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Monoamines and assessment of risks

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Over the past decade, neuroeconomics studies utilizing neurophysiology methods (fMRI or EEG) have flourished, revealing the neural basis of 'boundedly rational' or 'irrational' decision-making that violates normative theory. The next question is how modulatory neurotransmission is involved in these central processes. Here I focused on recent efforts to understand how central monoamine transmission is related to nonlinear probability weighting and loss aversion, central features of prospect theory, which is a leading alternative to normative theory for decision-making under risk. Circumstantial evidence suggests that dopamine tone might be related to distortion of subjective reward probability and noradrenaline and serotonin tone might influence aversive emotional reaction to potential loss.

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Introduction

Should I take an umbrella with me this morning? Should I buy life insurance? To answer these questions, and choose, we need to estimate the probability of the possible outcomes and magnitudes of possible gain and loss. For instance, we need to take into account the possible damage due to a severe health problem, the insurance premium, and the probability of being involved in a serious health problem.

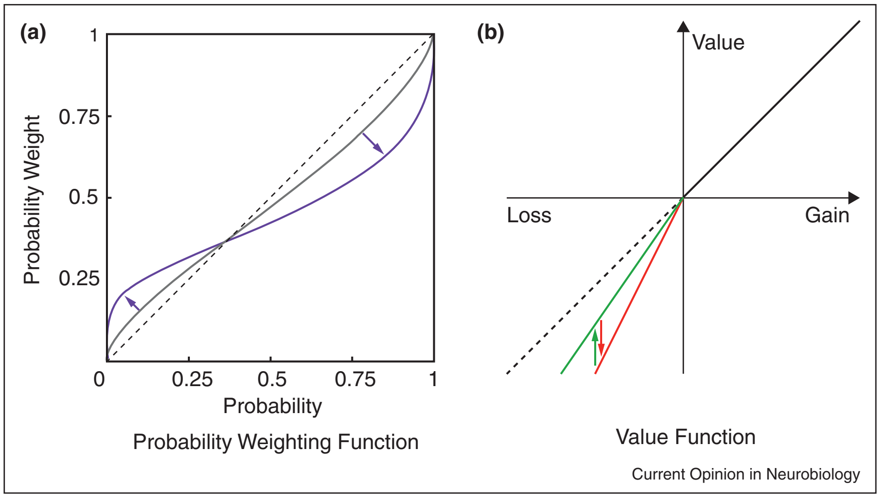
Normative theory in decision-making under risks assumes that people combine probabilities and valuation (utility) of possible outcomes in some way, most typically by taking the probability-weighted expectation over possible utilities. While this expected utility theory is the dominant model, experimental and field studies have repeatedly shown that decision-makers systematically violate it [1]. Over the past decade, a synthesis of economics and neuroscience called neuroeconomics utilizing neurophysiology methods (fMRI or EEG) has flourished, revealing the neural basis of 'boundedly rational' or 'irrational' decision-making that violates normative theory. Past neuroeconomics studies have demonstrated that, in addition to cortical regions such as the prefrontal cortex (PFC), subcortical emotion-related brain structures play a major role in 'irrational' decision-making [2]. The next question is how modulatory neurotransmission is involved in these central processes [3,4]. Here, I provide an overview of recent efforts to understand the neurochemical basis of 'irrational' decision-making under risks especially with regard to prospect theory.

Nonlinear probability weighting

One type of systematic departure from normative economic theory is that subjective weights on probabilities appear to be nonlinear. Decision-makers often overestimate low probabilities (e.g. playing lotteries) and underestimate high probabilities. A leading alternative to the expected utility theory is the prospect theory [5], a central feature of which is nonlinear probability weighting. Objective probabilities, p, are transformed nonlinearly into decision weights $w(p)$ by a weighting function (Figure 1a). Experimental studies suggest that the weighting function is regressive, asymmetric, and inverse S-shaped, crossing the diagonal from above at an inflection point (around 1/3) where $p = w(p)$. Although several functions have been proposed to express nonlinear probability weighting, the one-parameter function derived axiomatically by Prelec [6], $w(p) = \exp\{-(\ln(1/p))^{\alpha}\}$ with $0 \leq \alpha \leq 1$, is widely used because it typically fits as well as other functions with one or two parameters [7]. And because nonlinearity is fully captured by a single parameter, it is simple to correlate the degree of nonlinearity (α) across individuals with biological measures such as receptor density. This $w(p)$ function has an inverted-S shape with a fixed inflection point at $p = 1/e = 0.37$ (at this point the probability $1/e$ also receives decision weight $1/e$). In an inverse S-shaped nonlinear weighting function, low probabilities are overweighted and moderate to high probabilities are underweighted. The function neatly explains the typically observed pattern of risk-seeking for low probability gain and risk aversion toward high probability gain.

Paulus and Frank [8] investigated the neural substrates that are related to nonlinear probability transformation using fMRI with a certainty equivalent procedure. During this procedure, a gamble's certainty equivalent,

Figure 1



Hypothesized model showing the contribution of central monoamine tone to violation of normative decision theory. **(a)** DA tone might play a central role in distorting probability weighting function nonlinearly. Excessive DA tone might cause exaggerated overestimation of low probability and underestimation of moderate to high probabilities. A smaller value of α (closer to 0) means a more nonlinear inflected weighting function and a higher value (closer to 1) means a more linear weighting function. At $\alpha = 1$ the function is linear. Therefore, excessive DA tone is related to smaller α. **(b)** 5-HT and NE might contribute to shaping the slope of value function for loss. 5-HT might ease the slope of value function for loss (loss tolerance: green), and NE might intensify the slope (loss aversion: red). The value function is usually assumed to be a power function $v(x) = x^{\sigma}$, but we used common simplifying assumptions that σ is 1 for both value functions in gain and loss domain. The ratio (loss/gain) of the slope of linear functions was determined as λ.

the amount of sure payoff at which a player is indifferent between the sure payoff and the gamble, was determined. The authors found that differential anterior cingulate activation during estimation of high probabilities relative to low probabilities was positively correlated with Prelec's nonlinearity parameter α across subjects. Another fMRI study with risks of electric shocks found similar nonlinear response in brain regions including the caudate/subgenual anterior cingulate [9]. Tobler *et al.* [10] reported that the dorsolateral PFC was involved in overweighting low probabilities and underweighting high probabilities, and that the ventral frontal regions showed the opposite pattern. More recently, Hsu *et al.* [7] reported that the degree of nonlinearity in the neural response to anticipated reward in the striatum reflected the nonlinearity parameter as estimated behaviorally. The discrepancies regarding the loci of activation are thought to stem from differences in the task (probability range, context, etc.) and analysis of parameter estimation. However, it is reasonable to investigate the relationship between the dopamine (DA) system and nonlinear probability weighting, considering the fact that DA is linked to risk-seeking behavior [11] and excessive DA release was observed in pathological gambling in Parkinson's disease patients [12]. Trepel *et al.* [4] hypothesized in a thoughtful review that DA transmission in the striatum might be involved in shaping probability weighting. In order to test this speculation, we utilized *in vivo* molecular neuroimaging by positron emission tomography (PET) to examine central DA transmission and nonlinear probability weighting.

Certainty equivalents were determined outside the PET scanner, and we estimated probability weighting using the Prelec's one-parameter function [6].

The finding was that striatal D1 receptor binding measured by [^{11}C]SCH23390 PET (but not D2 receptor binding measured by [^{11}C]raclopride PET) was correlated with the nonlinearity parameter α of weighting function (Figure 2) [13•]. That is, people with lower striatal D1 receptor binding tend to show more pronounced overestimation of low probabilities and underestimation of high probabilities. [^{11}C]SCH23390 is a selective radioligand for D1 receptors, but it also has some affinity for serotonin (5-HT) 2A receptors. 5HT2A receptor density in the striatum is negligible compared to D1 receptor density. However, 5HT2A receptor density is never negligible in extrastriatal regions, and a recent *in vivo* study reported that approximately one-fourth of the cortical signal of [^{11}C]SCH23390 was due to binding to 5HT2A receptors [14]. The role of extrastriatal D1 receptors in nonlinear weighting needs to be tested with a more selective radioligand in future studies.

Although nonlinear probability weighting is a combination of risk-seeking (overestimation of low probability) and risk-aversion (underestimation of high probability), in