REVIEW

Neurobiology of Decision Making: A Selective Review from a Neurocognitive and Clinical Perspective

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We present a temporal map of key processes that occur during decision making, which consists of three stages: 1) formation of preferences among options, 2) selection and execution of an action, and 3) experience or evaluation of an outcome. This framework can be used to integrate findings of traditional choice psychology, neuropsychology, brain lesion studies, and functional neuroimaging. Decision making is distributed across various brain centers, which are differentially active across these stages of decision making. This approach can be used to follow developmental trajectories of the different stages of decision making and to identify unique deficits associated with distinct psychiatric disorders.

Key Words: Anticipation, anxiety, choice selection, development, motivation, schizophrenia

Decision making refers to the process of forming preferences, selecting and executing actions, and evaluating outcomes. Here we define decision making as encompassing a wide range of behaviors having in common the basic generic structure of input–process–output–feedback. *Input* refers to the presentation of separate stimuli, each predicting a measurable rewarding or aversive outcome; *process* refers to the appraisal of these stimuli and formation of preference; *output* refers to the action carried out in response to the selected stimulus. *Feedback* is the experience and evaluation of the outcome that follows the action perpetuated on the selected stimulus. It is used for learning about the values of the stimuli. The goal of this work is to provide a framework, or generic template, along which the various psychologic and neural processes underlying decision making can be examined. We show how findings from various fields of research can be integrated into this framework.

Decision making has received considerable attention from psychologists and economists (Loewenstein et al 2001; Slovic et al 2002; Tversky and Kahneman 1975), neurologists and neuropsychologists (Bechara 2004a; Clark et al., 2003; Damasio et al 1996; Lhermitte et al 1986; Shallice and Burgess 1991), psychiatrists (Ernst et al 2004; Paulus et al 2003; Rogers et al 1999), and neuroscientists (Clark et al 2004; Glimcher 2002; Gold and Shadlen 2001; Platt and Glimcher 1999). Initial forays in the clinical realm of decision making came from the systematic examinations of patients with well-defined brain lesions (for review, see Bechara 2004a; Damasio et al 1996). This unique body of work has not only identified brain regions essential for adaptive decision making but has also provided conceptual models of critical aspects of decision making (e.g., the somatic marker theory, Damasio et al 1996). Most important, lesion studies have supplied experimental paradigms (e.g., development of the Gambling Task, Bechara et al 1994), as well as hypotheses to the relatively new field of functional neuroimaging research. Finally, the integration of psychoeconomics that examines rules guiding choices (Kahneman 1991) and neuroscience that establishes neural models of reward-modulated behavior (Schultz 2002; Schultz et al 1997) has pushed research on decision making to a new level of scrutiny.

This review focuses on biological processes, keeping simple and constant the input component, that is, the presentation, in a neutral environment, of external cues defined by distinct physical features (e.g., volume, color, shape) that predict distinct measurable outcomes (e.g., dollar amounts). A large psychologic and social literature has examined the influence of context–environment on decision making, which operates at multiple levels, sensory, cognitive, affective, and social. These influences could also be tracked along the various stages of decision making.

The model presented here is anchored on a neural systems framework primarily based on functional neuroanatomy. Although we do not address directly the neurochemical substrates of the various processes involved in decision making, several neurotransmitter systems have been hypothesized to critically influence decision making. For example, dopamine is implicated in reward systems (Di Chiara et al 2004; Wise 1996) and associative learning (Schultz 2002), serotonin in impulsivity and emotion (Hollander and Rosen 2000), acetylcholine in memory (Gold 2003), and noradrenaline in attention and arousal (Berridge and Waterhouse 2003; Robbins 1997). Interaction among these neurochemical modulators and the translation of their actions at the molecular level (e.g., Nestler 2001) is an active area of research that is beyond the scope of this review.

Psychological Modulators and Neural Substrates of the Three Stages of Decision Making

Decision making depends on three temporally and partially functionally distinct sets of processes: 1) the assessment and formation of preferences among possible options, 2) the selection and execution of an action, and 3) the experience or evaluation of an outcome (Figure 1). The analysis of these stages helps to distinguish which aspect of decision making may be differentially affected in various psychiatric disorders. Although we address cognitive processes specific to each of these stages, a number of psychologic constructs, such as attention, working memory, motivation, anticipation, and impulsivity, can be involved in various degrees throughout these stages.

Stage 1. Forming Preferences

Human and animal studies have strived to identify factors and rules that govern choices. Identification of these rules have led

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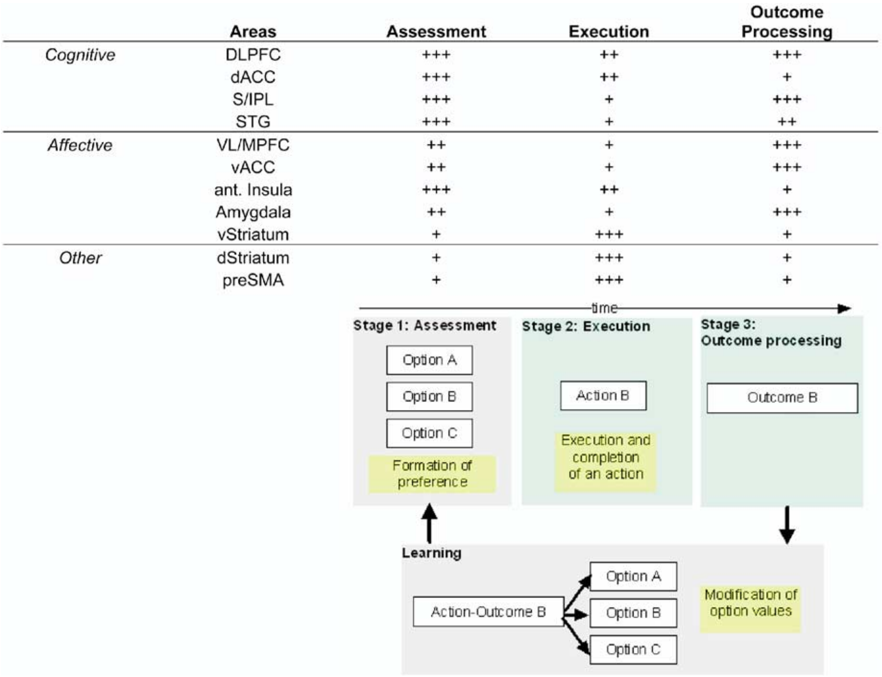

	Areas	Assessment	Execution	Outcome Processing
Cognitive	DLPFC	+++	++	+++
	dACC	+++	++	+
	S/IPL	+++	+	+++
	STG	+++	+	++
Affective	VL/MPFC	++	+	+++
	vACC	++	+	+++
	ant. Insula	+++	++	+
	Amygdala	++	+	+++
	vStriatum	+	+++	+
Other	dStriatum	+	+++	+
	preSMA	+	+++	+

Figure 1. Hypothetical model of the basic processes and brain areas involved in the different stages of decision making. Decision making is divided into three stages: 1) the assessment and formation of preferences among possible options, 2) the selection and execution of an action, and 3) the experience or evaluation of an outcome. Table of neural circuitry (top): We propose that a distributed network of both cognitive and affective brain areas process these stages differentially. Below is a possible decision-making scenario. In this scenario, the hypothesized neural substrates are involved in the three stages of decision making to varying degrees. The degree of their involvement is reflected by the number of + signs. Conceivably, certain types of decision making require relatively less emotional involvement, whereas others require more cognitive involvement. The balance between the engagements of these neural substrates is hypothesized to be altered in psychiatric disorders. Taken together, we predict that patients with different psychiatric disorders will exhibit stage-dependent degrees of decision-making dysfunctions. Decision-making schema (bottom): Stage 1 shows three available options (A, B, and C) among which one option must be selected. Stage 2 is the stage during which the selected option (option B) is being executed. Stage 3 is the stage during which the outcome of the action is being experienced and processed (outcome B). The fourth box represents processes involved in learning, which occurs when the action–outcome sequence is completed. Learning modifies the value associated with each option of stage 1, the next time these options are presented. Knowing outcome B not only influences the value of option B, but also has a profound influence on the nonselected options. Ant Insula, anterior insula; dACC, dorsal anterior cingulate cortex; DLPFC, dorsolateral prefrontal cortex; dStriatum, dorsal striatum; preSMA, presupplementary motor area; S/IPL, superior/intraparietal lobule; STG, superior temporal gyrus; vACC, ventral anterior cingulate; VL/MPFC, ventral lateral/medial prefrontal cortex; vStriatum, ventral striatum.

some to formalize mathematical models of choice behavior. Most prevalent psychologic theories and mathematical models applied to the formation of choices include learning theories with classical conditioning (Pavlov 2005), operant conditioning (Skinner 1953), and a mathematical rendition of classical conditioning (Rescorla and Wagner 1972); Matching law theory, which posits that over time, the pattern of choices is a direct function of the probability of outcomes (Hernstein 1961); game theory, which describes choice behavior in the context of several decision makers, setting a "competitive" or "cooperative" environment (Bernoulli 1954; Lewontin 1961; Nash 1953); and prospect theory, which describes decisions under uncertainty (Kahneman and Tversky 1979).

From a neural systems perspective, the formation of values involves both "cognitive" and "emotional" brain circuits. A host of factors influence the development of preferences, including physical features of the options; characteristics of outcomes predicted by the options, such as valence (positive, negative), salience (intensity, magnitude), probability (degree of certainty), and timing (delay); relative values and number of options to select from; previous experience with these options and their outcomes; and external and internal context in which the decisions are made (e.g., social, affective state). Each of these factors may be coded by specific neural circuits and modulated by distinct neurochemical systems. Some of these functional circuits are described later.

Coding the probability or certainty of outcomes predicted by available options is specific to the process of forming preferences. The parietal cortex has been shown to be involved in computation (Dehaene et al 1999) and in assessment of probability (Ernst et al 2004; Platt and Glimcher 1999; Shadlen and Newsome 2001). The anterior cingulate cortex (ACC) has been associated with processes of uncertainty (Critchley et al 2001; Elliott et al 1999), perhaps by integrating successes and errors over time (Carter et al 1999).

Editing options (e.g., ignoring least attractive options, pairing options of similar values, etc.) serves to simplify choices (Tversky and Kahneman 1981). These operations can be mostly automatic or can involve conscious deliberative effort. The right dorsolateral and orbitofrontal cortex have been suggested to underlie these processes (Cummings 1995; Dias et al 1997). Reasoning, part of deliberation, has been proposed to be carried out by left middle and inferior frontal gyri (Goel et al 1998).

Affective appraisal of options also involves both automatic and conscious processes. Theories of emotions (Cannon 1987; Schachter and Singer 1962) have helped to shape cognitive neuroscience approaches to decision making. Particularly, the James–Lange theory of emotion (Cannon 1987), which underlies the role of physiologic and cognitive responses in the formation of emotion, has paved the way to the contemporary somatic marker theory (Bechara 2004a; Damasio et al 1996).

The affective attribute of an option is expected to recruit limbic regions, such as amygdala, insula, orbitofrontal cortex, and anterior cingulate. An intermediate step in this operation is the production of "somatic markers," which signals the intensity (salience) of the valence (negative or positive value) of stimuli experienced by individuals. Although the relative contribution of the somatic markers in decision making continues to be debated (Heims et al 2004; Hornak et al 2003; Maia and McClelland 2004), it remains a central aspect of emotional tagging of stimuli. Structures involved in the somatic marker model comprise the orbitofrontal cortex, amygdala, and ventral striatum. This model, described later, also applies to the assessment of outcome stimuli in stage 3.

The amygdala belongs to a network of structures, which includes the insula, anterior cingulate gyrus, and medial prefrontal cortex. This network helps to identify the emotional significance of a stimulus, generate an affective response, and regulate the affective state (Phillips et al 2003). The insula has afferent and efferent connections to medial and orbital prefrontal cortex, ACC, and several nuclei of the amygdala (Augustine 1996). Together with the amygdala, the insula underlies the generation of somatic markers (autonomic changes such as skin conductance, blood pressure, heart rate), or the activation of the representations of somatic markers (Bechara 2004a). These somatic markers, in turn, send feedback signals to cortical structures, particularly to insula–somatosensory and orbitofrontal cortices, and perhaps ACC. The insular cortex appears to be important for subjective feeling states and interoceptive awareness (Craig 2002; Critchley et al 2004). Finally, the emotional intensity (salience) carried by stimuli has been associated with enhanced activation of ventral striatum, particularly nucleus accumbens (Zink et al 2004).

Stage 2. Execution of Action(s)

The goal of this stage is to initiate, perform, and complete an action according to the preferences established during the first stage. Cognitively, competing actions have to be suppressed or inhibited, and sequences of actions have to be implemented; appropriate subgoals have to be monitored; correction of errors has to take place; and timing of actions has to be planned. The general model of control of actions formulated by Shallice et al (1989) could be best articulated at this juncture, although it refers more specifically to the planning and execution of complex multitasks.

This stage engages the neural systems supporting initiation, monitoring, and completion of actions. The ACC has been consistently found to be recruited in error monitoring (Carter et al 1998; Holroyd and Coles 2002) and in conflict detection (Van Veen et al 2004). The lateral prefrontal cortex may also contribute to the monitoring of action through its interaction with the ACC during error monitoring (Mathalon et al 2003) and in guiding compensatory actions (Gehring and Knight 2000).

Motivation is functionally defined as the determinant of the direction and the energy of an action. The nucleus accumbens, a component of the ventral striatum, has been shown to modulate the motivational aspects of an action (Ernst et al 2002, 2004; Knutson et al 2001; Mogenson and Yang 1991; Salamone and Correa 2002). The amygdala and the sublenticular extended amygdala of the basal forebrain (Breiter and Rosen 1999), and ventrolateral prefrontal cortex (Taylor et al 2004) may also contribute to this process. Thus far, it has been difficult to separate motivation from arousal. For example, larger activation in premotor cortex with greater incentives (Roesch and Olson 2004) could reflect enhanced arousal rather than enhanced motivation.

A number of abnormalities, including prematurely initiated actions (e.g., impulsivity), incomplete actions (e.g., behavioral fragmentation), or delayed and insufficiently motivated actions (e.g., psychomotor retardation) can be observed during this stage. The stage 2 multiprocesses, that is, action selection, online monitoring of performance accuracy, motivation to act, and anticipation of outcome, interact in a manner not yet fully understood. Thus, not surprisingly, this complex equilibrium is often perturbed in psychiatric disorders.

Stage 3. Experiencing the Outcome

The outcome of the selected action is experienced (or consumed) at this stage. Like during Stage 1, values are attributed to the outcome experience. Thus, assessment processes such as coding physical and emotional characteristics of stimuli occur in both stage 1 and stage 3. The somatic marker theory (Damasio 1996) is also operative during this last step. Stage 1 and stage 3, however, differ critically in their ultimate function: the function of stage 1 is to form preference based on *expected* values, and that of stage 3 is to consume and learn the *actual* values of option stimuli for the supreme goal of adaptive behavior.

A number of factors that are specific to stage 3 influence the formation of actual values. For example, experienced outcome strongly depends on counterfactual possibilities, that is, what might have happened if a different choice had been made in stage 1 (Shepperd and Mcnulty 2002; Zeelenberg et al 1996). Regret and disappointment profoundly influence future behavior (Zeelenberg 1998). The degree of surprise associated with the outcome experience is also tantamount to the computation of the actual value. Surprise can emerge from earlier than expected time of occurrence or from the nature of the expected outcome. By definition, surprise infers a difference between actual value and expected value.

In daily experience, outcome or actual values, coded during stage 3, often differ from the option or expected values, coded during stage 1 (Kahneman and Snell 1990). A number of factors may contribute to the difference between expected and actual values, such as the contrast between imagined and experienced event (Mellers and McGraw 2001) or the adjustment of the expected value as a function of the time interval between the two stages (Ainslie 1992).

This value difference is critical to learning processes. Electrophysiologic work in monkeys has demonstrated that dopamine neurons code the value difference between the expected and actual value of outcomes, and this value difference serves as a learning signal that permits behavior to become adaptive (Schultz 2002). The larger the difference, the more unexpected the outcome and the greater the learning signal. This prediction is supported by behavioral (Coughlan and Connolly 2001; Mellers et al 1997), neuroimaging (Berns et al 2001), and neurophysiologic studies (Schultz 1998), all showing greater emotional and neural impact with unexpected outcome than with expected outcomes.

Processing the difference between the expected and observed outcomes is central to the temporal difference model. Functional neuroimaging experiments have shown that ventral striatum (Pagnoni et al 2002) and orbitofrontal cortex (O'Doherty et al

2003b) are involved in generating this difference signal in humans (McClure et al 2003).

In addition to the already mentioned regions implicated in emotion processing (amygdala, nucleus accumbens, orbitofrontal cortex, and insula), the medial prefrontal cortex, particularly within Brodmann area 10, seems to be uniquely involved in feedback processes (Knutson et al 2003). The ventral medial prefrontal cortex, including the orbitofrontal cortex, receives sensory inputs from several modalities and provides the major cortical output to visceromotor structures of the hypothalamus and brainstem (Ongur and Price 2000). The medial prefrontal cortex has been implicated in assessment of pleasurability (Mitterschiffthaler et al 2003), tracking of rewarding outcomes (Knutson et al 2003), and formation of hedonic associations (Passingham et al 2000).

Finally, associative learning is triggered when events occur repeatedly in close temporal proximity. Specifically, if feedback occurs close enough to stimulus presentation or to the action, associative learning is initiated. The amygdala and the nucleus accumbens have been critically involved in this process (Baxter and Murray 2002; Cardinal et al 2002; Gabriel et al 2003; Salamone and Correa 2002; Schoenbaum and Setlow 2003).

In conclusion, psychologic and neural correlates of decision making can be anchored on a cognitive–affective neuroscience framework that will permit a more systematic approach to developmental milestones of decision making and perturbations of motivated behaviors in distinct psychiatric disorders.

Clinical Applications

Neurodevelopment

The cognitive and affective components that contribute to decision making reviewed in the previous section are all subject to developmental changes. These developmental changes occur at a biological and environmental level. There is a large neuropsychologic literature addressing age-related changes in cognitive, affective, and social domains (Spear 2000), although few studies have focused directly on decision making (Byrnes 2002). Most work has focused on economic perspectives of decision making in adults, but none of this work has been conducted in children. Normative neurodevelopmental investigations in humans are beginning to emerge, particularly since the advent of noninvasive functional neuroimaging. At present, however, only three neuroimaging studies address specifically decision-making processes in young people (Bjork et al 2004; Ernst et al 2005; May et al 2004). These studies have explored in adolescents the neural substrates of motivation for action (stage 2), and response to feedback (stage 3). From an ontogenic perspective, decision making seems to be first under the primacy of emotional controls and then evolves toward a progressively larger involvement of cognitive function, to bring the decision-making process to a mature level of optimizing goal achievement.

This evolving balance between affective and cognitive components of decision making can be conceptualized along the framework of two putative parallel decision-making systems, a fast, mostly automatic system and a slow, deliberate system described by Denes-Raj and Epstein (1994). The fast, more rudimentary, system is present early in life, and the second system develops progressively with age, and, at times, competes with the older system. In addition, brain lesion studies suggest that the initial formation of emotional tags attached to stimuli depend on the integrity of the amygdala and that the representation of the affective tags are accessed through the ventromedial frontal cortex (for review, see Bechara 2004b). Early dysfunction in these regions and associated networks could compromise significantly the development of adaptive decision making.

Another formulation, particularly applicable to adolescence, relates to the balance between reward seeking (approach behavior) and harm avoidance (avoidance behavior). Both appetitive and aversive stimuli are found to be processed by the same structures, including amygdala, ventral striatum, and orbitofrontal cortex, suggesting that these structures can carry opposite functions, based on different modulatory controls affecting neuronal output. This imbalance may be most influential on the incentive value of stimuli presented in stage 1 and the experience of outcome in stage 3 of decision making. Such hypothesis can be tested behaviorally and in the functional magnetic resonance imaging environment using appropriate decision-making paradigms.

Adolescence is a transition period that is marked by changes in behavior reflecting a distinct pattern of decision making (Byrnes 2002; Chambers and Potenza 2003; Larson et al 2002; Spear 2000). This pattern of decision making underlies risk-taking and novelty-seeking behaviors, which confer a high level of morbidity and mortality to adolescents (Grunbaum et al 2004). The heightened fascination for novelty during this period may represent an evolutionary adaptive motivational force that facilitates learning and the move toward independence. It is accompanied by a sense of invulnerability, which has not yet been examined from a neuroscience perspective. Risk taking implies the prominence of sensation seeking over harm avoidance, suggesting a distinct balance within the neural systems involved in these processes. In support of this model, adolescents have been found to be more sensitive to the rewarding effects of illicit substances, as evidence by high incidence rates of substance abuse, and to be less aware of negative consequences of events (Clayton 1992). The balance between approach and avoidance may be translated differently at the various stages of decision making delineated in this review (Bjork et al 2004; Ernst et al 2005).

Substance Use Disorder

Several altered decision-making patterns have been observed in substance-dependent subjects. First, these individuals show a propensity to select actions associated with large short-term gains and long-term losses preferentially to those associated with small short-term gains and long-term gains (Bechara and Damasio 2002; Grant et al 2000). Second, they are more likely to select risky options (Lane and Cherek 2000) and show an altered temporal horizon of risks and benefits (i.e., a steeper temporal discounting function; Madden et al 1999; Petry et al 1998). Third, these subjects do not value appropriately the probability and magnitude of potential outcomes (Rogers et al 1999; Rogers and Robbins 2001). Fourth, they generate perseverative responses when making a prediction and select actions that are more stimulus bound and less dependent on changes in the frequency of prediction errors (Paulus et al 2002, 2003).

It is unclear whether these altered decision-making patterns reflect dysfunction in a single or several processes that contribute to decision making (Monterosso et al 2001). Several investigators have shown an increased activation of the inferior medial and lateral prefrontal cortex in substance-dependent subjects in response to cues that elicit craving responses (Breiter et al 1997; Childress et al 1999; Grant et al 1996; Wang et al 1999). This altered activation pattern could reflect an increased valuation of the drug-related stimuli and, therefore, fundamentally affect stage 1 (the formation of preferences) of the decision-making process. Specifically, an option, which is associated with sensitized stimuli, may have acquired an overwhelming weight, which results in an altered decision-making pattern.

Several neuroimaging studies have revealed dysfunctions of the ventromedial, ventrolateral, and dorsolateral prefrontal cortex in stimulant-dependent subjects (London et al 2000; Paulus et al 2002; Volkow and Fowler 2000). Based on their pattern of decision making just described, stimulant-dependent individuals are expected to show a lack of flexible association of outcomes with advantageous actions (attenuated trend detection). The inferior prefrontal cortex, including orbitofrontal cortex, has been shown to play an essential role in this process. This is consistent with studies that found altered inferior prefrontal activation at baseline and during decision making in stimulant-dependent subjects (Bolla et al 2003; Volkow and Fowler 2000). Dysfunction of the anterior insula may also be involved in substance abuse. Paulus et al (2003) reported a close correlation between risky responses, harm avoidance, and insula activation, a finding that is consistent with the insula's role in punishment (Critchley et al 2001; O'Doherty et al 2003a). Substance-dependent subjects may show attenuated insula activation, which is associated with increased risk taking. It is unclear, however, whether this process occurs at a particular stage of decision making or whether attenuated processing of aversive values occurs throughout the decision-making process.

A key question is whether decision-making dysfunctions and their underlying neural substrates are a preexisting condition and contribute to the initiation of drug use or are a consequence of the repeated use of these drugs. Altered processing of the value of available options during stage 1, which affects prediction of outcome, may represent preexisting deficits. Alternatively, deficient processing of the outcome value, which can lead to poorer acquisition of advantageous over disadvantageous actions, may result from altered dopaminergic signaling secondary to a residual error signal as a consequence of substance use (Redish 2004). Some investigators have suggested that the development of drug dependence may require the presence of both altered drug initiating and drug maintaining behaviors (Kendler 2001). Thus, perturbed decision making in drug-dependent individuals may reflect both a preexisting alteration of assessment of options and a substance-related attenuation of outcome processing.

Schizophrenia

Experimental evidence supports the general hypothesis that schizophrenia patients may exhibit dysfunctions during formation of preference, execution, and outcome evaluation. Kraepelin (Kraepelin and Robertson 1919) conceptualized schizophrenia as a disorder of volition rather than one of intellect, which refers to the ability to make and carry out conscious decisions (Zec 1995) and to the capacity for motivation to act (stage 2). A large body of literature evidences cognitive deficits in schizophrenia affecting attention and executive functioning (i.e., working memory and planning). We limit our discussion to the findings directly applicable to the decision-making model.

A number of data relevant to decision-making processes in schizophrenia concern the stage 1 of formation of preference. These patients seem to request less information before reaching a decision as evidenced in a probability inference task (Garety et al 1991), although they take longer to make their decisions (Hutton et al 2002). Aspects of learning, that is, use of previous outcome experiences to make appropriate decisions, seem to be impaired. Schizophrenia patients are more ready to change their estimates of the likelihood of an event when confronted with potentially disconfirmatory information (Garety et al 1991), and they show deficits on measures of risk adjustment (Hutton et al 2002). They also fail to show a priming effect, that is, facilitation of performance based on previous exposure to stimulus (Passerieux et al 1997; Vinogradov et al 1992).

Other cognitive processes seem to contribute to poor decision making, for example, inadequate discrimination of old items from new, insufficient distinction between self-generated items and externally generated items, and poor recognition of the modality in which an event was presented (Brebion et al 1998). These various abnormalities may point toward a mixture of assessment and executive dysfunctions. Several investigators have proposed a relationship between semantic processing and decision making. Schizophrenia patients may show an impairment of action selection because they do not benefit from the automatic retrieval of processing information about the options available (Baving et al 2001).

Thus far, no neuroimaging studies have investigated the different stages of decision making in this population. Neuropsychologic and clinical observations suggest the deficient integration of assessment and action selection processes (stage 1 and stage 2). Accordingly, an inadequate formation of values of options would result in a poorly formed internal model to guide the selection of action in a decision-making situation. Studies using an experimental probe that can manipulate each component process could assess each process separately and isolate the one(s) most significantly disrupted in schizophrenia patients.

As with substance dependence, schizophrenia has been associated with dopaminergic dysfunction, perhaps secondary to glutamatergic deficits (Laruelle et al 2003). In view of the central role of dopamine in learning and reward processes, its contribution to behavioral symptoms and neuroimaging findings in schizophrenia needs to be further examined. In the same vein, the influence of antipsychotic medications on decision making needs further evaluation (Kapur, 2004).

Anxiety Disorders

To our knowledge, characteristics of decision making in anxiety disorders have not yet been systematically examined; however, a number of investigations report on cognitive substrates of anxiety, the most widespread substrate being attentional bias toward threat (Mogg and Bradley 1999). An obvious difficulty in the study of anxiety is the heterogeneity of disorders placed under the umbrella of anxiety disorders. Nonetheless, several theoretical models of generic anxiety have been proposed that focus on the interaction between cognition, affect, physiology, and behavior (for review, Wilken et al 2000).

The association of stimuli with adverse affective experiences is a critical determinant of hyperarousal (Dowden and Allen 1997) and anxious apprehension (Nitschke et al 1999), which occur across anxiety disorders. Accordingly, the neural substrates engaged in the processing of aversive stimuli have been implicated in the pathophysiology of anxiety. These include limbic (amygdala, ventral striatum) and paralimbic structures (orbitofrontal cortex, insula, ACC).

For example, subjects with obsessive–compulsive disorder show increased error-related activity in the ACC (Ursu et al 2003), which could hypothetically affect stage 2 (error monitoring during execution) and stage 3 (error detection during feedback) of decision making. Posttraumatic stress disorder has been associated with dysfunction of medial prefrontal cortex and ACC

(Liberzon et al 2003), which could underlie impaired feedback processing (stage 3).

Recently, a "risk-as-feelings" hypothesis, which highlights the role of affect experienced at the moment of decision making, has been proposed (Loewenstein et al 2001). Accordingly, anticipated outcomes are translated into different body states based on previous experiences. This process critically depends on the orbitofrontal cortex, insula, amygdala, and ACC. Given the importance of hyperarousal and related autonomic changes in anxiety, anxious patients may show an altered pattern of aversive somatic markers during the assessment stage of decision making (stage 1), as well as during the experience of outcome (stage 3). A number of processes can contribute to disturbed assessment, for example, appraisal processes (Mogg and Bradley 1999), encoding and recall biases (Pury and Mineka 2001; Reidy and Richards 1997; Russo et al 2001), expectancy changes (Chan and Lovibond 1996), or increased sensitivity to punishment (Corr et al 1997).

In conclusion, the systems neuroscience framework based on distinct stages of decision making can provide a road map to determine which component of decision making is dysfunctional in psychiatric populations. This line of investigation can prove to be critical for the development and testing of new interventions aimed to improve decision making and ensuing quality of life in impaired populations. (Craig 2003).

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