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Commentary

The Importance of Animal Models of Decision Making, Gambling, and Related Behaviors: Implications for Translational Research in Addiction

Marc N Potenza*,[1]

[1] *Departments of Psychiatry and Child Study Center, Yale University School of Medicine, Connecticut Mental Health Center, New Haven, CT, USA*

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Addictions are arguably the most costly medical disorders, with annual costs to the US society estimated to exceed $500 billion dollars and to be larger than those associated with stroke, heart disease, and diabetes combined (Uhl and Grow, 2004). Despite the immense costs associated with addictions, relatively few effective treatments exist, particularly for specific addictions such as cocaine dependence for which no pharmacotherapies are currently approved by the US Food and Drug Administration. As such, there exists a significant need for more research into the etiologies and neurobiologies of addictions such that more effective treatment strategies may be developed for these currently costly disorders. Given that addictions, similar to other psychiatric disorders, are complex processes for which etiologies likely involve multiple genetic and environmental determinants that interact in a dynamic manner, using multiple approaches and disciplines in an integrative manner will be important to make substantial inroads into our understanding of addictions and to translate this knowledge into prevention and treatment advances.

Addictions have been conceptualized as disorders of misdirected motivation in which one typically hedonic and maladaptive behavior (eg, drug use) takes precedence over other more adaptive ones (eg, performing well at work or attending to familial concerns) (Potenza, 2006). This conceptualization is consistent with descriptions of the core components of addictions that typically include an element of continued engagement in a behavior despite adverse consequences (Potenza, 2006). Consistently, much research over the past decade has involved assessments of decision making in individuals with addictions (Bechara, 2003). Neuroeconomic paradigms have investigated temporal discounting of monetary rewards (as well as drug rewards) in individuals with addictions and have found that individuals with addictions tend to discount rewards more rapidly than do those without addictions, and that the discounting behaviors are associated with clinically relevant features, such as treatment outcome (Krishnan-Sarin *et al*, 2007). More complex paradigms, such as the Iowa Gambling Task (IGT) that involves risk-reward decision making coupled with the learning of a strategy that is not intuitively obvious, have also demonstrated deficits in individuals with addictions (Bechara, 2003). Moreover, an association between IGT performance and real-life measures of functioning (eg, ability to hold a job) has been reported in addicted individuals, highlighting the real-life relevance of performance on this task (Bechara, 2003). As such, an improved understanding of the neurobiology of decision making holds significant promise for generating clinical advances for the prevention and treatment of addictions.

Precisely how decision making is related to addiction remains relatively poorly understood. That is, individual differences in decision making may relate to genetic and/or early life environmental factors, or their interactions, and may exist before the drug exposure experienced in drug addictions. Alternatively and not mutually exclusively, drug exposure may influence the neural structures and functions underlying decision making. Animal models are important in investigating these questions, and animal data indicate roles for each possibility. For example, in the first instance, individual differences in impulsivity before drug exposure have been linked to drug use behaviors. In a model of cocaine dependence, response impulsivity predicted compulsive drug use (Belin *et al*, 2008), and in investigations of nicotine administration, response impulsivity predicted enhanced motivation to initiate and maintain nicotine self-administration, and impulsive choice on a delayed reward task predicted reinitiation of nicotine use after abstinence (Diergaarde *et al*, 2008). With respect to the second possibility, alcohol exposure during adolescence has been found to lead to risky decision making later in life (Nasrallah *et al*, (in press)), indicating that both individual differences in decision making before substance exposure

*Correspondence: Dr MN Potenza, Departments of Psychiatry and Child Study Center, Yale University School of Medicine, Connecticut Mental Health Center, Room S-104, 34 Park Street, New Haven, CT 06519, USA, Tel: +1 203 9747356, Fax: +1 203 9747366, E-mail: marc.potenza@yale.edu
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and substance exposure itself (as well as the timing and duration of such) are important considerations in addictions. These animal studies, that include pre-drug-exposure assessments, controlled experimental conditions, longitudinal characterization, and (in some cases) nondrug-exposed experimental groups, provide important information that could not be obtained in human studies because of the lack of feasibility. As such, they offer a critical complement to human investigations.

The recent investigation by Zeeb *et al* (2009), as well as another recent one by Rivalan *et al* (2009), models the IGT in rats. Both groups use the task to investigate important aspects of decision making: influences on task performance of serotonergic and dopaminergic drugs as well as individual differences in reward sensitivity and anxiogenic risk taking, respectively. Although each study provides important information in its own right, there is significant hope that they represent the initial basis for multiple investigations that deconstruct and probe specific aspects of decision making as related to addiction. As evidenced by other examples mentioned above, such investigations could use carefully controlled longitudinal experimental conditions that are not practical or feasible in human studies. Such investigations could also adopt additional approaches (eg, genetic manipulations, proteomic analyses, electrophysiological recordings, or neurochemical assessments) that are also typically not feasible in people, yet provide important information on neurobiological processes. In addition, careful coordination between preclinical and clinical investigations, such as those that model the same behavior or paradigm (herein, the IGT) across species could facilitate the translation of information in a manner that could help dissect and clarify complex processes underlying addiction and generate clinical advances. Importantly, the availability of animal models of the IGT also holds promise for better understanding gambling behaviors and human conditions such as pathological gambling, for which the lack of availability of appropriate animals models has slowed research into the disorder. As such, these studies hold significant implications of a broad range of neuropsychiatric conditions and thus could contribute to multiple clinical advances that could benefit many individuals, their families, and the society as a whole.

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See related article by Zeeb *et al* on page 2329 in NPP, Volume 34, Number 10.