This report is required by law (7 USC 2143). Failure to report according to the regulations can result in an order to cease and desist and to be subject to penalties as provided for in Section 2150.

See reverse side for additional information.

Interagency Report Control No 0180-DOA-AN

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

ANNUAL REPORT OF RESEARCH FACILITY
(TYPE OR PRINT)

1. CERTIFICATE NUMBER: 57-R-0003

CUSTOMER NUMBER: 896

FORM APPROVED
OMB NO. 0579-0036

Emory University
1599 Clifton Rd NE, 1599-001-1BE
Atlanta, GA 30322

Telephone: (404) 727-3889

3. REPORTING FACILITY (List all locations where animals were housed or used in actual research, testing, or experimentation or held for these purposes. Attach additional sheets if necessary)

FACILITY LOCATIONS (Sites) – See Attached Listing

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 teaching, research, experiments, 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 NUMBER OF ANIMALS (COLUMNS C + D + E)
4. Dogs	0	3	27	0	30
5. Cats	0	0	17	0	17
6. Guinea Pigs	0	8	43	88	139
7. Hamsters	0	0	0	0	0
8. Rabbits	1	40	253	0	293
9. Non-human Primates	1664	400	1778	17	2195
10. Sheep	0	0	27	10	37
11. Pigs	0	0	294	0	294
12. Other Farm Animals	0	0	0	0	0
13. Other Animals					
VOLES	156	1054	135	124	1313
GERBILS	0	8	12	0	20

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 such 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)

(b)(6), (b)(7)c

DATE SIGNED
11/25/2008

APHIS FORM 7023
(AUG 91)

(Replaces VS FORM 18-23 (OCT 88), which is obsolete)

PART I - HEADQUARTERS

NOV 26 2008

Thirty "stimulus" prairie voles pups were used to test maternal behavior. In order to test the appropriate behavioral response, the adult subjects must establish physical contact with the pups and the pups need to be awake, warm and emit all stimuli that normally trigger the attention of the subjects. Replacement of pups by objects or anesthetized pups would not trigger the appropriate maternal responses from the adult subjects. In order to reduce the number of pups, they are reuse at different ages 2, 3, 4, and 5 days. The risk of the mother attacking the pups cannot be avoided in any maternal behavior test. The animals are under continuous observation during the test. The major goal of this study is understanding variability in the response to pups within and across species that ranges from spontaneous caring activities to neglecting or infanticidal behavior.

Finally, seventy voles were used in the tail suspension test and forced swim tests. These tests are designed to assess active versus passive behavior when challenged by either tail suspension or forced swimming. The tail suspension and forced swim test are well-described and currently accepted assays for depressive-like behavior in rodents. Each test is brief and does not produce long term distress in the animal. Since the main question is how these animals respond to the mildly stressful situations, distress relieving measures cannot be used.

Protocol #	Title	# Species
025-2006Y	Neuropeptide Basis of Social Loss and Depression	94 voles
060-2007Y	Oxytocin and Social Attachment	30 voles

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 parkinsoniansim 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. The five animals reported with this work were carried-over from 2007 and do not represent new acquisitions.

Protocol #	Title	# Species
072-2008	Modulation of the sleep/wake state by dopamine	5 Rhesus Macaques

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-alpha therapeutically develop depression. In these studies, the administration of IFN-alpha 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

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 that are being well maintained.

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

Protocol #	Title	# Species
004-2006Y	Effects of Viewing Distance on Eye Growth and Refractive Development	11 rhesus macaques
264-2007Y	Binocular Coordination of Eye Movements; Surgical Treatment of Strabismus in Juvenile Monkeys	11 rhesus macaques
087-2007Y	Cellular Mechanisms Underlying the Therapeutic Benefit of High-Frequency Stimulation of the Subthalamic Nucleus for Parkison's Disease	2 rhesus macaques
091-2005Y	Episodic Memory in Rhesus Monkeys: Spatial and Temporal Contexts	6 rhesus macaques
124-2008Y	Laminar Specific Neural Mechanisms for Memory in the Entorhinal Cortex	2 rhesus macaques
178-2008Y	Local Field Potentials in the Basal Ganglia	2 rhesus macaques
040-2007Y	Transgenic Monkey: Inherited Neurodegenerative Disease	45 rhesus macaques
204-2008Y	Hippocampal-Cortical Interaction and Memory Formation	4 rhesus macaques
173-2008Y	Neural Control of Visual-Vestibular Behavior	4 rhesus macaques
204-2008Y	Hippocampal-Cortical Interaction and Memory Formation	4 rhesus macaques
242-2007Y	The neurology of memory in the nonhuman primate	15 cynomolgus macaques
003-2006Y	Imaging Medial Temporal Lobe Activity Related to Memory and Emotion in Awake, Behaving Primates	2 rhesus macaques
249-2005Y	Cocaine Use and Monoamine Function in Nonhuman Primates	44 squirrel monkeys

2. Short-term physical restraint only:

Protocol #	Title	# Species
264-2007Y	Binocular Coordination of Eye Movements; Surgical Treatment of Strabismus in Juvenile Monkeys	11 rhesus macaques
003-2006Y	Imaging Medial Temporal Lobe Activity Related to Memory and Emotion in Awake, Behaving Primates	2 rhesus macaques
087-2007Y	Cellular Mechanisms Underlying the Therapeutic Benefit of High-Frequency Stimulation of the Subthalamic	2 rhesus macaques

	Nucleus for Parkison's Disease	
095-2008Y	Development of a Reversible Deactivation, via Cooling Technique of Study Higher Cognitive Function in Monkeys	2 rhesus macaques
134-2008Y	Development of a Focal Transgenic Model of Huntington's Disease	1 rhesus macaque
112-2006Y	Glutamate Receptors: Novel Targets for Parkinson's Disease Therapy	11 rhesus macaques
178-2008Y	Local Field Potential in the Basal Ganglia	2 rhesus macaques
187-2006Y	Evolution of Aging and Dementia in Female Primates, Cores A-D and Projects 1-3	25 rhesus macaques
195-2008Y	Visual Processing and Smooth Eye Movements & Novel Immunotoxin and IGF Therapy for Strabismus	18 rhesus macaques
217-2006Y	Function of Dopamine in the Primate Substantia Nigra	2 rhesus macaques
031-2006Y	Maintenance of Yerkes Primate Center Animal Colony	148 rhesus macaques
012-2008Y	Transition States of Drug Addiction in Non-human Primates	16 rhesus macaques
070-2006Y	Behavioral, neural and endocrine effects of differential rearing history in rhesus monkeys (Macaca mulatta)	70 rhesus macaques
079-2007Y	PET Neuroimaging and Cocaine Neuropharmacology in Monkeys; PET in conscious monkeys	39 rhesus macaques
112-2007Y	Orbitofrontal-limbic ontogeny and early dysfunction; The integration of multisensory social cues and its neural basis in monkeys	18 rhesus macaques
076-2007Y	Development of Reversible Inactivation Technique for the Study of Higher Cognitive Functions in Monkeys	2 rhesus macaques
144-2007Y	Development of Medial Temporal Lobe Function	22 rhesus macaques
124-2008Y	Laminar Specific Neural Mechanisms for Memory in the Entorhinal Cortex	2 rhesus macaques
173-2008Y	Neural Control of Visual-Vestibular Behavior	4 rhesus macaques
040-2007Y	Transgenic Monkey: Inherited Neurodegenerative Disease	48 rhesus macaques
242-2007Y	The neurology of memory in the nonhuman primate	15 cynomolgus macaques
249-2005Y	Cocaine Use and Monoamine Function in Nonhuman Primates	44 squirrel monkeys

Summary of Studies (Animal) Listed in Column E

Animals are used to study the effect of social deprivation during infancy in the prairie vole, to model maternal neglect, which occurs in humans. Pups are separated from their mother and placed in a warm incubator. Since the aim is to study the effects of the stress of maternal separation on the pups, drugs or other procedures cannot be used to alleviate the stress. The pups do not experience pain but only the psychosocial stress of being without their mother.

K. Recent studies have shown that a molecule called Programmed Death-1 (PD-1) is highly expressed by killer CD8 T cells during lymphochorio meningitis virus (LCMV) infection and that the binding of PD-1 with its counter part PD-L1 on cells that present the viral protein (antigen presenting cell) results in the loss of killing ability of killer T cells[1]. Blocking the binding between PD-1 and PD-L1 in mice by injecting anti-PD-1 antibody recovered the killing ability of killer CD8 T cells and improved the control the of LCMV infection. Recent studies have extended these observations to killer CD8 T cells in individuals infected with human immunodeficiency virus (HIV). These studies show that these killer CD8 T cells express high levels of PD-1 and this expression is higher in individuals with high viral burden. Blocking binding between PD-1 and PD-1 ligand (PD-L1) in the laboratory in culture dish recovered the function of these killer CD8 T cells. Data from our laboratory also show that rhesus monkey killer T cells express high levels of PD-1 following infection with a simian immunodeficiency virus (SIV, virus that causes AIDS in monkeys) and blocking binding between PD-1 and PD-L1 in culture dish recovers the killing function of SIV-specific T cells. Collectively, these results strongly suggest that blocking the binding between PD-1 and PD-L1 in SIV-infected monkeys by injecting anti-PD-1 or anti-PD-L1 antibody (*in vivo* blockade) may recover the function of anti-viral killer cells and lower the levels of SIV in blood. Thus, *in vivo* blockade of PD-1 or PD-L1 may represent a novel therapeutic approach for HIV/AIDS.

Protocol #	Title	# Species
149-2007Y	PD-1 Blockade as Therapy for SIV/AIDS	26 rhesus macaques
260-2007Y	PD-1 Ligand Blockade as a Therapy for SIV	22 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

our rhesus monkeys, reduce the numbers of euthanasia due to these conditions, and improve animal welfare.

Protocol #	Title	# Species
067-2008Y	Does CRH Receptor Antagonism Reduce Self-Injurious Behavior and Improve Gastrointestinal Health in Rhesus Macaques	3 rhesus macaques

I. 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.

Protocol #	Title	# Species
005-2008Y	Transplant Tolerance in Nonhuman Primates	82 rhesus macaques
098-2008Y	Pre-Clinical Non-human Primate Islet Allotransplantation Model for Tolerance Induction Testing with CTLA-4-Ig (Abatacept), LFA-3-Ig (Alefacept), and Sirolimus; Improving the Efficacy of Costimulation Blockade by Targeting T Cell Memory	3 rhesus macaques
192-2007Y	Creating a non-human primate model of graft-versus host disease: Determining Mechanism and Assessing Novel Therapeutics	17 rhesus macaques
240-2008Y	Immune Function and Biodefense in Children, Elderly and Immunocompromised Populations: Project 3	29 rhesus macaques
208-2007Y	Non-human Primate Renal Transplantation as a Preclinical Model for Testing Genzyme 29155 for Allospecific Tolerance Induction	20 rhesus macaques

J. The following project investigates the alterations in behavioral, neuroendocrine and neuroanatomical development of rhesus macaque infants who are physically abused (examples of abuse: infant dragging, throwing) or neglected by their mothers, from birth through adulthood. Specifically, we intend to investigate possible long-term changes in social behavior, emotional regulation and reactivity to stress induced by early abuse and the neural and neuroendocrine mechanisms underlying these changes. Because infant abuse in monkeys and humans share several important characteristics, this study could enhance our understanding of the consequences of child abuse as well as make an important contribution to the prevention and treatment of this phenomenon.

Protocol #	Title	# Species
107-2007Y	Developmental Consequences of Infant Abuse in Primates	39 rhesus macaques

NOV 06 2008

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.

Protocol #	Title	# Species
173-2008Y	Neural Control of Visual Vestibular Behavior	4 rhesus macaques
195-2008Y	Visual Processing and Smooth Eye Movements & Novel Immunotoxin and IGF Therapy for Strabismus	18 rhesus macaques
264-2007Y	Binocular Coordination of Eye Movements; Surgical Treatment of Strabismus in Juvenile Monkeys	11 rhesus macaques

G. Neuroreceptor imaging studies in postpartum women have provided preliminary support for several mechanisms that may contribute to the maternal behavior and mood changes observed in postpartum depression. First, based on neuroimaging studies there are significant alterations in serotonin-1A (5HT1A) receptor binding in limbic regions of the brain involved in emotionality and in dopamine-2 (D2) receptor binding in striatal regions of the brain associated with emotion and reward in healthy control postpartum relative to healthy control non-postpartum women. These results converge with animal models to suggest a process of perinatal neuroplasticity in the service of maternal behavior that occurs in recently delivered mothers compared to non-postpartum women. Second, postpartum depressed women had significant 5HT1A and D2 receptor binding alterations relative to postpartum healthy control women. These changes are consistent with the literature that describes monoamine deficits in major depressive disorder, anxiety disorders, and social stress. These cumulative findings suggest three potential mechanisms of perinatal mood disorder: pre-existing neurobiological vulnerability to mood disorder that persists perinatally, a failure of optimal perinatal neuroplasticity in susceptible women, or both processes.

Peripartum rhesus monkeys represent an ideal model to begin to better understand how changes in monoamine systems emerge during pregnancy that may predict what females may be more likely to exhibit PPD symptomatology. This proposal represents a pilot study to show the feasibility of using microPET neuroimaging to quantify changes in 5HT1A and D2 receptor binding during late pregnancy and the early post partum period.

Protocol #	Title	# Species
062-2008Y	Peripartum Changes in Monoamine Activity	2 rhesus macaques
139-2005Y	Genetics of Neuropathogenic SIV Infection	6 pigtailed macaques

H. Evaluates the efficacy of a corticotropin releasing hormone type 1 (CRH_1) receptor antagonist in reducing chronic diarrhea and self-injurious behavior (SIB) in captive housed rhesus macaques. Chronic diarrhea in the absence of identifiable pathogens and SIB are two of the most troublesome clinical conditions in rhesus monkeys housed in biomedical research facilities, for which current treatment methods are often ineffective. Chronic exposure to psychosocial stress is thought to play a role in these conditions. Emerging data indicate that corticotropin releasing hormone (CRH) mediates stress-induced anxiety and depression, and that these emotional problems are corrected by treatment with specific CRH_1 receptor antagonists. Furthermore, this treatment also attenuates stress-induced gut motility and the incidence of diarrhea. We aim to determine whether treatment with a CRH_1 receptor antagonist can ameliorate chronic diarrhea in the absence of enteric pathogens and/or reduce SIB in rhesus macaques. Data obtained from this study has the potential to greatly impact the clinical health of

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.

One of the primary brain structures coordinating emotional responses is the amygdala. Much of our understanding of how the amygdala coordinates our behavior has come from whole animal research. However, the amygdala is not a simple structure in that it consists of at least 15 subdivisions, and contains at least 5 types of neurons. If we are to understand how the amygdala helps to coordinate our behavior, we must first understand the functional properties of the individual subdivisions and the properties of the neurons contained therein. Despite the importance of the amygdala as a structure, there is still relatively little information available concerning the properties of amygdala neurons. It is now possible to keep thin sections of the brain "alive" for several hours in an artificial environment. This "slice" preparation gives us direct access to the individual neurons from which we can record their electrical activity in response to drug application. Moreover, by stimulating input pathways to these neurons we can begin to construct a simple model of how the neurons in the amygdala may be connected.

Protocol #	Title	# Species
012-2008Y	Transitional States of Drug Addiction in Non-human Primates	16 rhesus macaques
076-2007Y	Development of Reversible Inactivation Technique for the Study of Higher Cognitive Functions in monkeys	2 rhesus macaques
079-2007Y	PET Neuroimaging and Cocaine Neuropharmacology in Monkeys; PET in conscious monkeys	39 rhesus macaques
203-2007Y	Development of a Monkey Dystonia Model	3 rhesus macaques
249-2005Y	Cocaine use and Monoamine Function in Nonhuman Primates	44 squirrel monkeys
254-2007Y	Studies of the natural SIV infection of sooty mangabeys	2 sooty mangabeys and 5 rhesus macaques
139-2005Y	Genetics of Neuropathogenic SIV Infection	6 pigtailed macaques
224-2007Y	Modulating HIV Immunity with Dendritic Cells	52 rhesus macaques
102-2006Y	Functional Neuroanatomy of the Basolateral Amygdala	3 rhesus macaques
112-2007Y	Orbitofrontal-limbic ontogeny and early dysfunction; The integration of multisensory social cues and its neural basis in monkeys	18 rhesus macaques
163-2007Y	Imaging Estrogen Receptors with PET	4 rhesus macaques
126-2008Y	Analysis of the Neuronal Microcircuitry of the Basal Ganglia	2 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, sclera 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

031-2006Y	Maintenance of Yerkes Primate Center Animal Colony	148 rhesus macaques
142-2007Y	Project 3: Attenuated Listeria Vectors as an AIDS Vaccine in Macaques	10 rhesus macaques
177-2006Y	Poxvirus Immunity and DNA/MVA HIV Vaccines	4 rhesus macaques
077-2007Y	Therapeutic DNA/MVA Vaccines for HIV	18 rhesus macaques
176-2007Y	Determinants of Vaccine-Induced Memory T-Cell Development	24 rhesus macaques
224-2007Y	Modulating HIV Immunity with Dendritic Cells	52 rhesus macaques
062-2007Y	Virus Turnover and T Cell Responses During SIV Infection	10 rhesus 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.

Protocol #	Title	# Species
069-2007Y	Use of Osteoinductive Factors (BMP) to Enhance Spine Fusion	9 rhesus macaques

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 in dwelling 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

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.

Dengue is one of the most important mosquito-borne viral diseases affecting humans, with over half of the world's population living in Dengue endemic areas. A wide spectrum of clinical manifestations has been noted which range from asymptomatic, mild febrile (dengue fever, DF) to dengue hemorrhagic fever (DHF)/dengue shock syndrome (DSS), and a severe form associated with a life-threatening illness. The incidence rate of the latter disease form is 1-5% and predominantly occurs in children under the age of 15. The pathological hallmarks that determine disease severity and distinguish DHF from DF and other viral hemorrhagic fevers are plasma leakage resulting from increased vascular permeability and abnormal blood clotting.

The objectives of this pilot proposal are to generate sufficient data to further pursue for the more completed underlying mechanisms triggering DHF/DSS and to better define and understand the initial target cells infected by dengue virus, which may correlate with hematopoietic suppression. The proposed study, therefore, may potentially provide a new insight and shed a new light on human immunology in response to dengue virus infection.

Protocol #	Title	# Species
013-2008Y	Evaluation of infection, viral dissemination and immune responses to the gamma human retrovirus XMRV in rhesus macaques	3 rhesus macaques
088-2007Y	Evaluation of anti-HIV Interventions for the prevention of SHIV Transmission in Pig-tailed Macaques	28 pigtail macaques
198-2008Y	Non-human Primate Models of Malarial Anemia	18 rhesus macaques
247-2007Y	Early Innate Immune Response in Dengue Virus Infection	3 rhesus macaques
142-2008Y	Innate Immunity and affects of Macrophage Depletion in SIV-Infected Non-Human Primates	3 rhesus macaques
256-2008Y	Molecular Evolution of Multiply Deleted SIV in Vivo	23 rhesus macaques
261-2008Y	Vaccination Against mucosal HIV Clade C Transmission	71 rhesus macaques
010-2006Y	Infant Immunoprophylaxis Against a Primate Lentivirus	21 rhesus macaques
061-2007Y	SHIV Transmission Through Oral versus Other Mucosae	22 rhesus macaques
030-2007Y	Role of virus specific immunity in primate AIDS; CD4 T cell activation in SIV+ disease resistant mangabeys; Role of CTL in indian macaques with live attenuated deglycoslated SIV	6 mangabeys and 20 rhesus macaques
259-2007Y	Molecular Analysis of Antigenic Variation in Malaria	18 rhesus macaques

081-2007Y	Regulation of Motor Function in Parkinson's Disease: Effects of Cannabinoid Antagonists in the MPTP Primate Model of Parkinson's Disease	8 rhesus macaques
094-2007Y	Neuropsychology of Primate Social Cognition	8 rhesus macaques and 10 chimpanzee

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.

Protocol #	Title	# Species
066-2007Y	Alzheimers Immunotherapy in Primate Model of Cerebral Amyloid Angiopathy	7 squirrel monkeys
255-2008Y	Focal Alzheimer transgene expression in rhesus monkeys	4 rhesus macaques
068-2007Y	Relationship between Serum and CSF Drug Levels and Central D2 Occupancy for Two Atypical Antipsychotics	5 rhesus macaques

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

Exceptions to Regulations and Standards

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 14 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 up to 8 times per month for 6-10 hours per session. This is done either to facilitate brain mapping, intracerebral recording, and neurochemical microdialysis or for fear-potential startle testing.

Protocol #	Title	# Species
072-2008	Modulation of the sleep/wake state by dopamine	5 rhesus monkeys
182-2006	Cytokine-induced depression: A rhesus monkey model	12 rhesus monkeys

Exemptions from Social Enrichment for Nonhuman Primates: Social Isolation

The male capuchin monkeys on census have repeatedly injured each other when paired or given protected contact housing opportunities. For their safety and well-being, they have been exempted from social housing. These animals are no longer used experimentally and are awaiting donation to a sanctuary.

Protocol #	Title	# Species
072-2008	Modulation of the sleep/wake state by dopamine	2 capuchin monkeys

Physical Restraint of Swine

Pigs are used in studies of reperfusion injury – that injury to the myocardium that occurs in patients after the blockage of a coronary artery is relieved and blood flow to poorly perfused tissue is restored. At one week following surgical implantation of an occluding device on the left anterior descending coronary artery, pigs are sedated with midzolam, provided intravenous fluids, and restrained in a porcine sling. The occluder is inflated to obstruct coronary artery blood flow for one hour simulating a myocardial infarction and microspheres are injected at the beginning and end of the procedure. The occluder is then deflated and the heart reperfused with or without pharmacologic intervention and the pig is removed from the sling and recovered from sedation.

Protocol #	Title	# Species
225-2006	Consortium to investigate myocardial protection strategies to reduce infarct size	8 swine

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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 five hours to enable hemodynamic and pulmonary physiology measurements while under continuous observation.

Protocol #	Title	# Species
080-2007	C/EBPbeta regulation of lung inflammation	10 sheep

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.

Protocol #	Title	Species
126-2008Y	Analysis of the Neuronal Microcircuitry of the Basal Ganglia	2 rhesus macaques
037-2005Y	Glutamate and GABA Related Therapies in Parkinson's Disease	4 rhesus macaques
178-2008Y	Local Field Potentials in the Basal Ganglia	2 rhesus macaques
112-2006Y	Glutamate receptors: Novel targets for Parkinson's Disease Therapy	11 rhesus macaques
213-2006Y	The Thalamostrital System as a Target for Tourette's Syndrome	2 rhesus macaques
217-2006Y	Function of Dopamine in the Primate Substantia nigra	2 rhesus macaques
212-2006Y	GABA-B Receptors and Parkinson's Disease	1 rhesus macaque

depression and aspiration. The 12 animals reported with this study were carried-over from the 2007 census and do not represent new acquisitions.

Protocol #	Title	# Species
182-2006	Cytokine-Induced Depression: A Rhesus Monkey Model	12 Rhesus Macaques

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. All 10 of these sheep were new acquisitions.

Protocol #	Title	# Species
080-2007	C/EBPbeta regulation of lung inflammation	10 Sheep

Infection with the arenavirus of Lassa fever causes a potentially lethal human hemorrhagic disease where it is endemic in West Africa. Unlike Lassa fever, the infection of guinea pigs with the related Pichinde arenavirus does not pose a human health hazard, but is an important model in the study of the pathogenesis and possible treatments or vaccines for diseases caused by arenaviruses. Guinea pigs infected with Pichinde virus develop Lassa fever-like symptoms of fever progressing to hypothermia and weight loss. The regular administration of pain-relieving drugs during the clinical course might inhibit fever (nonsteroidal inflammatory agents) and can alter immune function (opioids) and their use is contraindicated in this model. Instead, the guinea pigs are humanely euthanatized when they show a combination of weight loss and hypothermia or any signs of hemorrhage, dyspnea, or distress.

Protocol #	Title	# Species
204-2007	Pichinde virus infection of guinea pigs as an animal model for Lassa fever	88 guinea pigs