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Can We Make Animal Models of Human Mental Illness? A Critical Review

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BACKGROUND

The use of animal models in studies of psychiatric disorders is increasingly controversial. Arguments for their use note that while imperfect, they are indispensable for research; those against argue that because they are imperfect, they are at best inadequate and at worst misleading.

DETAIL

The participants in this Banbury meeting critically reviewed the state of animal models in studies of psychiatric disorders, including:

- Current models and their effectiveness;
- Utility of models that reproduce some symptoms through lesion, chemical, environmental, or behavioral manipulations;
- Interpreting mutant models that do not, or only partially, reproduce the symptoms found in patients with that mutation;
- Integration of genetic and environmental factors in animal models;
- Approaches to the heterogeneity and overlap of symptoms
- Application of new gene editing techniques;
- Arguments that only primate models are valid, and the implications of this approach.

Participants were drawn from the psychiatric neuroscience fields within a framework, based on the National Institute of Mental Health's Research Domain Criteria (RDoC), involving dysfunctions in social processing, positive valence systems, negative valence systems and cognitive systems, as well as researchers with interests in genetics, development and sex differences.

There was a strong consensus among the participants that animal models are critical for investigating and finding better treatments for mental illnesses, though many current models are inadequate to the task. Attention should be paid to the limitations of any model, and researchers must acknowledge these rather than extrapolating directly from nonhuman models to human disease. Among other requirements, participants called for:

- The use of as many complementary models as possible;
- Continual validation of against new genetic, molecular, and circuit findings from humans;
- Sufficient sample sizes and attention to study complexity and statistical challenges in studies that involve multiple genes and/or environmental, developmental, or sex influence.

With appropriate attention to these matters, the technological advances in studying neural circuits in more specific ways, the use of CRISPR technology to manipulate genes, and the ability to obtain complete transcriptome maps of single cell types (and even individual cells) promises to bring new perspectives to the modeling of mental disorders.

Eric Nestler & Hakon Heimer

MEETING PARTICIPANTS

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