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Simulated opioid withdrawal engenders risk-prone choice: A comparison of intravenous and intranasal-using populations☆

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Abstract

Risk-sensitive foraging theory refers to a group of different models that predict the occurrence of risk-prone behavior; therefore, these models may help to characterize the risky behavior that is a hallmark of opioid dependence. The daily energy budget (DEB) rule, one model of risk-sensitivity, suggests that foragers will prefer highly variable food sources over less variable ones when all current options provide means that are insufficient to meet metabolic requirements. The tenets of the DEB rule were tested in the context of opioid dependence, the primary hypothesis being that opioid withdrawal may foster risky choice. Intravenous and intranasal-using opioid-dependent patients enrolled in a buprenorphine treatment program read scripts simulating opioid-agonist and -antagonist symptoms, and then made a series of decisions between two different opioid dealers. One dealer provided a constant source of heroin, and the other, a variable source. Separate measures were utilized to expose participants to either variability in delay of opioids or quantity of opioids. Participants were also required to complete a money questionnaire in which two hypothetical slot machines differed in respect to payoff amounts and probabilities. Results demonstrate that preference for the risky option was mediated by hypothetical drug deprivation in all circumstances, but this effect was more considerable in opioid-dependent participants who used intravenously. The current findings suggest that intravenous delivery places greater metabolic constraints on the user and therefore engenders greater risk-taking during withdrawal. The DEB rule is applicable to opioid dependence and provides a useful framework from which to examine the behaviors associated with opioid withdrawal.

Keywords: Risk sensitivity; Opioid dependence; Withdrawal; Risky choice; Intravenous administration; Intranasal administration

1. Introduction

Risky behavior is a hallmark of opioid dependence (Calsyn et al., 1992; Odum et al., 2000). Obtaining opioids frequently requires involvement in an illegal market system in which a host of other high-risk activities are within reach, such as theft or prostitution. Furthermore, self-administering heroin often entails health consequences associated with unsanitary needle use. Rationally, these risks outweigh the potential gains, but for the dependent individual, the risks are an inherent and accepted aspect of continued use.

This research report examines the conditions under which risk-prone behavior occurs in opioid-dependence and explores whether opioid withdrawal precipitates risky choice. Drug dependence is a behavioral state that operates upon neural-limbic circuitry normally activated by food reinforcement (Nestler and Landsman, 2001). Opioids, like food, have both negative and positive reinforcing effects in drug-dependent individuals, and withdrawal may be analogous to hunger in promoting foraging behavior. Therefore, approaching the problem of drug dependence from the perspective of foraging theory may help to characterize the features of the disorder as well as provide new opportunities for research and treatment.

Sustenance is primary to survival and adaptive foraging strategies contribute positively to evolutionary fitness.

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Contemporary views of foraging theory place great importance on risk as a determinant of foraging strategy and understanding the organism's response to resource variability (i.e. risk) is the primary focus of risk-sensitive foraging (RSF) theory. Several different models of RSF exist, and investigations of RSF behavior traditionally involve a dilemma between two different reinforcement schedules and each provides nearly equivalent reward quantities per unit time. One option is arranged to be more variable than the other, so the degree of risk-prone behavior is assessed by preference for the variable alternative. Several studies have investigated RSF behavior in humans (Bickel et al., 2004; Egelman et al., 1998; Pietras and Hackenberg, 2001; Pietras et al., 2003; Wang, 1996), and the results demonstrate that humans are sensitive to resource variability and that perceived risk guides decision-making strategy.

1.1. The daily energy budget rule

One model of RSF, called the daily energy budget rule (DEB; Houston, 1991; Stephens, 1981), posits that risky choice is dependent upon the economic relationship between caloric income and energy expenditure. More specifically, the DEB rule states that foraging strategy is determined by an interaction of initial energy reserves (X), the mean rate-of-gain (μ), the time available for foraging (T), and the organism's survival requirement (R). When energy budgets are positive ($X + \mu T > R$) and energetic income exceeds expense, foraging organisms ought to avoid risk. When energy budgets are negative ($X + \mu T < R$), foragers ought to behave in a risk-prone manner because a riskier option may occasionally yield a greater return. Given a run of good luck, repeated risk-prone choice could potentially resolve a negative energy budget.

The present experiment explores the implications of the DEB rule to opioid dependence, the fundamental question being whether opioid withdrawal symptoms promote risky choice. Because withdrawal symptoms are noxious and tended to with great urgency, the dependent individual may choose to engage in high-risk behaviors in order to alleviate withdrawal. Although withdrawal does not threaten survival, its noxious effects may prompt risky behavior in a similar manner to how a negative energy budget may produce risk-prone choice. When satiated, the stimuli that occasion the behaviors associated with withdrawal relief are not present, and opioid-dependent individuals may behave in a more risk-averse manner.

1.2. The mean rate-of-gain parameter and method of drug delivery

Reward magnitude and the delay-to-receipt of that reward are two factors that determine the mean rate-of-gain (μ, in the equations above). Investigators have manipulated both the quantity of food (e.g., Caraco, 1981) and the delay to the next rewarding event (e.g., Bateson and Kacelnik, 1995) in order to obtain a better understanding of the mechanics of μ on risk-sensitive choice. Specifically, μ refers to the integration of mean reward magnitudes and delays-to-reward. The utility of μ is determined by the energy expended to obtain food and the forager's metabolism. One of the tenets of the DEB rule is that this relationship between caloric intake and the subjective energy obtained is nonlinear (Stephens, 1981). For instance, an organism with a rapid metabolism needs to acquire a proportionately large amount of food before caloric intake translates into a meaningful and sufficient energetic gain.

If the DEB rule is applied in the context of opioid dependence, μ may be substantially influenced by the method of drug delivery. Opioids are absorbed more rapidly via intravenous (IV) than intranasal (IN) self-administration (Cone, 1998), and the half-life of IV-administered is more abrupt than IN-delivered opioids (Takala et al., 1997; Helmers et al., 1989), producing a more proximal and more severe withdrawal syndrome upon discontinuation (Farre and Cami, 1991, 2003; Sellers et al., 1991). Therefore, in order to avoid withdrawal, IV-using dependent individuals would necessarily need to administer opioids more frequently than IN-using individuals. Assuming resources are scarce or at least constrained, IV users are less likely to meet their energetic requirements and evade withdrawal. According to the DEB rule, intravenous users ought to have a higher overall probability of behaving in a risky fashion because symptoms of withdrawal are more proximal, severe, and more likely than for intranasal users. Alternatively, intranasal users may behave in a less risk-prone manner relative to their intravenous-using counterparts.

1.3. Empirical evidence of risk-sensitivity in opioid dependence

When given a series of choices between two hypothetical heroin dealers, Bickel et al. (2004) demonstrated that opioid-dependent participants were more likely to behave in a risk-prone manner after being exposed to a script that presented symptoms of heroin withdrawal. Participants were risk-averse after being exposed to a script that presented symptoms of heroin satiation. The choices involved one heroin dealer who hypothetically provided a fixed amount of the drug while the second dealer provided a variable amount of the drug with the same mean. Each successive choice yielded a greater average return. A second series of questions presented variability in the delay-to-receipt of heroin (quantities were equivalent between the two dealers) and the average delay until the receipt of the drug was successively increased. Results over the series of choices demonstrated that symptoms of withdrawal produced risk-prone heroin choice. Furthermore, the researchers concluded that the magnitude of the drug reward influenced the degree of risk-prone responding such that more exclusive risk-prone behavior was exhibited at high quantities. Although this study provides support for the applicability of the DEB rule in opioid dependence, these results need to be critically evaluated because the variability of the risky option increased in a linear fashion as mean quantity increased (hereafter noted as the mean-variance confound). While the mean-variance confound does not negate the importance of Bickel et al. findings, the confound prevents speculation about systematic relationships between reward magnitude and risk-sensitive choice.