Neural Correlates of Risk and Reward Signals in Smokers Using an MRI-Compatible Vaping Device: A Preliminary Study

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Abstract

Reward and risk processing are fundamental for decision-making, which can be altered by addiction. While it's crucial to utilize drug rewards to capture the drug-specific neural processes, less is known about reward and risk encoding in the context of actual drug use. This study aims to fill this gap by investigating how reward and risk processing differ between smokers and non-smokers, using both monetary and nicotine rewards in a structured gambling task and an MRI-compatible vaping device. Preliminary fMRI results with monetary rewards showed significant striatal activation correlated with reward prediction errors and detected risk prediction error-related activity in the posterior parietal cortex (PPC) and dorsolateral prefrontal cortex (dlPFC). Notably, smokers exhibited altered neural responses in these regions, indicating their distorted risk and reward processing compared to non-smokers. This study will shed light on our understanding of the distinct neural processing of primary drug rewards, such as nicotine, within the framework of risk and reward evaluation, providing valuable insights into the neurocognitive aspects of addiction.

Keywords: Reward, Risk, Nicotine Use Disorder, fMRI, Mean-Variance Theory

Introduction

Encoding risk, quantified by variance in the mean-variance choice theory (Kroll et al., 1984) is important for learning optimal strategies in unpredictable environments. Understanding the neural mechanisms of reward and risk processing is crucial for understanding the impaired decision-making in addiction, where evaluation of reward and risk is often altered. Previous research suggests that the reward system in substance misusers, particularly the striatum, exhibits a selectively heightened sensitivity to drug cues, contrasting with their reduced sensitivity to non-drug rewards such as monetary incentives (Goldstein et al., 2007; Sweitzer et al., 2014). This underscores the necessity of employing drug rewards in neuroimaging studies of addiction, as monetary rewards may not fully capture the decision-making nuances of drug-seeking behavior in dependent individuals.

While studies examining the neural response to nicotine rewards exist (Modak et al., 2021), a direct investigation into how reward and risk prediction and errors are processed in the context of drug usage is lacking. Regarding risk, previous studies identified key brain regions implicated in risk and uncertainty including the insular, prefrontal, and parietal cortices (Huettel et al., 2005; Preuschoff et al., 2008). Yet, the alteration of risk encoding in individuals with substance use disorders, and their varied responses to drug versus non-drug rewards, remains poorly understood.

Here, we aim to address this gap by developing a novel MRI-compatible vaping device (**Figure 1**), enabling direct comparison of neural activation for nicotine and monetary rewards. Furthermore, we utilized a gambling task to manipulate both reward and risk prediction and their prediction errors to investigate the neural underpinnings of both reward and risk encoding in smokers.

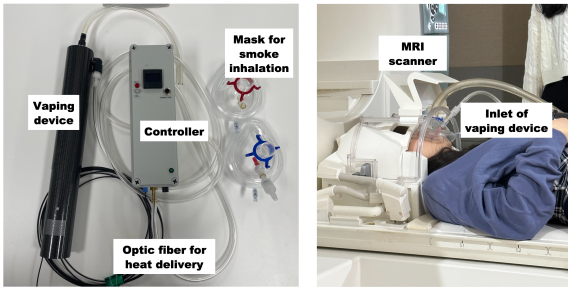

Figure 1. MRI-compatible vaping device.

Figure 2 outlines the central hypotheses of our investigation. Regarding the reward circuit, including the striatum, we hypothesized that smokers would demonstrate an increased fMRI response to nicotine rewards, while their response to monetary rewards will be diminished (Modak et al., 2021; Tolomeo et al., 2021). As for the risk circuit, encompassing the prefrontal and parietal cortices, we hypothesized that smokers would exhibit reduced fMRI response to both types of rewards, in line with previous studies suggesting their reduced risk representation (Naqvi & Bechara, 2015). While we are collecting participants with both nicotine and monetary conditions, we reported preliminary results with the monetary condition only, which replicate the previous findings.

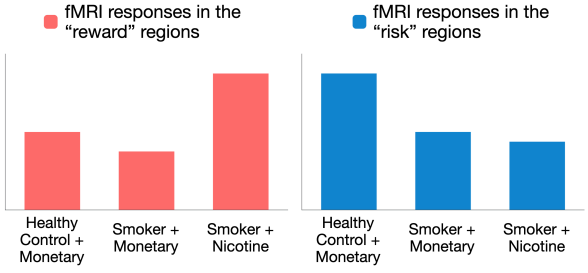

Figure 2. Hypotheses for fMRI responses in the regions implicated in reward and risk processing.

Methods

Participants included 6 smokers (mean age 22.33 ± 2.25 years old, all male) and 7 non-smokers (mean age (mean age 23.71 ± 5.99 years old, 2 males and 5 females). We plan to recruit up to 50 participants in total. Participants engaged in a gambling task (**Figure 3**; Preuschoff et al., 2008), designed to manipulate reward

and risk predictions. In each trial, two cards were drawn consecutively from a randomly shuffled deck of 10. Before seeing the cards, players guessed whether the second card would be higher or lower than the first card. After both cards were revealed, participants answered whether they won or not for each trial. Monetary rewards were allocated for correct predictions, with a fixed amount for each win.

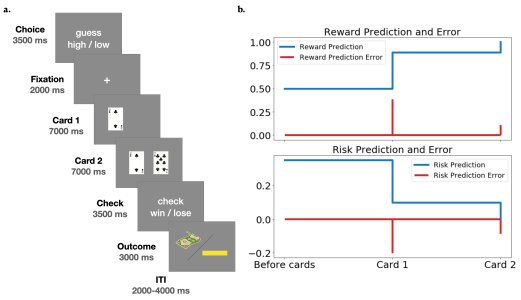

Figure 3: **a** Task design; **b** Reward and risk predictions and errors

Modeling The initial reward prediction (denoted as $P0$) was always 0.5 in our task design. After the first card is displayed, expected reward was updated accordingly (denoted as $P1$) and produced a reward prediction error, $P1 - P0$. Likewise, the reward prediction error at the onset of the second card presentation was calculated as the difference between the actual reward (denoted as $P2$) and the prediction after the first card ($P1$).

Risk prediction before card 1 was the expected variance of the reward prediction error, calculated as $E[(P1 - P0)^2]$. Risk prediction error after the first card presentation was the difference between the actual squared prediction error and the expected squared prediction error, expressed as $(P1 - P0)^2 - E[(P1 - P0)^2]$. Likewise, risk prediction before card 2 and risk prediction error after the second card were $E[(P2 - P1)^2]$ and $(P2 - P1)^2 - E[(P2 - P1)^2]$, respectively (Preuschoff et al., 2008).

Data Analysis We used SPM12 and the general linear model (GLM) to analyze the fMRI data, including task-related regressors including card presentations, feedback onsets, and button presses. Separate parametric modulators for reward prediction errors and risk prediction errors were included at the onsets of both cards.

Results

As shown in **Figure 4a**, consistent with previous research, we found the neural correlates of reward prediction errors in the striatum (MNI coordinates x = -13, y = 9, z = -5, Z = 3.42, p < .001 uncorrected). Furthermore, we found group differences between smokers and non-smokers. In smokers, the caudate exhibited significantly reduced activation (M = -0.06, SD = 0.26) compared to non-smokers (M = 0.31, SD = 0.34) (**Figure 4b**; t(11) = -2.19, p = .05).

We also identified the neural correlates of risk prediction error, in the dorsolateral prefrontal cortex (dlPFC) and the posterior parietal cortex (PPC) (**Figure 4c**; MNI coordinates x = 36, y = 14, z = 59, Z = 3.14; x = 43, y = -60, z = 55, Z = 3.91, p < .001 uncorrected). Notably, smokers exhibit increased PPC activation in response to risk prediction errors, contrary to our initial hypotheses, which warrants further investigation with a larger sample and nicotine rewards (**Figure 4d**; t(11) = 3.21, p < .05)

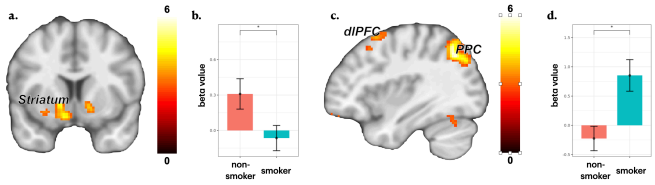

Figure 4: Overlays are presented at a threshold of p < .005 (uncorrected). The color scale indicates t values. Colored bars are group means, and black error bars are ± SEM.

Conclusion

This study contributes to our understanding of neurocognitive mechanisms involved in drug use, by demonstrating altered neural processing of risk and reward in smokers compared to non-smokers. The attenuated response of the striatum to monetary rewards in smokers supports the hypothesis of addiction-related reward system desensitization. Furthermore, the unexpected increase in PPC activation during risk prediction error processing in smokers may suggest altered risk encoding in nicotine addiction, necessitating further investigation to unravel the interplay between risk processing and addictive behaviors.

This study's initial findings, centered on monetary rewards, set the groundwork for forthcoming experiments with the novel MRI-compatible vaping device to directly assess responses to nicotine, promising to shed light on the drug-specific neural responses involved in risk and reward processing. These efforts could advance the understanding of the neural mechanics underlying nicotine use disorder, particularly the role of reward and risk processing.

Acknowledgments

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