Welcome

FASEB Webinar on
“Why Do We Study Nonhuman Primates, and How is This Research Regulated?”

THE WEBINAR WILL BEGIN IN A FEW MINUTES

Click the join link in your Confirmation email.
If you don’t have your link, go to https://www.gotomeeting.com/webinar/join-webinar and enter Webinar ID: 255-900-283

To use your telephone to hear the audio, call (415) 655-0060 and enter Access Code: 833-956-297

If you experience trouble joining the webinar, please contact Customer Support at http://care.citrixonline.com/gotowebsinar/join
Agenda for Today’s Webinar

- Welcome & Background

- Introduction of Part One Speaker, Sabine Kastner, MD, PhD

- Part One: We do we study nonhuman primates?

- Introduction of Part Two Speaker, Doty Kempf, DVM, ACLAM

- Part Two: Laboratory Animal Use Regulations

- Questions and Answers
Sabine Kastner, M.D., Ph.D.

- 1986 – B.A., University of Gottingen (History & Philosophy)
- 1993 – M.D., University of Dusseldorf
- 1994 – Ph.D., University of Gottingen (Neurobiology)
- 2000 – Faculty member at Princeton University
- Clinical training in neurology and psychiatry
- Graduate studies in primate neurophysiology
- Postdoctoral training at NIMH in human brain imaging
Why do we study non-human primates?

Sabine Kastner, MD, PhD
Why non-human primates?

Adults

Cognitive Neuroscience
Why non-human primates?

Adults
Cognitive Neuroscience

Kids
Development of cognition
Why non-human primates?

Adults
Cognitive Neuroscience

Kids
Development of cognition

Pathology of cognition

Patients
Why non-human primates?

Adults

Kids

Non-human primate research is central for understanding the human brain.

Cognitive Neuroscience

Development of cognition

Macaque

Pathology of cognition

Patients
Why non-human primates?

The non-human primate brain provides the closest model for human brain function in the domains of:

- perception
- action
- cognition
Basic knowledge is not ‘knowledge for knowledge’s sake’.

Basic knowledge has been responsible for our greatest scientific advancements and provided the foundation for breakthroughs in biomedical research that saved millions of lives.

- Infectious diseases/vaccinations (e.g. polio, measles, HIV, Zika)
- Rh factor and safe blood transfusions
- Kidney, liver, lung and heart transplants
- Alzheimer’s, Parkinson’s, and schizophrenia
- Diabetes and obesity
- Pregnancy outcomes
Ca. 30% of the primate brain is dedicated to processing visual information.
Monkey vision
Mouse vision
Primate visual system

Nobel Prize in Physiology & Medicine, 1981

David Hubel & Torsten Wiesel
Primate visual system

Discoveries laid the ground for our current understanding of
• the functional architecture of primary visual cortex
• and the development and plasticity of the brain

Hubel & Wiesel
Primate visual system

Hubel & Wiesel

Primary visual cortex
Primate visual system

Primary visual cortex
Primate visual system

Primary visual cortex

Visual stimulus
Receptive field
Cell discharge
Primate visual system

Primary visual cortex
The development of this functional architecture, particularly of ocular dominance, depends on visual experience early in life, during a ‘critical period’.
The development of this functional architecture, particularly of ocular dominance, depends on visual experience early in life, during a ‘critical period’.

Visual deprivation leads to a massive loss of binocular neurons.
The development of this functional architecture, particularly of ocular dominance, depends on visual experience early in life, during a ‘critical period’.

Visual deprivation leads to a massive loss of binocular neurons.
Hubel and Wiesel’s discoveries on the development and plasticity of the visual system led to changes in the treatment of amblyopia.

In amblyopia (1-5% of the population), or ‘lazy eye’, inputs from the two eyes do not converge in the cortex. If untreated until after the ‘critical period’ (~2 years of age in humans), binocular vision is greatly compromised.

Hubel and Wiesel’s basic research led to today’s standard treatments of early intervention.
The motor system of non-human primates is similar to that of humans due to their rich action repertoire and advanced motor skill level.
Primate motor system
Primate motor system
Primate motor system

Movement disorders due to basal ganglia dysfunction:

- Parkinson’s Disease
- Chorea Huntington
- Hemiballism
Parkinson’s disease affects ~ 1 million people in the U.S. alone and is characterized by ...

- Tremor
- Changes in posture/muscle tone (‘rigidity’)
- Slowness of movements
Basal ganglia circuitry

Movie #1
Basal ganglia circuitry

Normal DOPAMINE

Striatum

Direct pathway facilitates movement
Indirect pathway inhibits movement

Thalamus
From SNc
GPi
GPe
Indirect
Direct

Pedunculopontine nucleus
STN

Spinal cord
Basal ganglia circuitry

**Normal**

- **DOPAMINE**
- **Striatum**
  - Direct pathway facilitates movement
  - Indirect pathway inhibits movement
- **Pallidum**
  - From SNc
  - Gpi
  - GPe
  - Indirect

**Pedunculopontine nucleus**

**Spinal cord**
Basal ganglia circuitry

Normal

DOPAMINE

Subthalamic nucleus

Pallidum

Striatum
Basal ganglia circuitry

Normal DOPAMINE

Substantia nigra

Striatum

Subthalamic nucleus

Pallidum
Basal ganglia circuitry

Normal

DOPAMINE

Substantia nigra

Striatum

Subthalamic nucleus

Pallidum
Basal ganglia circuitry

Normal

DOPAMINE

Substantia nigra

Striatum

Subthalamic nucleus

Pallidum
Primate motor system

Normal

Substantia nigra

Striatum

Pallidum

Subthalamic nucleus

DOPAMINE

Direct pathway facilitates movement

Indirect pathway inhibits movement

Normal

Parkinson’s Disease

DOPAMINE

Direct

Indirect

+ 

-
~1957: Dopamine deficit identified in basal ganglia (particularly substantia nigra)

1961: L-Dopa introduced as first treatment

1983: MPTP induces parkinsonism

1995: Deep brain stimulation and other surgical approaches
Deep Brain Stimulation (DBS)
Basal ganglia circuitry

Movie #2
Basal ganglia circuitry

Movie #3
Deep Brain Stimulation (DBS)

100,000+ Parkinson’s patients treated with DBS
The non-human primate brain provides the closest model for human brain function in the domains of:

- perception
- action
- cognition

Basic research is the bedrock for future scientific discoveries.
Acknowledgments

Thanks to Michele Basso, Karla Ewalt, Michael Graziano, Bill Newsome, Dario Ringach, David Tank, Stu Leland and other colleagues for helpful discussions.

Sources:
• Kandel, Schwartz, Principles of neural science, 4th edition
• Bear, Connors, Exploring the brain, 4th edition
• Gazzaniga, Cognitive neuroscience, 5th edition
Laboratory Animal Use Regulations

Doty Kempf, DVM, DACLAM
Doty Kempf, DVM, DACLAM

2001 - B.S., University of Louisiana at Lafayette
2009 – DVM, Louisiana State University
2011 – Faculty at YNPRC

- Residency training in laboratory animal medicine with focus on nonhuman primates at Tulane National Primate Research Center
- Diplomate of the American College of Laboratory Animal Medicine
Animals in Research

► Use is subject to laws, regulations, policies, and standards
► Quality of scientific results assured by veterinary care, good husbandry, facility management, laboratory techniques
How did use become regulated?

◆ 28-hr Law (1873)
  - Farms animals provided food, water, and rest at least once every 28 hr during transit

◆ Pressure for federal legislation mounted in the 1950s and 1960s
How did use become regulated?

1965 - Sports Illustrated and Life Magazine publish revealing articles on the procurement process for finding and delivering dogs for biomedical research.
How did use become regulated?

1965 - Sports Illustrated and Life Magazine publish revealing articles on the procurement process for finding and delivering dogs for biomedical research.
Laboratory Animal Welfare Act

◆ 1966 – *Set minimum standards* for the handling, sale, and transport of cats, dogs, nonhuman primates, rabbits, hamsters, and guinea pigs held by animal dealers or pre-research in laboratories

◆ Laboratories were required to be licensed and to provide identification
AWA Amendments

◆ 1970 – Animal Welfare Act
  ■ Annual report
  ■ Assurance

◆ 1976 – Transportation standards
Animal welfare movement gained momentum in 1980s

- 1982 - Institute for Biological Research, Silver Spring, MD
- 1984 – Penn’s Head Injury Clinic
- 1985 – City of Hope National Medical Center
AWA Amendments

1985 – Health Research Extension Act

- Public Health Service Policy on Human Care and Use of Laboratory Animals.
  - IACUC
    - Veterinarian and non-affiliated member
    - Semiannual review
  - Training
  - Assurances
  - Justification

www.faseb.org
AWA Amendments

1985 – The Food Security Act

- Improved Standards for Laboratory Animal Welfare Act
- IACUC
  - Veterinarian and non-affiliated member
  - Inspections and corrective actions
- Pain
- Psychological well-being for NHPs
- Exercise requirements for dogs
- Pre/post-surgical care
- Major survival surgery
AWA Amendments

1985 – The Food Security Act

- National Agricultural Library
- Alternative testing
- Reduce duplication
PHS Policy

- Appropriate care and use of all vertebrate animals
  - 2002 – AWA amendment
- Proper treatment of animals
- Euthanasia
  - AVMA guidelines
- *Guide for the Care and Use of Laboratory Animals*
- AAALAC
PHS Policy

IACUC

- 5 members
  - Veterinarian, practicing scientist, non-scientific, non-affiliated
- Review
- Inspect
- Records
- Report
- Suspend
PHS Policy

◆ Animal Welfare Assurance

- Submitted every 5 years
- Care and use
- Site Visits
- Suspension or revocation of funding

www.faseb.org
The Guide

◆ The *Guide for the Care and Use of Laboratory Animals*
◆ 1\(^{\text{st}}\) Edition – 1963 (45 pages)
◆ 8\(^{\text{th}}\) Edition – 2011 (220 pages)
◆ Framework for animal care and use

◆ Subject to modification
◆ Scientific principles
◆ Professional judgement.
Association for Assessment and Accreditation of Laboratory Animal Care

- Private, nonprofit organization that promotes the humane treatment of animals in science through voluntary accreditation and assessment programs

- Value of Accreditation
  - Symbol of quality
  - Scientific validity
  - Public assurance

- Gold standard in animal care
Development of Alternatives

◆ The Three Rs

■ Replace
  ■ Substitute with non-animal systems
  ■ Replace with less sentient species

■ Reduce
  ■ Decrease animal numbers

■ Refine
  ■ Decrease or eliminate pain and distress

◆ NIH Revitalization Act of 1993
◆ ICCVAM Authorization Act of 2000
Replacement

**BCOP Testing – Bovine Corneal Opacity/Permeability Assay**

- Draize eye test
Refinement with NHPs

- Eye-tracking
NPRCs

- Laws and regulations
- AAALAC accredited
- Allocation committees
- Animal Care
  - Veterinary care
  - Animal care
  - Behavioral management
  - Enrichment
Behavioral Management

- Socialization
- Behavior assessment
- Enrichment
  - Structural
  - Physical
  - Feeding
- Training methods
Enrichment
Conclusions

◆ Excellent Care
◆ Animal well-being
◆ Professional standards
◆ Expertise
  ■ Scientists, veterinarians, support teams
◆ Animal welfare policies
Acknowledgments

Thanks to Dr. Joyce Cohen and Lisa Newbern
Everyone taking care of our animals:
Vets
Vet techs
Animal Care staff
Behavioral enrichment staff
Investigators
Lab personnel
To Ask A Question

Type your question in the white box and click “Send” (gray button)
Naomi Charalambakis, PhD
Staff Liaison, FASEB Animals in Research and Education Subcommittee
ncharalambakis@faseb.org