Environment	10 rhesus macaques
• Development of a Reversible Deactivation, via Cooling Technique to Study Higher Cognitive Function in Monkeys	2 rhesus macaques
• PET Neuroimaging and Cocaine Neuropharmacology in Monkeys	37 rhesus macaques
• Orbitofrontal Limbic Ontogeny and Early Dysfunction	18 rhesus macaques
• Development of Reversible Inactivation Technique for the Study of Higher Cognitive Functions in Monkeys	2 rhesus macaques
• Development of Medial Temporal Lobe Function	12 rhesus macaques

• Basal Ganglia Discharge Patterns in Parkinsonism	4 rhesus macaques
• Development of Functional Magnetic Resonance Imaging (MRI) for Behavioral Studies in Nonhuman Primates	6 rhesus macaques
• Laminar Specific Neural Mechanisms for Memory in the Entorhinal Cortex	2 rhesus macaques
• Influence of Subthalamic Nucleus on Striatal Dopamine	4 rhesus macaques
• Local Field Potentials in the Basal Ganglia	2 rhesus macaques
• Effects of Self Administered MDMA on Brain and Behavior in Rhesus Monkeys	6 rhesus macaques
• Neural Control of Visual Vestibular Behavior	8 rhesus macaques
• Relationship between Nearwork and the Development of Myopia	2 rhesus macaques
• Visual Processing & Smooth Eye Movements	21 rhesus macaques
• Transgenic Monkey Inherited Neurodegenerative Disease	37 rhesus macaques
• Neurology of Memory in the Nonhuman Primate	15 cynomolgus macaques
• Cocaine Use and Monoamine Function in Nonhuman Primates	53 squirrel monkeys

Physical Restraint and Exemptions from Social Enrichment for Nonhuman Primates: Social Isolation

There are a variety of human diseases (Parkinson's Disease, Huntington's Disease, progressive supranuclear palsy, narcolepsy, and periodic leg movements during sleep) that are associated with uncontrolled movements in sleep that cause injury. Studies described here are on monkeys with Parkinsonism induced by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). Monkeys given MPTP are kept in social isolation for periods of three days after drug administration while MPTP and its toxic metabolites are excreted. On a scheduled basis afterwards, these animals are placed in a cage specially designed for behavioral testing and telemetric recording in a room separated from the other monkeys. Individual monkeys may be maintained in the observation and recording room for a maximum of 7 days and are then returned to their home cage in a colony with other monkeys of the same species for at least 7 days before repetition. Isolation from other monkeys is necessary in order to permit sleep undisturbed by commotion caused by other monkeys or human traffic in and out of the room. Monkeys under study are instrumented with backpack transmitters which telemeter their EEG, EOG and EMG signals. This telemetric approach allows studying sleep behavior in monkeys that are unrestrained. In addition, physical restraint in a chair is done 3 times a week for up to 4.5 hours per session. This is done either to facilitate brain mapping, intracerebral recording, and neurochemical microdialysis or for fear-potential startle testing.

• Modulation of the sleep/wake state by dopamine	5 rhesus monkeys
• Cytokine-induced depression: A rhesus monkey model	12 rhesus monkeys

Physical Restraint and Exemptions from Social Enrichment for Nonhuman Primates: Social Isolation

Capuchin monkeys under these conditions are used in studies to determine how the brain is organized to control limb movement and how the brain reorganizes during the learning and acquisition of new skilled motor movements. Information gained from this research may improve the understanding of the neural basis of learning and may be applicable to better understanding of the brain response to stroke, trauma or other cerebral injuries. Physical restraint in a chair is done 3-5 times a week and lasts up to 1.5-4 hours per session in order to allow cortical stimulation testing and for conscious behavioral assessments. The

animals are also housed singly, but otherwise in close proximity and within sight and sound of conspecifics. This must be done to prevent fight injuries to the hands and digits that would compromise motoneuron function or risk damage to subcutaneously implanted microelectrodes. Otherwise, full environmental and nutritional enrichments are provided.

• Muscle re-assembly in MI during skill acquisition	2 capuchin monkeys
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Physical Restraint

Monkeys in these studies are trained to do simple motor tasks such as reaching, depressing a lever, touching a target on a video screen, depressing a key to make a video target appear, or controlling a joystick to move a cursor to a target on a video screen. The monkeys are loosely restrained in a chair and typically spend 1-3 hours per daily session in the laboratory and for up to 5 sessions per week.

• Behavioral Pharmacology of Narcotic Antagonists	9 squirrel monkeys
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Food or Water Restriction of Dogs - none

Exemptions from Exercise for Dogs

Dogs with an inherited motoneuron disease may be restricted from exercise for 3-4 days while acutely recovering from surgery.

• Functional studies in motoneuron disease	7 dogs
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Food or Water Restriction of Swine - none

Physical Restraint of Sheep

Sheep are used in studies of the effect of gene therapy or pharmacologic agents (including inhaled) upon the pulmonary epithelium and general physiology. These studies are intended to better understand the pathophysiology and improvement treatment of conditions such as pulmonary hypertension, acute lung injury, and ARDS. In the conduct of the research procedures, sheep are loosely restrained in small ruminant stanchions for up to four hours to enable hemodynamic and pulmonary physiology measurements while under continuous observation.

• C/EBPbeta regulation of lung inflammation	40 sheep
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Summary of Studies (Animal) Listed in Column E

• Behavioral Pharmacology of Narcotic Antagonists	9 squirrel monkeys
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Squirrel monkeys were used in drug discrimination studies for studies of opioid receptors (μ , κ , δ , others) in the brain. In these studies, opioid drugs with differing or unknown profiles of receptor interactions were evaluated. The objective was to identify and study those components of drug action that underlie potential for abuse. It should be noted that an alternative species, rats, is used for most of these studies and squirrel monkeys were involved to a lesser extent.

Squirrel monkeys were trained to discriminate between a reference drug, such as cocaine or morphine, and a placebo in a trial avoidance paradigm. Monkeys were loosely seated in a primate chair during these studies. During the training phase and as an aversive stimulus to respond during discrimination trials, a 0.5-1.0 second mild electrical stimulus might be delivered to the monkey's tail after 5 seconds from the beginning of the trial. The monkeys could terminate the trial and prevent the electrical shock by pushing on one of two levers (corresponding to the reference drug or the placebo). The monkeys quickly learned to avoid the stimulus by responding during the five seconds after the start of the trial. After the initial training session, the monkeys rarely, if ever, received an electrical stimulus. Shocks were never given indiscriminately or without providing the monkey the opportunity, through lever manipulation, to prevent the shock.

Pain-relieving drugs were not used in these studies because any pain experienced would be transient (one second or less) and the animal could take action to avoid all pain (by pushing a lever within 5 seconds of a clear cue). Additionally, pain-relieving drugs, such as narcotics, would have confounded the pharmacological effects of the opioid compounds studied.

This study was terminated during calendar year 2006 and is no longer active.

• Modulation of the sleep/wake state by dopamine	5 Rhesus Macaques
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Disorders affecting dopamine transmission, such as Parkinson's Disease, are associated with disrupted sleep patterns and arousal. Rhesus monkeys are used in this study to investigate the cellular mechanism of these sleep disorders and how medications act and can be better used to manage them. Nonhuman primates given the neurotoxin MPTP are used as a model of parkinsonianism. Induction of parkinsonianism with MPTP causes impaired movement, blunted motivation, apathy and drowsiness that may be distressful. This condition cannot be relieved with pain-relieving drugs. In fact, analgesics, anesthetics and tranquilizers are medically contraindicated for the condition potentially enhancing drowsiness and creating risk of aspiration or respiratory distress. Although the federal reporting requirements only considers the use of anesthetics, analgesics and tranquilizers to relieve pain or distress, it should be noted that dopaminomimetic agents, a more specific and appropriate intervention, may be used to reverse acute signs of MPTP intoxication in animals on this study.

• Cytokine-Induced Depression: A Rhesus Monkey Model	12 Rhesus Macaques
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Human patients with a wide range of illnesses may exhibit a high rate of depression mediated by activation of the immune system and the release of cytokines. The latter can exert effects upon the brain leading to altered behavior. For example, about 50% of humans given the cytokine IFN- α therapeutically develop depression. In these studies, the administration of IFN- α causes chronic immune activation and a behavioral syndrome in macaques similar to depression in humans. Monkeys given the cytokine are used to study how it disrupts brain neurochemistry and to develop treatment interventions. The syndrome may also be characterized by apathy, poor motivation and sleepiness.

Potentially animals may also experience heightened sensitivity to painful stimuli and other neurological abnormalities. Pain relieving drugs, except during and immediately following surgery, cannot be used because of the potential confounding effects upon the neurological effects of the model as well as increasing the risk of sleepiness, respiratory depression and aspiration.

• C/EBPbeta regulation of lung inflammation	15 sheep
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Inflammatory diseases of the lung cause respiratory dysfunction, may involve infectious agents and often with a septic component, and may cause high mortality. To simulate sepsis and associated pulmonary pathology in a controlled and self-limiting fashion, sheep are administered endotoxin by intravenous injection. The host response to the endotoxin elicits a cascade of events resulting in hypoxemia, pulmonary hypertension, pulmonary inflammation and edema, and respiratory distress lasting for several hours. Additionally, sheep experience transient fever, malaise and other flu-like symptoms lasting 12-15 hours before restoration to normal health. The administration of pain relieving agents, both narcotics and nonsteroidal anti-inflammatory drugs, may alter inflammatory effect, immune response and, if tranquilizing, respiratory function. Such would confound the interpretation of scientific data making the use of anesthetics, analgesics or tranquilizers contraindicated in the model.

Annual Report to USDA
Facility Locations



(b)(2)High, (b)(7)f

* rats and/or mice only; not regulated by AWAR.