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Molecular neuroimaging of emotional decision-making

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ABSTRACT

With the dissemination of non-invasive human neuroimaging techniques such as fMRI and the advancement of cognitive science, neuroimaging studies focusing on emotions and social cognition have become established. Along with this advancement, behavioral economics taking emotional and social factors into account for economic decisions has been merged with neuroscientific studies, and this interdisciplinary approach is called neuroeconomics. Past neuroeconomics studies have demonstrated that subcortical emotion-related brain structures play an important role in "irrational" decision-making. The research field that investigates the role of central neurotransmitters in this process is worthy of further development. Here, we provide an overview of recent molecular neuroimaging studies to further the understanding of the neurochemical basis of "irrational" or emotional decision-making and the future direction, including clinical implications, of the field.

1. Introduction

With the dissemination of non-invasive human neuroimaging techniques such as fMRI and the advancement of cognitive science, neuroimaging studies regarding emotions, social cognition (Theory of Mind) and moral cognition became established from the late 1990s (Adolphs, 2002; Frith and Frith, 2003; Lamm et al., 2011; Moll et al., 2005; Takahashi et al., 2004). This general period was also an important time for the advancement of behavioral or experimental economics. In normative economics theory, decision makers are assumed to be "rational" and purely self-interested. However, we are not always rational, and sometimes show other regarding preference (e.g. charity, moral decision etc.). Laboratory and field evidence from behavioral economics has shown that decision-makers systematically depart from normative theory (Camerer and Loewenstein, 2004; Camerer and Fehr, 2006; Tversky and Kahneman, 1992). Because behavioral economics deals with the effects of emotional and social factors on economic decisions, not surprisingly, it has been merged with neuroscientific studies about emotions or social cognition, and this interdisciplinary approach is called neuroeconomics (Fehr and Camerer, 2007; Levallois et al., 2012). Since Daniel Kahneman and Vernon Smith were awarded the Nobel Prize in Economics for their contributions to the establishment of behavioral or experimental economics in 2002, neuroeconomics research has been accelerating (Fehr and Camerer, 2007; Glimcher et al., 2005; Sanfey et al., 2003; Takahashi et al., 2009). Past neuroeconomics studies have investigated the neural basis of "irrational" or "emotional" decision-making that violates normative theory, demonstrating 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 (Fehr and Camerer, 2007). The next question then is how modulatory neurotransmission is involved in these central processes (Rangel et al., 2008). Here, we provide an overview of recent efforts to understand the neurochemical basis of "emotional" decision-making under risks.

2. Emotional decision-making under risks

2.1. Neuroscientific studies of nonlinear probability weighting

Normative economics theory in decision-making under risks assumes that decision-makers combine probabilities and valuation (utility) of possible outcomes in some way, most typically by taking the probability-weighted expectation over possible utilities. However, our daily experiences and empirical evidence tell us that we systematically violate the normative theory. One type of systematic violation of normative economics theory is that people tend to weight objective probabilities nonlinearly. Decision-makers often overestimate low probabilities (e.g. playing lotteries) and

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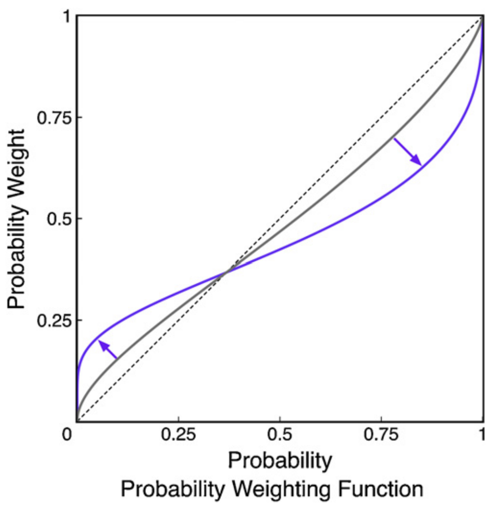

Fig. 1. Hypothesized model showing the contribution of central DA tone to nonlinear probability weighting. A smaller value of α (closer to 0) means a more nonlinear inflected weighting function and a higher value (closer to 1) means a more linear weighting function. At $\alpha = 1$ the function is linear. 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.

underestimate high probabilities. A leading alternative to normative theory (expected utility theory) is the prospect theory (Tversky and Kahneman, 1992). One of the important components of the prospect theory is nonlinear probability weighting, where objective probabilities, p, are transformed nonlinearly into decision weights $w(p)$ by a weighting function (Fig. 1).

From a psychological point of view, the overweighting of low-probability gains may reflect the hope of winning, and underweighting of high-probability gains may reflect the fear of losing a "near sure thing". In this sense, nonlinear probability weighting is called "emotional" decision-making. 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 (1998), $w(p) = \exp\{-(\ln(1/p))^{\alpha}\}$ with $0 < \alpha < 1$, is widely used. 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.

The neural correlates related to nonlinear probability transformation were investigated using fMRI with a certainty equivalent procedure (Paulus and Frank, 2006). During this procedure, a gamble's certainty equivalent, the amount of sure payoff at which a player is indifferent between the sure payoff and the gamble, was determined. It was reported 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 negative outcomes (electric shocks) found similar nonlinear response in brain regions including the caudate/subgenual anterior cingulate (Berns et al., 2008). Tobler et al. (2008) 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. However, more recently, the degree of nonlinearity in the striatal response to anticipated reward was shown to reflect the nonlinearity parameter as estimated behaviorally (Hsu et al., 2009). The discrepancies regarding the loci of activation are thought to stem from differences in the task (probability range, context, etc.) and parameter estimation method. However, elucidating the role of the dopamine (DA) system in nonlinear probability weighting would seem promising, considering the fact that DA is linked to risk-seeking behavior (Leyton et al., 2002) and excessive DA release was observed in pathological gambling in Parkinson's disease patients (Steeves et al., 2009). Trepel et al. (2005) hypothesized in an insightful review that DA transmission in the striatum might be involved in shaping probability weighting. Taking advantage of in vivo molecular neuroimaging, we investigated the relationship between central DA transmission and nonlinear probability weighting by positron emission tomography (PET).

Using a certainty equivalent procedure, we estimated probability weighting with Prelec's one-parameter function outside the PET scanner. There was positive correlation between striatal D1 receptor binding measured by [^{11}C]SCH23390 PET and the nonlinearity parameter α of weighting function (Fig. 2) (Takahashi et al., 2010a). No correlation was found between D2 receptor binding measured by [^{11}C]raclopride PET and nonlinearity parameter α. That is, subjects with lower striatal D1 receptor binding tend to show more pronounced overestimation of low probabilities and underestimation of high probabilities. Although [^{11}C]SCH23390 is a selective radioligand for D1 receptors, 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 it was reported that approximately one-fourth of the cortical signal of [^{11}C]SCH23390 was due to binding to 5HT2A receptors (Ekelund et al., 2007). Future studies with a more selective radioligand are recommended to test the role of extrastriatal (cortical) D1 receptors in nonlinear weighting.

Mis-estimation of probabilities, especially of low probabilities, might be related to some problematic behaviors in neuropsychiatric disorders. Clinical studies have reported the emergence of pathological gambling in Parkinson's disease patients taking DA agonist medication (Dagher and Robbins, 2009; Gallagher et al., 2007), and such patients showed exaggerated DA release in the ventral striatum measured by [^{11}C]raclopride PET during gambling (Steeves et al., 2009). Although pathological gambling is a heterogeneous disorder and cannot be solely attributed to mis-estimating probability, these observations can lead to the hypothesis that excessive DA transmission might cause distortion of subjective probability weights for gains (positive outcomes) (Fig. 1). On the basis of this hypothesis, circumstantial evidence can lead us to the conjecture of a vicious-cycle mechanism for developing drug/gambling addiction as follows: Reduced striatal D1 binding (which might in part be determined by genetic information) is linked to a risk-seeking trait. The risk-seeking trait is linked to enhanced activation and DA release in the striatum during risk-seeking behavior (Leyton et al., 2002; St Onge and Floresco, 2009). Chronic exposure to unusually high release of DA might lead to down-regulation of D1 receptors (Moore et al., 1998; Yasuno et al., 2007). Further decrease in D1 receptor binding would then lead to further risk-seeking. Reduced striatal D1 binding could therefore be a gateway to a vicious cycle, creating a predisposition to drug addiction and pathological gambling. In fact, a recent study suggested that reduced D1 receptor binding may be associated with an increased risk of relapse in drug addiction (Martinez et al., 2009).

However, nonlinear probability weighting is a combination of risk-seeking (overestimation of low probability) and risk-aversion (underestimation of high probability). In fact, a recent study reported that pathological gamblers demonstrated an overall shift toward risk, rather than excessive distortion of nonlinear probability weighting in decision-making under risks (Ligneul et al., 2012). Thus, the shape of weighting function, especially in the