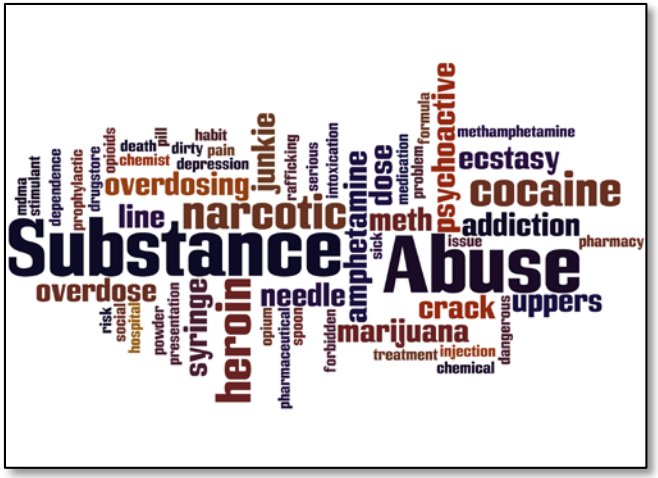

Introduction to the Use of Non-Human Primates (NHP) in Addiction Research

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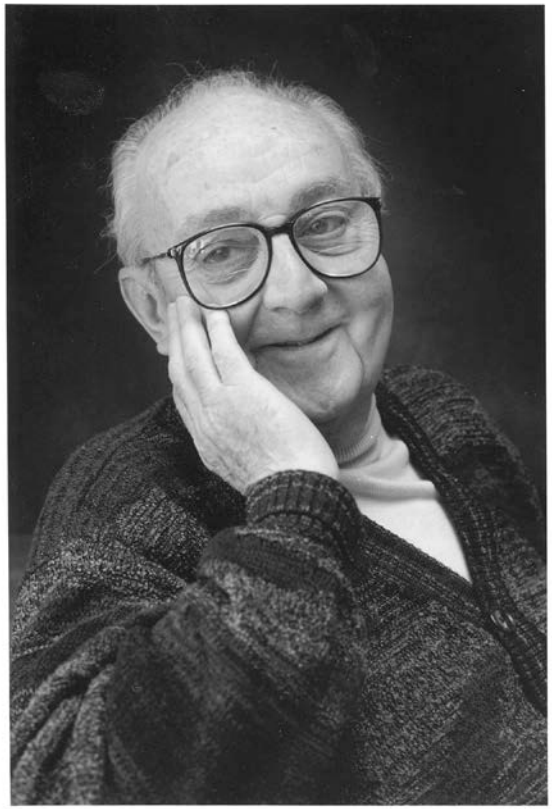
NIH Council of Councils, May 18, 2018

“ All models are approximations. Essentially, all models are wrong, but some are useful. However, the approximate nature of the model must always be borne in mind . . .”



George E.P. Box

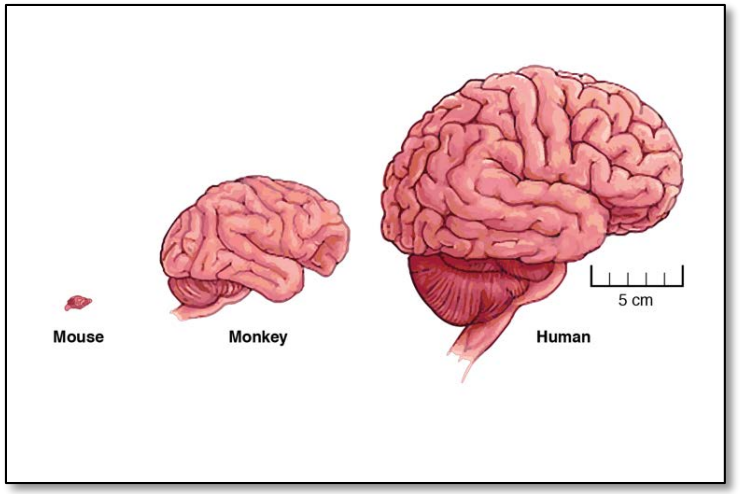
Limitations of Rodent Models for Substance Abuse Research

Despite many important contributions, limitations of rodent models include:

- Relatively distant phylogenetic relationship between rodents and humans
- Challenges in modeling addictive behaviors and self-administration in rodents
  - Smaller: more difficult to instrument and image
  - Shorter life spans
- Potential for differences in pharmacokinetics and drug metabolism

Advantages of Nonhuman Primate Models for Substance Abuse Research-I

- Relatively close phylogenetic relationship between NHP and humans
- Ability to establish procedures for drug self-administration (reflecting both anatomy and behavior)
- Ability to carry out longitudinal studies of chronic drug self-administration

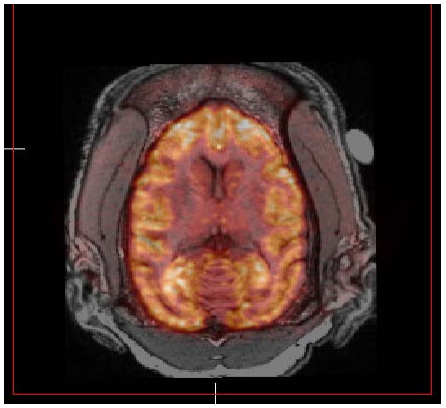


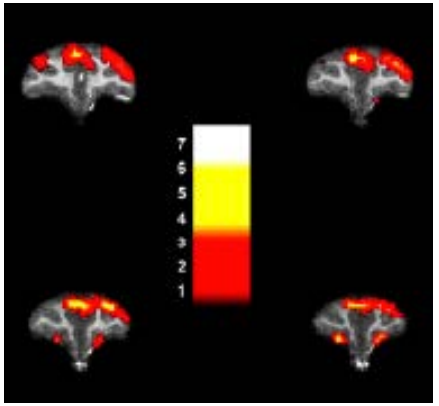
https://blogs.ntu.edu.sg

Advantages of Nonhuman Primate Models for Substance Abuse Research-II

- Ability to integrate functional imaging studies (PET, fMRI)
- Established paradigms of stress and social dominance in NHP
- Use of homologous rewards and testing strategies in humans and NHP
- Ability to examine novel therapeutic approaches

Serotonin 5-HT$_{2A}$





Murnane, *J Neuro Methods* 2010

Limitations of Nonhuman Primate Models for Substance Abuse Research

- Monkeys are not humans
- Limited number of subjects translates into limited statistical power
- NHP experiments generally study ‘all comers’, not a subset of subjects with an enhanced propensity for substance abuse
- Challenges in studying effects of psychiatric comorbidities associated with substance abuse

Future Directions for NHP Substance Abuse Research

- Leveraging the rapid expansion of NHP genetic data
- Increased efforts to validate results from NHP studies with those in humans using concordant imaging and testing techniques
- Enhanced definition of the molecular mechanisms that underlie substance abuse (incorporating optogenetics, DREADDs)
- Expanded focus on novel approaches to the prevention and treatment of opiate abuse

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Professor of Physiology and Pharmacology

Professor of Radiology

Director, Center for Neurobiology of Addiction Treatment

Director, The Nonhuman Primate Imaging of Behavior Program