

affect us—has relevance from the broadest levels of public policy to our most immediate interpersonal interactions. There is little doubt that the combination of Game Theory tasks, with their formal, detailed mathematical models, and the techniques of modern neuroscience offers fruitful opportunities for the study of social decision-making. This approach can both advance the predictive accuracy of theoretical models by constraining them based on behavioral performance and the underlying neurobiology, as well as further our knowledge of how people make decisions in a social context.

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REVIEW

Decision-Making Dysfunctions in Psychiatry—Altered Homeostatic Processing?

Martin P. Paulus

Decision-making consists of selecting an action from a set of available options. This results in an outcome that changes the state of the decision-maker. Therefore, decision-making is part of a homeostatic process. Individuals with psychiatric disorders show altered decision-making. They select options that are either non-optimal or nonhomeostatic. These dysfunctional patterns of decision-making in individuals with psychiatric disorders may fundamentally relate to problems with homeostatic regulation. These may manifest themselves in (i) how the length of time between decisions and their outcomes influences subsequent decision-making, (ii) how gain and loss feedback are integrated to determine the optimal decision, (iii) how individuals adapt their decision strategies to match the specific context, or (iv) how seemingly maladaptive responses result from an attempt to establish an unstable homeostatic balance.

Before considering what goes wrong with decision-making in psychiatric patients, it is useful to summarize some of the basic conceptualizations and findings regarding decision-making in general. Generically, decision-making is selecting an action from a set of available options, which may result in an outcome that

leads to a different psychological and physiological state of the decision-maker. Decision-making consists of a complex set of processes that are orchestrated in various brain systems to find an optimal outcome. Optimal decision-making requires a set of higher-order cognitive functions by which individuals regulate their

actions, thoughts, and emotions according to current psychological or physiological states, goals, and environmental conditions. In particular, individuals must be able to appraise the momentary status of their needs. Therefore, decision-making is part of a homeostatic process. Homeostasis can be defined as a dynamic physiological, cognitive, and affective steady state (*I*) that integrates multiple bottom-up sensory afferents and top-down cognitive and affective control processes, resulting in dynamic stability (i.e., resistance to internal and external perturbations). Decisions maintain or bring individuals into a new homeostatic state. Temporally, decision-making can be divided into three stages (2): (i) the assessment and formation of preferences among possible options, (ii) the selection and execution of an action (and the inhibition of alternative actions), and (iii) the experience or evaluation of an outcome. Initially, a value or utility is assigned to each available option (3), which determines the preference structure of the decision-making situation. The brain must evaluate not only what is occurring now but also what may or may not

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occur in the future (4). The current state of the individual, the time to experience an outcome, the degree to which the outcome is advantageous, and the likelihood that an outcome will be observed are important variables that determine this preference structure. The decision-maker incorporates previous outcome-related information, action-related information, and contextual or situational information to select an action. Each of these factors has to be considered in the context of the homeostatic balance of the individual to better understand decision-making dysfunctions in psychiatric-disorder populations.

Traditional approaches to understanding decision-making are based on economic theory (5) and mathematical choice psychology (6). Several investigators have augmented this approach to include affective or visceral factors (7–9), which profoundly affect the preference structure of available options. Individuals often underestimate, hardly remember, and have difficulty explaining the influence of these factors (8). Nevertheless, the effect of these factors is consistent with the emerging understanding of how the brain computes decisions as derived from systems-neuroscience approaches (10–12) and neurobiologically informed theories (13, 14). For example, the somatic-marker hypothesis (15) posits that options are tagged with positive and negative somatic states to guide individuals in making optimal choices (16). Thus, there is growing evidence that decision-making and homeostatic processing are inextricably linked (17) and that dysfunctions of decision-making cannot be understood without the reference to changes in homeostasis.

The inclusion of visceral factors (8) and affect heuristics (7) as part of decision-making has moved this process from a rational selection of options based on preference structures into the realm of homeostatic maintenance behaviors. One cannot separate decision-making from the current state of the individual (6) and/or understand decision-making dysfunctions in psychiatric patients without delineating how the disorder affects homeostasis. This view highlights an important but experimentally often underappreciated aspect of decision-making; that is, the interoceptive valuation of available options and the general role of interoceptive neural systems in decision-making. Interoception refers to the homeostatic sensing of the internal state of the body (1). This process combines the limbic sensory representation of subjective “feelings” within the anterior insula and the limbic motor representation of volitional agency within the anterior cingulate as the neuroanatomical basis for all human emotions (18). In this framework, affective/visceral processes are not simply occasional events but are ongoing and continuous, which is critical for the notion that visceral factors influence decision-making (8).

Two recent neuroimaging studies provide strong support for the homeostatic nature of decision-making. First, the preference structure in

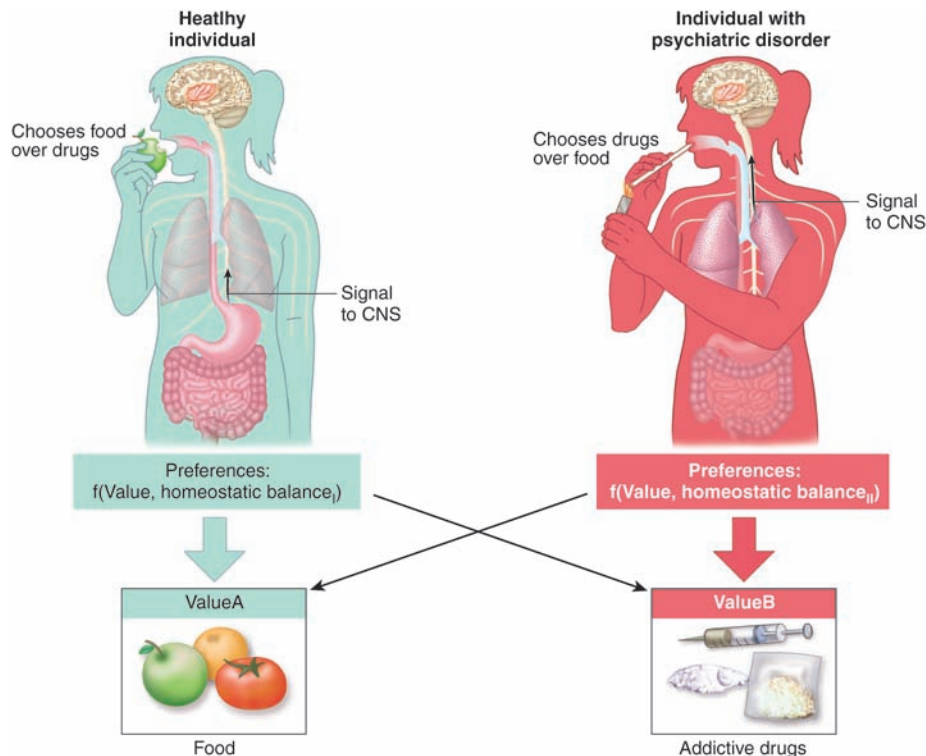


Fig. 1. Schematic illustration of two individuals who are in a different homeostatic balance in relation to each other (a person who is hungry and about to eat on the left and a person who is about to use methamphetamine on the right). It is presumed that interoceptive information transmitted via C-fibers and integrated in the anterior insular cortex plays a pivotal role in instantiating the current homeostatic balance. As a consequence, the value of an option (fruits on the left, methamphetamine on the right) is transformed via a complex function f , which takes into account probabilities and reward magnitudes but also the interoceptive state, into a different set of preferences based on the current status of the individual. The central hypothesis put forth here is that individuals with psychiatric disorders do not necessarily value the options differently in themselves but establish a different preference structure (represented by the thickness of the arrows pointing toward the options) based on their altered homeostatic balance.

repeated decision-making situations is fundamentally affected by the sampling of the available options. An individual who makes a decision needs to determine strategically whether to gather or to exploit option-related information. There is evidence that cortical and subcortical systems compete to moderate this conflict and balance the individual toward exploratory and exploitative action strategies (19). Second, a fundamental observation in classical choice psychology is that the value of an option is relative to a contextual reference point (the so-called “framing effect”). Limbic processing areas, which are also critically involved in homeostatic maintenance behaviors (such as the amygdala), are important for this effect, and top-down modulatory areas (such as the medial prefrontal cortex) can predict the susceptibility to the framing effect (20).

Homeostatic Processes in Psychiatric Disorders

Decision-making dysfunctions in individuals with psychiatric disorders are most likely due to several different alterations of component processes.

These alterations may be due to a primary processing dysfunction (for instance, an altered contribution of outcome magnitude, probability, or delay to computing the preference structure) or to a secondary dysfunction resulting from a primary dysregulation of the homeostatic balance. Although many investigators have argued the former, here I argue that decision-making dysfunctions in psychiatry are largely consequences of homeostatic dysregulation (Fig. 1). This approach is similar but not identical to the allostasis model (21)—the notion that a disease process is a result of the continued attempt to achieve stability—which has been proposed for addiction. Here, homeostasis is not a simple bottom-up determined physiological set point, but rather a bottom-up and top-down determined dynamical state. Therefore, the altered assessment and formation of preferences, the suboptimal selection and execution of an action, and the attenuated or exaggerated experience or evaluation of an outcome are hypothesized to be due to compensatory processes, albeit dysfunctional, aimed to bring the individual into a homeostasis. As a

consequence, the valuation of options changes the preference structure in different disorder populations. This homeostatic formulation of decision-making dysfunctions has important implications. First, it asserts that in many cases primary processing of the preference structure is intact, which is consistent with the finding that decision-making dysfunctions are often absent in asymptomatic individuals. Second, seemingly irrational decision-making may be adaptive and explicable within the context of attempting to maintain homeostasis. For example, increased risk-taking in substance-using individuals is often referred to as nonadaptive. However, studies of risk-sensitive foraging show that the degree of risk is a function of the homeostatic balance of the animal or individual (22, 23). For example, the frequency of visiting artificial flowers containing high-variance rewards is directly related to the degree to which foraging birds find themselves in a precarious energy balance. Thus, increased risk-taking may represent an adaptive mechanism of the drug-using individual. Third, this approach calls for experimental modulation of the homeostatic equilibrium during decision-making experiments with psychiatric populations to determine whether dysfunctional decision-making can be remedied.

Specific Examples of Dysfunctional Decision-Making in Psychiatric Populations

Substance-use disorders. Various deficits in decision-making have been reported in people with substance-use disorders (24). Specifically, these individuals do not appropriately take into account outcomes that occur sometime in the future versus those that occur now, and they therefore discount delayed rewards at significantly higher rates than do comparison subjects (25–27). Some have argued that this behavior occurs because of an underlying disposition of impulsivity rather than a substance-induced problem (28). This presumes a discounting model of impulsiveness (29) (impulsivity is a direct consequence of an increased attenuation of rewards as a function of delay), which is supported by the finding that the degree of temporal discounting is correlated with ratings of impulsivity (30). Thus, altered discounting may be a predisposing characteristic but not a consequence of years of substance use, because individuals reporting illicit drug use at a younger age tend to discount the value of future hypothetical rewards more steeply than do their peers (31).

Individuals with substance-related problems, irrespective of the substance used, perform poorly on the Iowa gambling task (IGT) (32–36), which measures the degree to which individuals select small immediate gains associated with long-term gains (advantageous option) over large immediate gains associated with long-term losses (disadvantageous option). These decision-making problems occur with and without concomitant working memory or executive-functioning problems, suggesting that decision-making is not simply a result of

impairments in executive functioning. Individuals with alcohol-related problems also perform worse on this task (37). Addicted individuals either show attenuated learning of selecting advantageous options or do not choose preferentially advantageous options over disadvantageous ones. It is not clear which behavioral processes or neural systems are responsible for this deficit. In one study, a κ -antagonist, buprenorphine, improved performance on the IGT in opiate-dependent subjects relative to methadone-maintained individuals, which points toward an opioid mechanism (38). Both predisposing characteristics and consequences of use (i.e., duration of abstinence, years of abuse, number of relapses, and times in treatment) predict these performance deficits (39). However, it is not clear whether these deficits are related to abnormal orbitofrontal functioning, a consequence of years of drug use, related to poorer outcomes, or even generalizable to other decision-making situations.

Substance users also exhibit altered decision-making on other tasks. Amphetamine abusers select suboptimally when presented with low-probability options and deliberate longer before making their choices (40). As opposed to healthy volunteers, outcome success does not modulate changes in win-stay/lose-shift strategies in methamphetamine-dependent individuals (41). Cocaine-dependent individuals show related but not identical abnormalities on different decision-making tasks (42). Taken together, there is substantial evidence for altered behavioral decision-making in substance-using individuals, irrespective of the behavioral probe that was used. These dysfunctions include altered processing of future outcomes, reduced ability to adapt to short- versus long-term gains, selection of suboptimal choices based on probability, and/or reduced ability to incorporate outcomes into altering the preference structure of available options. Nevertheless, it is not yet clear whether these dysfunctions are due to primary differences in establishing the preference structure of the available options or, alternatively, represent an attempt to generate a preference structure that is optimal for an individual with an altered homeostasis.

In decision-making neuroimaging studies, methamphetamine-dependent individuals show altered fronto-parietal activity during “hard” decisions, which may point to inefficient cortical processing (43). We found less decision-making-related activation in the orbitofrontal cortex (OFC), the dorsolateral prefrontal cortex, the anterior cingulate cortex (ACC), and the parietal cortex (41, 44) in these subjects. Cocaine users show greater activation during performance of the IGT in the right OFC but less activation in the right dorsolateral and left medial prefrontal cortex, which may reflect differences in the anticipation of reward and/or planning and working memory (45). These altered brain-activation patterns may be the consequence of an imbalance between an impulsive, amygdala system for sig-

naling pain or pleasure of immediate prospects and a reflective, prefrontal cortex system for signaling pain or pleasure of future prospects (46). Others have pointed out that an altered link between affect and decision is the key to understanding decision-making dysfunctions in substance-using individuals (47).

Are changes in decision-making behavior (and associated brain functions) a result of a preexisting characteristic, which may predispose subjects to use drugs and become dependent on them, or a consequence of years of use? Two complementary approaches have been used to examine this question. First, a high-risk population of individuals who have not yet developed substance dependence can be assessed to determine whether decision-making dysfunction predates the consequences of years of use. Second, acute effects of abused drugs on decision-making processes can be used to gauge whether acute administration of these substances has the potential to alter such processes.

Increased risk-related behaviors have been observed in “high-risk” populations (48). Individuals who use stimulants but are not dependent select risky responses more frequently than do comparison subjects, but the nondependent stimulant users also select risky choices less often after punishment. This risk-taking behavior correlates with measures of sensation-seeking and impulsivity but not with other personality measures, anxiety, or a tendency toward using alcohol (49). In these individuals, an increase in caudate nucleus activation during a simple decision-making paradigm aimed to determine the influence of outcome uncertainty is correlated with impulsivity (50). Thus, those at risk show altered decision-making and brain-activation patterns before developing substance dependence. Ultimately, however, the continued use of substances despite adverse consequences that lead to dependence may have additional effects on the brain and behavior.

Acute administrations of drugs with abuse potential have shown effects on decision-making behavior that are not completely consistent with those observed in substance-using individuals. The stimulant methylphenidate reduces risk-taking behavior in healthy volunteers (51), amphetamine [and in some (52) but not other (53) studies, alcohol] attenuates the delayed discounting curves (54), and acute administration of (\pm)3,4-methylenedioxymethamphetamine increases the degree to which the previous stimulus influences the selection of the current response (55). Neither the benzodiazepine diazepam (56) nor cannabinoids altered impulsive behavior (57), but these drugs have been shown to increase risky decision-making (58, 59). Taken together, the results from acute administration studies are only partially consistent with findings in substance-dependent individuals. Thus, decision-making dysfunctions and associated altered neural-

substrate processing could reflect a behavioral- and neural-systems biomarker to identify high-risk individuals. However, much more work is needed to better delineate the altered homeostatic processes that give rise to the behavioral- and neural-systems dysfunctions before one can begin to use this approach as an endophenotype for substance-use disorders.

Mood and anxiety disorders. Reward processing is part of assessing the value of options and occurs during the first stage of the decision-making process. Altered reward processing has been implicated in the basic pathophysiology of depression. Depressed patients show less activation in bilateral ventral striatal activation, which is believed to be involved in reward processing. This, in turn, has been shown to correlate with decreased interest and/or pleasure in the performance of activities (60), but not with levels of anxiety (61). Individuals with major depressive disorder (62) and bipolar disorder (63) also perform more poorly on the IGT. These findings have been replicated in a related but experimentally different decision-making task for manic and depressed patients (64). As compared to healthy subjects, bipolar individuals during a manic episode are more sensitive to feedback and switch more frequently during high-error rate conditions (65). Thus, those suffering from mood disorders present decision-making dysfunctions characterized by assigning different values to available options, probably because of reward-processing abnormalities in the ventral striatum.

Uncertainty is an important component of decision-making, and cognitive models of generalized anxiety disorder highlight the role of intolerance of uncertainty (66). Accordingly, decision-making by anxious subjects is influenced to a greater extent by ambiguous stimuli (67). Moreover, the sensitivity of high-trait anxious individuals to infrequent errors is associated with increased activation in the ACC and the medial prefrontal cortex (68). Finally, the intolerance of uncertainty is positively related to the degree of ACC activity (69). These results may be related to the sensitivity of anxious individuals to interoceptive sensations. These bodily sensations are associated with the assessment of available options as dangerous or threatening (70), a process that may be mediated by altered anterior insula functioning (71). In particular, risky options that are associated with uncertain and possible aversive outcomes may invoke more aversive anticipation of negative consequences, which could result in reduced numbers of risk-taking behaviors. Not surprisingly, increased activation in the anterior insular cortex is related to reduced risk-taking and increased neuroticism or harm avoidance (72, 73), which are temperamental characteristics of individuals prone to develop anxiety disorders. Therefore, increased sensitivity to possible aversive out-

comes during the assessment stage of decision-making because of hyperactivity in both the anterior cingulate and the anterior insular cortex may be a key feature of anxiety disorders. From a homeostatic perspective, anxious individuals find themselves in a state that is characterized by increased top-down modulation of bottom-up interoceptive afferents that heighten sensitivity to and bias interpretation toward aversive outcomes.

There is substantial evidence of orbitofrontal pathology in individuals with obsessive compulsive disorder (OCD) (74). Some (75), but not others (76), find impaired decision-making on the IGT in OCD patients to be associated with greater error-related activation in the rostral ACC, which is correlated with symptom severity (77). Although the behavior of OCD individuals is sensitive to changing contingencies, these people show decreased responsiveness in the right medial and lateral OFC, as well as in the right caudate nucleus during outcome processing (74). These individuals may experience an altered processing of reward history and valuation of options because of the relative disconnect between the dorsolateral, orbitofrontal, and anterior cingulate cortices with limbic regions (especially the amygdala) and with the basal ganglia (78).

Schizophrenia. Surprisingly, several studies have shown that individuals with schizophrenia perform normally on the IGT (79). Both first-episode and chronic schizophrenic patients take longer than controls to make decisions, and both groups are also impaired on a measure of risk adjustment. This impairment is more severe in the chronic patients than in first-episode patients (80). Decision-making dysfunctions in schizophrenia subjects may be due to an intermittent disruption of decision-strategies, which leads to choice patterns that can be both highly predictable and highly unpredictable (81–83). This pattern is particularly evident in deficit, but not in nondeficit, schizophrenia patients (84). Brain-imaging studies of decision-making show that the bilateral parietal cortex in schizophrenic patients is more involved in the assessment of uncertainty and less involved in success-related processing (85). Overall, evidence for experimental decision-making dysfunctions in schizophrenia is more mixed than that for other disorders. This may be due to inadequate experimental assessment or to the heterogeneity of the population characterized as being schizophrenic. The experimental findings are clearly at odds with a growing literature on the reduced capacity to make decisions using questionnaire approaches (86). Future investigations will need to develop experimental paradigms that can better probe the components of impaired decision-making capacity.

Future Directions

Decision-making is a complex process that engages numerous neural systems to optimally

select an option. There is clear evidence of dysfunctional decision-making in psychiatric populations. However, many of the studies have so far used a limited number of behavioral tasks, which are complex and probe multiple decision-related processes. Several approaches will be necessary to gain a deeper and disease-relevant understanding of such dysfunctions. First, instead of one decision-making task, a set of behavioral paradigms will need to be developed to probe different aspects of decision-making and to provide converging validity of some of the proposed decision-making constructs. Second, clinical populations need to be better defined, sampled across sites, and examined using multi-level descriptions to better delineate the specificity of the dysfunction, relation to the clinical syndrome, and degree to which decision-making dysfunctions are preexisting characteristics or consequences of the disorder or treatment. Third, decision-making will need to be examined within the homeostatic context of the individual. It is not yet clear whether dysfunctional decision-making in individuals with psychiatric disorders is a consequence of altered assessment, execution, or evaluation stages of decision-making, or whether it is adequate decision-making in the context of an altered homeostatic balance. Fourth, neuroimaging laboratories will need to collaborate with clinical researchers to better delineate the neural substrates involved in disorder-related decision-making dysfunctions. Fifth, systems and theoretical neuroscientists will need to work with clinical researchers to develop novel computational hypotheses and examine their relevance in making meaningful predictions. For example, a specific aberrant computational process has been suggested to underlie learning and discounting dysfunctions in a recent addiction model (87). However, this model needs to be tested in various populations of substance-using individuals and refined to make clinically useful predictions. Nevertheless, the experimental study of decision-making provides an opportunity for meaningful interdisciplinary approaches that can help to reveal how brain processes go awry in individuals with psychiatric disorders.

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REVIEW

Decision Theory: What “Should” the Nervous System Do?

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The purpose of our nervous system is to allow us to successfully interact with our environment. This normative idea is formalized by decision theory that defines which choices would be most beneficial. We live in an uncertain world, and each decision may have many possible outcomes; choosing the best decision is thus complicated. Bayesian decision theory formalizes these problems in the presence of uncertainty and often provides compact models that predict observed behavior. With its elegant formalization of the problems faced by the nervous system, it promises to become a major inspiration for studies in neuroscience.

Evolutionary psychology has found that many human behaviors can be well understood assuming adaptation of psychology to the past social environment of humans

[e.g., (1)]. Similarly, ethology, the study of animal behavior [e.g., (2)], has shown that many of the properties of the nervous system and the bodies of animals are remarkably well adapted to their eco-

logical niche. These disciplines have shown that, over the course of evolution, animals are often endowed with solutions to common problems that are close to optimal [(1), but see (3)]. Many studies in neuroscience analyze low-level processes. For example, researchers study how animals control their limbs, how they infer events in the world, and how they choose one of several possible rewards. Such processes may have remained conserved for very long periods of time. We can thus expect the solution used by the nervous system for such problems to be close to optimal.

Normative models formalize how the idea of adaptation predicts properties of the nervous system. These models assume that a process has

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