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Behavior matters for neuroscience and neuroscience matters for behavior

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The study of behavior matters for neuroscience. The main function of the central nervous system is to integrate information from the internal and external environment, and to generate responses that facilitate survival. These adaptive responses are, by definition, both physiological and behavioral. However, maladaptive behavior can also occur, and in humans, such behavior is characteristic of psychiatric illness. Our goal, as behavioral neuroscientists, is to better understand the brain mechanisms underlying adaptive and maladaptive behaviors, and to contribute to the development of novel treatments for brain disorders. To do so effectively, we argue that behavior is critical to understanding brain function and vice versa.

During the last two decades, remarkable technological progress has been made to probe brain function, with optogenetic and chemogenetic methods at the forefront. These methods enable manipulation of specific cell types within a brain area, and the investigation of functional connections between cell groups or brain areas. This has resulted in a resurgence of interest in systems neuroscience in relation to both adaptive and maladaptive behaviors. However, these technological advances can only reach their full potential if they are combined with a detailed study of behavior. Krakauer et al. (2017) recently argued that in order to investigate the underlying brain mechanisms, behavior must be dissected it into its component processes. They note that this strategy will be most useful if applied to natural or innate behaviors. In this issue, Rutherford and Milton (2022) take a similar position, but argue that for some components of addiction-like behaviors, the decomposition of behavior should be done based on animal learning theory. They describe how cue-elicited addiction-like behaviors can be dissected into instrumental and Pavlovian conditioning processes. Rutherford and Milton do not suggest, however, that the learning-based approach is superior to the study of ethology-based behavior advocated by Krakauer et al. Rather, both approaches are necessary to understand behavior, so that combining the strengths of ethological approaches with animal learning approaches will benefit the behavioral neuroscience field. Another article in this issue (Venniro et al., 2022) summarizes how biological (sex and age) and environmental (exercise, enrichment, alternative rewards, and stress) factors contribute to the incubation of drug seeking in rats. This model captures the time-dependent increase in drug craving following abstinence that occurs under some conditions in human drug addicts. This work on the incubation of drug seeking is also grounded in animal learning theory.

Both the Rutherford and Milton (2022) and Venniro et al. (2022) articles note the importance of laboratory animal studies to understand human behavior and brain function, a point explicitly made in a recent paper by Homberg et al. (2021). These studies allow for manipulations of neural processes in ways that are not possible in humans. Additionally, because in a laboratory situation the history and living conditions of animals can be tightly controlled, causality can be more easily established than in humans. There are, of course, aspects of human behavior (e.g., language) that cannot readily be modeled in laboratory animals. Thus, advancements in understanding the relationship between behavior and brain function will only occur when knowledge gained from laboratory animal studies is combined with knowledge derived from human studies.

In relation to the latter point, Rutherford and Milton (2022) argue that integrated approaches to study neural mechanisms of psychiatric disorders are needed in order to develop new treatments. They argue that both translational (applying knowledge from laboratory animal studies to the human condition) and reverse translational (using information from the human condition to develop and improve animal models) approaches should be used in concert to turn new discoveries into clinical practice. Consonant with this position, Venniro et al. (2022) review reverse translational work on how the therapeutic effects of physical exercise, improved sleep, as well as interventions such as contingency management and the community reinforcement approach can be modelled in laboratory animals, and how the underlying neural mechanisms can be studied. They propose that such knowledge can be

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used for forward translation to develop novel treatments – pharmacological or behavioral – for addiction.

The Rutherford and Milton (2022) article also provides a thoughtful discussion on the strengths and drawbacks of translational and reverse translational approaches and argues that multiple techniques and approaches should be used in a convergent way to increase our understanding of psychiatric illness. This includes molecular biology, neurophysiology, functional imaging, and computational modelling. Here, we would like to add that an interdisciplinary approach will be critical since no single discipline is likely to provide a solution to prevent and treat psychiatric illness. Beyond neuroscientific, biological, psychological, and computational approaches, we must also incorporate relevant knowledge and expertise from other disciplines, including public health, sociology, and law to effectively prevent and treat a given psychiatric illness (Heilig et al., 2021).

In conclusion, a thorough study of behavior is an integral and critical part of neuroscientific investigation of brain-mediated conditions. The reviews by Venniro et al. (2022) and Rutherford and Milton (2022) eloquently point out how investigating human behavior on the basis of animal learning theory enhances our knowledge of the neurobehavioral mechanisms of psychiatric illness, with a focus on drug addiction. They also emphasize that understanding the brain mechanisms of innate and learned behaviors requires concerted efforts from multiple disciplines. This aligns very well with the ambitions of the European Behavioural Pharmacology Society, which operates at the crossroads of molecular biology, neurophysiology, genetics, epigenetics, pharmacology, experimental psychology, psychiatry, epidemiology, and neuroscience. As a Society, we welcome scientists working in these and related fields and we hope to provide a forum for the exchange of ideas that will advance our understanding of the fundamental relationship between brain function and behavior and the neural substrates of psychiatric illness.

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