What is the Importance of Animal Models to Neuropsychiatric Disease?

Submission ID 3010377

Submission Type Study Group

Topic scat1000127

Status Submitted

Submitter Tracy Bale

Affiliation University of Maryland School of Medicine

Affiliate Type Member

Gender Female

Participant(s) Tracy Bale (Chair), Kerry Ressler (Co-Chair), Eric Nestler (Participant), Scott Thompson (Participant), Joshua Gordon (Participant), Huda Akil (Participant), William Carlezon (Participant), Ted Abel (Participant), Bita Moghaddam (Participant)

SUBMISSION DETAILS

Secondary Category sscat1000114

Research Area Integrative

Request for Proposal Yes

RFP Categories What have we learned from the successes and failures of treatment approaches (pharmacologic, behavioral, neuromodulatory)? What do these approaches tell us about the underlying biology of disease? How ready is neuroscience to be translated into clinical practice?

Presenter Affiliations No

Neuroscience Based Nomenclature

Study Group Proposal Current changes to our thinking about neuropsychiatric disease mechanisms and classifications have prompted a dynamic discourse as to the importance and reliability of animal models. At a time when most major pharmaceutical companies are disbanding their R&D in neuroscience and mental health programs, academia is the remaining bastion in the development of novel drug targets and validation. ACNP is the ideal audience for this discussion, providing a professional setting in which all sides to this topic can be presented, and allowing voices from all arenas of basic and translational neuroscience to be heard. There is a growing concern in the field as to translational ability of outcomes in animal models matching that of human clinical trials. While it is clear we cannot completely model complex neuropsychiatric and neurodevelopmental disorders in most animals, there is certainly agreement across domain criteria

and endophenotypes, those factors that integrate many levels of outcomes, including cellular, circuits, genomics/epigenomics, and behavior, of disease that have proven informative. While the current ‘omics generation continues to provide novel and informative big data sets, the critical importance of how these results relate to disease risk and resilience requires validated measures. Similarly, while GWAS studies have given us valuable clues into the genes and pathways that are associated with disease risk, how these loci interact with the environment and their importance across developmental and life stages requires focused and pointed studies. How do we go from findings in rodents to complex diseases in humans? How do we control for the variables across labs and between species that make interpretation or translation difficult? At the cellular level, a recent push toward the utilization of human iPSC cells for phenotypic characterization, including organoids, migration assays and electrophysiology, have been suggested as an alternative to animal models. How these cells resemble the human disease condition and respond in a controlled environment is a critical question for this important area with great potential to provide molecular insight. Key factors and variables are still necessary, including sex as a biological variable and appropriate developmental stages, to draw reliable conclusions. There are key questions that remain as to the importance of animal models and require discussion and consensus across the field. What can we learn from animal models regarding the underlying causes and relevant interventions and treatments of mental health disorders? Can we map novel circuits and identify important gene x environment interactions? How does stress in animals influence these points, promote relevant dysregulation of physiological and behavioral measures, and are these analogous to the impact of stress in diseases such as depression and PTSD? Are some of the more translational behavioral measures, including fear conditioning, PPI, and sociality well validated, and can they be applied across species, sexes, and the lifespan of animals? Confidence and reliance on animal models has been a cornerstone of neuroscience and mental health research for decades. Can we determine a path forward in improving mental health?

Attestation and Affirmation Tracy L. Bale

Keywords

Keywords
Animal Models
Neurodevelopmental Disorders
Neuropsychiatric Disorders
Translational research

Participant Diversity Yes

Previously Published Material I attest that the information submitted has not been previously published.

DISCLOSURE

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Commercial Interest	Type of Financial Interest	Individuals Involved

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