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Dissociable contribution of nucleus accumbens and dorsolateral striatum to the acquisition of risk choice behavior in the rat

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ABSTRACT

While a growing body of research has suggested that the mesocorticolimbic dopamine systems play a key role in decision making under risk, how the nucleus accumbens (NAC) is involved in the acquisition of risk choice behavior remains unclear. This study used a T-maze task to assess risk-based decision making in which the rat was required to assess the risk by choosing to enter either a small and certain reward arm or a large but uncertain reward arm of the maze. The latter option, when chosen, resulted in provision of 2, 4, or 8 sweeten pellets with a probability (p) of 0.5, 0.25, or 0.125, respectively. Thus the latter arm provided three different conditions of reward ratio, compared to the choice of former arm, which always provided 1 pellet with $p = 1$. This risk choice task was then run with the expected value being equality between the binary choice options. The experimental rats first received an excitoneurotoxic lesion affecting either the NAC or the dorsolateral striatum (DLS) and this was followed by post-lesion behavioral examination. The sham lesion control rats acquired a stable risk choice with regard to each reward ratio over a 10-day test. The pattern of choice behavior appeared in risk-seeking when $p = 0.5$ to obtain 2 pellets, and was risk-averse when larger reward resulted in lower p. The NAC lesion significantly disrupted the acquisition of the aforementioned risk choice behavior and apparently shifted the choice into a risk-averse style for all three reward ratios. No such effect was observed in the rats with DLS lesions. Neither the gross motor action nor the discrimination of different reward magnitudes was impaired by the lesions affecting either the NAC or DLS as assessed by an additional experiment. These findings suggest that firstly there is heterogeneity between NAC and DLS with respect to risk-based decision making, and that secondly the NAC is involved and critical to the acquisition of behavioral choice under risk, specially when the expected value of the reward under the two choice options is equal.

1. Introduction

Animals including humans often make decisions that involve components of risk or uncertainty (Balci, Freestone, & Gallistel, 2009; Paglieri et al., 2014; Trimmer et al., 2011). The individual is not entirely sure about the future reward to be obtained. As a result, both a risk and an expected reward are associated with each choice option to be considered for the engendering action outcomes with respect to the more valuable that should lead to optimal survival. Thus the expected reward value of an action during risk-based decision making can be represented by the product of the value of an outcome and its relative probability of occurrence. The phenomenon of probability discounting occurs when the subject responds toward in a risk-averse manner, due to a decrease in the probability of obtaining a reward that has the appearance of risk (Cardinal, 2006; Green & Myerson, 2004). Recently, aberrant or maladaptive risk-related decision making has been observed in a number of psychiatric populations including those with drug addiction, mood disorders, and schizophrenia (Jentsch et al., 2014; Paulus, 2007; Stopper & Floresco, 2015). However, the causal relationship between psychiatric disorders and maladaptive decision making remains unclear. Thus, it is important to delineate the underlying neural substrates and mechanisms associated with risk decision making; this will assist our understanding of this phenomenon and help with the development of treatments for these brain/mental disorders (Lee, 2013).

In order to probe the underlying neural mechanisms, several types of animal model used to test risk-related decision making

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have been developed in the past two decades (see a review by Orsini, Moorman, Young, Setlow, & Floresco, in press). Of particular interest, when testing risk-based decision making, a typical binary choice task can be set up for a rodent subject during which there is choice between either a small but certain reward (probability; $p = 1$) and a larger reward that is obtained with a degree of uncertainty (e.g. $0 < p < 1$). Accumulating evidence from lesion and psychopharmacological studies has indicated that the midbrain dopamine (DA) systems are involved in modulating risk-based decision making. Using systemic drug treatments, amphetamine (an indirect DA agonist) and flupenthixol (a non-selective DA receptor antagonist) have been shown to increase and decrease, respectively, the preference for taking the risky large reward option when carrying out a probabilistic discounting task (Floresco & Whelan, 2009; Mai, Sommer, & Hauber, 2015; St. Onge, Chiu, & Floresco, 2010). The risk-prone response induced by amphetamine can be partially reversed by treatment with the selective DA D1 and D2 receptors antagonists, SCH23390 and eticlopride, respectively (St. Onge & Floresco, 2009). Further evidence for an involvement of the nucleus accumbens (NAC) in risk associated choice has been obtained through studies that have used brain lesions, microinjection, and neurochemical measurements. For example, the enhancement of DA release in the NAC has been found to be correlated with the individual differences in a risk-taking behavior as monitored by voltammetry (Sugam, Day, Wightman, & Carelli, 2012). Similarly, risk choice in relation to a probability discounting task has been measured by using a microdialysis approach (St. Onge, Ahn, Phillips, & Floresco, 2012). When intra-NAC microinjection of drugs that can selectively activate or block DA subtype receptors is carried out, it was found that NAC D1 receptors would seem to play a more important role in the modulation of the risk choice on a probability discounting task than NAC D2/D3 receptors (Stopper, Khayambashi, & Floresco, 2013). While the roles of DA receptor subtypes may not be clearly dissected yet, it would seem that the subareas of the NAC were thought to be in the control of risk choice behavior are heterogeneous in nature. The D1/D2 receptors in the core, but not the shell, subarea of the NAC would seem to be involved in the risk-based decision making; this has been validated by locally infusing flupenthixol into the NAC core, which was found to suppress a preference for the large/risky choice with respect to a probability discounting task (Mai et al., 2015). Several excitotoxic lesion studies have shown the involvement of NAC in risk choice behavior, but with the mixed results. That rats with a NAC lesion were found to display a risk-averse pattern of choice behavior with respect to a probability discounting task was initially reported by Cardinal and Howes (2005); however, Acheson et al. (2006) reported that a NAC lesion slightly, but not reach the statistical significance, affected the discounting of probabilistic rewards. Despite these inconsistent results, a more recent study has reported that inactivation of NAC by local infusion of GABA agonists was able to produce risk-averse response (Stopper & Floresco, 2011). These findings, when taken together, support a notion that the NAC or brain DA is involved in the modulation of risk-based decision making. It is important to note that all of the NAC-related data were collected when the experimental treatment was given after behavioral training (namely, they involved post-training lesions). Up to now, very few studies have used pre-training lesions when carrying out such behavioral task (Mai & Hauber, 2012). Thus, it remains to be determined whether the mesoaccumbens DA system makes a critical contribution to the acquisition/development of risk choice behavior when a pre-training lesion approach is used.

Risk, in a sense, can be defined as the variance in the desired reward outcome. If we take this into account, the level of risk can be directly manipulated by holding the overall reward or payoff constant while changing only the variance. If not, the reward magnitude is likely to be confounded by the risk. This concern, however, has been rarely given attention during the experimental design of the aforementioned studies. The previous studies as described above, namely those with a probability discounting task, were carried out by manipulating the reward probabilities and holding the reward magnitude of the risky option as a constant. With this set up, the expected value (EV) is shifted across each of the different reward probabilities. In other words, the binary choices options set in those previous studies yield unequal payoff and this will have caused the risk to vary, but not to increase along with a reward probability decreased. Thus, it is worth to disentangle the differences that potentially existed between a test associated risk as a behavioral choice and those of the reward probability discounting.

The present study used a T-maze set up to evaluate the risk choice behavior. As the task, the rat was required to assess the risk by choosing entry to either a risky large reward arm of the maze or to a certain small reward one. The former option was set up with a p of 0.5, 0.25, or 0.125 correspondingly being given 2, 4, or 8 sweeten pellets as the different reward ratio conditions, whereas the latter option was provided as a choice outcome that always gave 1 pellet ($p = 1$). Accordingly, this risk choice task was run under a condition with the EV being equal for these binary options. The present study investigated the role of the NAC on the acquisition of risk choice behavior by conducting excitotoxic lesions prior to behavioral training. A counterpart experiment where there were lesions of the dorsolateral striatum (DLS) conducted for a comparative purpose. The dorsal striatum is thought to be important to reward-mediated decision making (Balleine, Delgado, & Hikosaka, 2007), but how this region or its subareas are involved in behavioral choice under risk has not yet been examined. We expected to find differences in the profiles with respect to behavioral choice under risk for the rats with pre-taring lesions of NAC and DLS compared to the sham lesion controls.

2. Methods

2.1. Subjects

Male Wistar rats (BioLASCO Taiwan Co., Ltd.) were used that averaged approximately 200 g of body weight on arrival. The rats were housed individually. After 10 days of adaptation to the food and water provided *ad libitum*, the rats were maintained on a food-restriction regimen such that about 15 g of laboratory rodent pellets were provided in their home cage no sooner than 30 min after the end of each daily experimental session. The rats were monitored and kept at 85% of their pre-restriction body weight. Water was continuously available in each home cage. Training and/or test sessions were conducted daily at the same time (9:00–16:00) each day during the light portion of the vivarium's 12/12-h light/dark cycle (light on at 7:30 a.m.). The temperatures of the colony and the behavioral test room were kept constant around 22 ± 2 °C. Following the NIH Guide for the Care and Use of Laboratory Animals, the experimental procedures were approved by the Animal Care and Use Committee of National Cheng-Chi University.

2.2. Apparatus

The testing of the risk choice task was conducted in an acrylic-made T-maze that consisted of one start arm (55 × 15 × 25 cm) and two goal arms (55 × 15 × 25 cm each). Chocolate-flavored sweeten pellets (~0.15 g each; Chawkolo Co., Ltd., Taichung, Taiwan) were used as the reward in this task with the amount of reward varying according to the experimental protocol. Prior to