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Title

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Permalink

<https://escholarship.org/uc/item/15q6884g>

Journal

NEUROPSYCHOPHARMACOLOGY, 47(SUPPL 1)

ISSN

0893-133X

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Publication Date

2022

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Peer reviewed

29. Bridging the Gap Between Pre-Clinical and Clinical Studies: The Promise and Challenges of Forward and Reverse Translational Approaches

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Study Group Summary: There have been extensive advances in our knowledge of the neurobiology of mental health disorders over the past decade. The translation of findings from bench to bedside, however, remains slow, costly, and is often fraught with substantial limitations. There has been much discussion around how to improve components of the translational process—for example, by using different animal models, developing novel and innovative experimental tasks, or selecting appropriate research tools. Nevertheless, a major challenge in translational research has been the wide gap between the scientists conducting preclinical animal studies and those conducting clinical human studies. Most scientists focus exclusively on only animal or human models, leading to silo mentality. Among factors isolating camps include the use of different research approaches, methods, and terminology, as well as presenting data at conferences and publishing findings in journals most associated with one line of research. Funding mechanisms and study section assignments also contribute to separation of animal from human studies, and vice versa.

Despite these longstanding challenges, new approaches are beginning to emerge. This study group will highlight work by scientists dedicated to bridging gaps between animal and human studies through several perspectives. The first perspective is from scientists who have cross-trained in both human and experimental model research. A second perspective arises from scientists collaborating tightly across research modalities. Combining these perspectives can help mitigate silos by

developing transdisciplinary language, methods, and interpretations. Especially compelling are scientific partnerships that provide a foundation for rapid and iterative forward and reverse translational approaches. Forward translation has been a hallmark of the bench to bedside approach. However, reverse translation from human to animal models is equally important, as identifying the power and limitations of experimental systems and matching human questions to appropriate models is crucial. An iterative approach, that supports real-time forward and reverse translation, shows great potential for moving the field forward. A combination of reverse and forward translation can enhance identification of causality and mechanisms in animal models that can then be tested in human disease, and can encourage the application of findings from human studies to develop novel approaches and hypotheses to be tested in preclinical studies. An iterative, transdisciplinary process is critical for advancing construct-validated investigations of disorder-relevant neural circuitry, with the ultimate goal to guide the identification of novel treatment targets, development of novel therapeutics, and enhancement of current therapies.

This study group will include scientists who have cross-trained in animal models and human studies (Ressler, Milad, Silveri) and pairs of scientists who are actively collaborating to achieve iterative forward and reverse translations across their research programs (Winder-Blackford, Kalin-Pine, Baram-Yassa, Carlezon-Rosso).

Disclosure: Nothing to disclose.