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The Cognitive Neuroscience of Human Decision Making: A Review and Conceptual Framework

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Decision making, the process of choosing between options, is a fundamental human behavior that has been studied intensively by disciplines ranging from cognitive psychology to economics. Despite the importance of this behavior, the neural substrates of decision making are only beginning to be understood. Impaired decision making is recognized in neuropsychiatric conditions such as dementia and drug addiction, and the inconsistencies and biases of healthy decision makers have been intensively studied. However, the tools of cognitive neuroscience have only recently been applied to understanding the brain basis of this complex behavior. This article reviews the literature on the cognitive neuroscience of human decision making, focusing on the roles of the frontal lobes, and provides a conceptual framework for organizing this disparate body of work.

Key Words: executive function, prefrontal cortex, frontal lobes, amygdala, reward, impulsivity

Decision making is a vital component of human behavior. Like other executive processes, it involves the synthesis of a variety of kinds of information: multimodal sensory inputs, autonomic and emotional responses, past associations, and future goals. These inputs must be integrated with information about uncertainty, timing, cost-benefit, and risk and then applied to select appropriate actions. This processing has further practical constraints: It must be completed rapidly and must retain some degree of flexibility to be useful in a changing environment. Despite this daunting complexity, recent work using a variety of methods has begun to elucidate the component processes underlying decision making and to localize these processes in the human brain.

This is a new focus for cognitive neuroscience. Inroads have been made in understanding elements of decision making, but the connections between these elements remain unclear. However, there are long tradi-

tions of decision-making research in disciplines as varied as cognitive psychology, economics, and computer science (Baron, 1994; Kahneman, Slovic, & Tversky, 1982; Lipshitz, Klein, Orasanu, & Salas, 2001; Stirling, 2003), which may be very useful in guiding this fledgling field. This article will attempt to clarify what is known about the neural bases of human decision making and what is not. First, the literature on decision making in patients with frontal lobe damage will be reviewed. In the past several years, this work has had an important impact on the study of both normal and pathological decision making. However, the inconsistencies and difficulties in interpreting this growing body of work highlight the need for a more systematic approach. Although there is no true consensus model of decision making, consistent features can be found in theories emerging from various disciplines. These recurring themes can be distilled into a useful framework for beginning to understand how the general processes of decision making may be represented in the brain. In the second part of this article, I will propose such a framework and review the cognitive neuroscience literature that addresses these more fundamental aspects of decision making.

NEUROANATOMY

The cognitive neuroscience literature on decision making has focused on a limited set of brain regions.

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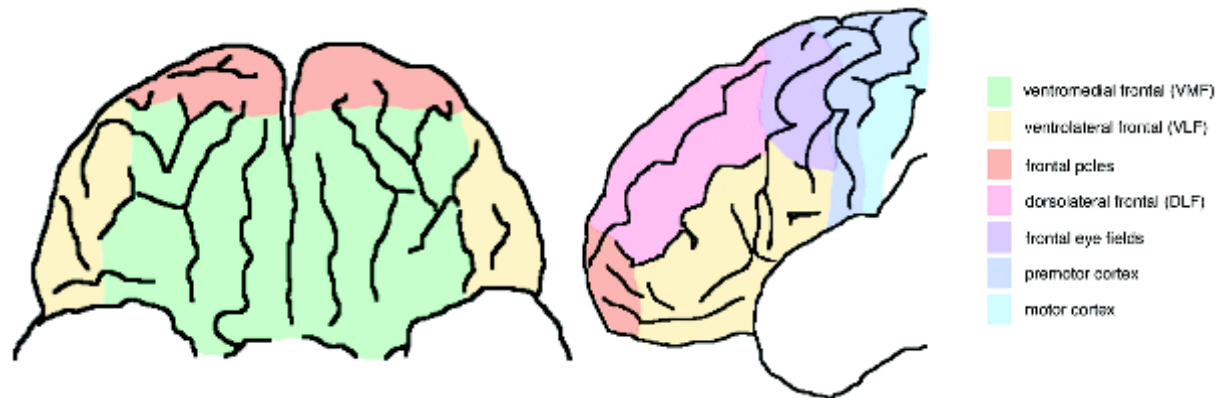


Figure 1: Ventral and Lateral Views of the Frontal Lobes, Showing the Approximate Borders of the Various Sectors Described in the Text.

There has been particular interest in the role of the prefrontal cortex in general and the ventromedial prefrontal cortex in particular. The terminology used to describe these regions can be confusing. Although strict boundaries are rarely defined, the ventromedial frontal lobe (VMF) includes the medial portion of orbitofrontal cortex (OFC) and the ventral portion of the medial wall of the frontal lobes. The lateral OFC is often grouped with the ventral portion of the lateral convexity of the frontal lobe and labeled the *ventrolateral frontal lobe* (VLF), although this distinction is more frequent in functional imaging than in lesion studies. Most commonly, these ventral areas are contrasted with dorsolateral prefrontal cortex (DLF; for a detailed discussion of the relationship between these areas and Brodmann's nomenclature, see Chiavaras, LeGoualher, Evans, & Petrides, 2001; Petrides & Pandya, 1999, 2002).

This broad division of prefrontal cortex is a reasonable starting point because, generally speaking, these three cortical areas have different cytoarchitecture and different patterns of connectivity, both in humans (Petrides & Pandya, 1999, 2002) and in nonhuman primates (Barbas, 2000; Dombrowski, Hilgetag, & Barbas, 2001). Ventral medial prefrontal and caudal orbitofrontal regions are classified as paralimbic cortex. These cortical areas are closely connected to limbic structures such as the amygdala and hypothalamus, provide descending inputs to midbrain structures including periaqueductal gray and substantia nigra, and receive polymodal sensory inputs (An, Bandler, Ongur, & Price, 1998; Barbas, 2000; Ghashghaei & Barbas, 2002; Ongur, An, & Price, 1998; Price, Carmichael, & Drevets, 1996; Rempel-Clower & Barbas, 1998). In contrast, DLF is heteromodal association cortex, with more restricted sensory inputs, and has been implicated in working memory and selective attentional processes. However, all areas of the prefrontal cortex are heavily intercon-

nected, emphasizing the synthetic and integrative role of the region in general (Barbas, 2000). The cortical anatomy is summarized in Figure 1; for additional accessible reviews of this anatomy, see Mesulam (2003) and Stuss and Levine (2002).

Several subcortical structures have been implicated in decision making. The amygdala appears to have a role, perhaps in part through its important interconnections with the OFC. Recent work has also begun to examine the role of mesolimbic and mesocortical dopaminergic projections (arising in the substantia nigra and ventral tegmental area of the midbrain and terminating in the ventral striatum-nucleus accumbens, dorsal striatum [caudate-putamen], and prefrontal cortex) that have been implicated in reward and addiction (Schultz, 2002; Wise, 2002). There is also some work supporting a role for prefrontal serotonin in aspects of reinforcement-driven learning and deciding (Clarke, Dalley, Crofts, Robbins, & Roberts, 2004; Rogers et al., 2003; Rogers, Owen, et al., 1999).

This should not be viewed as a definitive list of the neuroanatomical substrates of decision making but rather as a useful starting point for understanding the existing literature. It reflects the biases of the initial investigators in this relatively new field, primarily driven by clinical observations of patients with focal brain damage and more recently by the results of functional imaging studies of reward processing in humans and the insight that the poor choices of substance abusers suggests a role for the reward circuitry first identified in animal models of addiction in normal and pathologic human decision making (Bechara & Damasio, 2002; Bechara, Dolan, & Hinds, 2002; Cavedini, Riboldi, Keller, D'Annuncci, & Bellodi, 2002; Grant, Contoreggi, & London, 2000). Indeed, recent single-unit work in monkeys has demonstrated reward-sensitive neurons in a variety of other regions, including the sensory

thalamus (Komura et al., 2001) and parietal cortex (Platt & Glimcher, 1999; Sugrue, Corrado, & Newsome, 2004).

LESIONS

Most of the lesion studies of decision making in humans have focused on the ventromedial prefrontal cortex. Focal lesions in humans that involve VMF structures generally spare lateral prefrontal areas (and vice versa), so this division is theoretically sound, clinically relevant, and experimentally pragmatic. It is important to keep in mind that the common causes of VMF damage are generally different from the common causes of VLF or DLF damage (aneurysm rupture, tumor resection and traumatic brain injury in the former, ischemic or hemorrhagic stroke in the latter two). This may introduce confounds, in that the patient populations may differ systematically in other respects, such as older age and history of vascular risk factors in the case of ischemic stroke and the possibility of nonfocal damage due to acute hydrocephalus, edema, and surgical trauma in the case of aneurysm rupture, for example. In addition, lesions that affect these different cortical areas also tend to involve different subcortical structures. Individuals with VMF damage may also have involvement of the basal forebrain, the genu of the corpus callosum, and the septum; DLF damage may be associated with damage to the dorsal caudate-putamen and intervening white matter tracts; and VLF damage often extends posteriorly to involve the insula. Finally, VMF damage is frequently bilateral, whereas lateral frontal damage is rarely so.

FUNCTIONAL IMAGING

Susceptibility artifact limits the detectable blood oxygenation level dependent (BOLD) signal from the OFC, making this area challenging to image with standard functional magnetic resonance imaging (fMRI) techniques. Methods exist to address this limitation (Deichmann, Gottfried, Hutton, & Turner, 2003; Wilson & Jezzard, 2003). Positron emission tomography (PET) studies do not suffer from this problem. In addition, the surface anatomy of the human OFC is quite variable. A probability map has recently been developed to allow functional imaging results to be related more rigorously to the cytoarchitecture of this area (Chiavaras et al., 2001).

STUDIES OF COMPLEX DECISION MAKING

Clinicians have reported strikingly impaired decision making in patients with VMF damage many times over the past century (reviewed in Cottle & Klineberg, 1974; Eslinger & Damasio, 1985; Damasio, 1994; Loewenstein,

Weber, Hsee, & Welch, 2001). Such reports have emphasized impairments in the emotional aspect of decision making. Empirical studies of elements of decision making following frontal lobe damage have been undertaken more recently (e.g., Godefroy & Rousseaux, 1996, 1997; Miller, 1992; Miller & Milner, 1985). The work of Bechara et al. using a gambling task has been particularly influential in shaping the direction of such work in the past several years. This laboratory task was developed to capture the elements of risk, reward, and punishment that this group hypothesized were at the root of the decision-making impairment of VMF patients (Bechara, Damasio, Damasio, & Anderson, 1994). This now well-known task, here referred to as the Iowa gambling task (IGT), requires the participant to repeatedly choose from four decks of cards with the goal of winning as much play money as possible. Each card is associated with a win, and some cards also carry losses. Overall, choosing from two of the decks results in larger wins but even larger losses, whereas choosing from the other two results in small wins but even smaller losses. As participants progress through the 100 trials, they gradually learn to avoid the riskier (so-called disadvantageous) decks and choose more often from the lower stakes, overall advantageous decks. Bechara et al. (1994) reported that participants with VMF damage performed quite differently, persistently choosing more often from the riskier (ultimately disadvantageous) decks. This observation was extended by examining the skin conductance responses (SCR) in 6 VMF participants while performing the IGT. Control participants showed enhanced SCR prior to choosing cards, with choices from the risky decks preceded by larger SCR than choices from the safe decks even before controls were able to explicitly report deck contingencies. In contrast, the VMF participants showed minimal SCR prior to card choices, and this response did not distinguish between safe and risky decks (Bechara, Damasio, Tranel, & Damasio, 1997).

The authors of this study argued that VMF damage impaired the acquisition of emotional or “dispositional” knowledge about the decks, knowledge that biased controls away from the risky decks. A similar pattern of behavioral and autonomic results has been reported following bilateral amygdala damage (Bechara, Damasio, Damasio, & Lee, 1999). These findings have led to the more general “somatic marker” hypothesis that emotional information, indexed by the autonomic state of the body, can influence decision making under uncertainty (Bechara, Damasio, & Damasio, 2000, 2003; Damasio, 1994). Dissenting evidence regarding the importance of the autonomic body state in risky decision making has come from a study of patients with high cervical spinal cord lesions who performed the IGT nor-

mally (despite the inability to generate normal sympathetic autonomic responses; North & O'Carroll, 2001) and from a study in young normal participants that found that SCR magnitude related to the magnitude of anticipated rewards or punishments in the IGT, rather than the riskiness of the choice (Tomb, Hauser, Deldin, & Caramazza, 2002). Recent work has also shown that normal participants acquire sufficient explicit knowledge of the contingencies to support good performance, even at very early stages of the task, making recourse to a somatic marker explanation unnecessary (Maia & McClelland, 2004).

The Iowa group has reported a number of follow-up studies in patients with frontal lobe damage. One contrasted the effects of VMF damage (9 participants) with the effects of dorsolateral or dorsomedial frontal damage (six left hemisphere, four right hemisphere) on the IGT. Although direct statistical comparison of the performance of the two groups is not provided in the article, VMF participants chose fewer than 50 cards from the safe decks, whereas participants with dorsal frontal damage, like normal participants, chose more than 50 cards. The role of working memory in IGT performance was also examined in this study; deficits in working memory were correlated with deficits on the IGT but were not the sole explanation for impaired IGT performance (Bechara, Damasio, Tranel, & Anderson, 1998). More recently, this group has reported that unilateral right VMF damage ($n = 4$) but not left VMF damage ($n = 3$) leads to impaired IGT performance compared to control participants (Tranel, Bechara, & Denburg, 2002).

Efforts by other centers to replicate these behavioral findings have led to mixed results. Manes et al. (2002) administered the IGT to 19 patients with focal frontal lobe damage. To pinpoint the key area(s) responsible for poor performance on this task, they studied participants with unilateral damage and classified the damage as involving one of three frontal regions (OFC, DLF, dorsomedial frontal) or as "large" if it extended into two or more of these regions. Damage to the OFC alone did not impair IGT performance, whereas isolated damage to DLF or dorsomedial regions and large lesions were all accompanied by impaired IGT performance. A follow-up study added another 27 patients to permit analysis of laterality effects (albeit collapsed across the frontal subregions). In keeping with the small series of Tranel et al. (2002), right frontal damage was associated with the worst performance on the IGT. However, left frontal damage was also associated with impairment (Clark, Manes, Antoun, Sahakian, & Robbins, 2003). The poor performance of participants with right hemisphere damage was evident even when ventromedial regions were spared.

Fellows and Farah (2005) replicated the original finding that VMF damage is associated with impaired IGT performance in a group of 9 participants, most of whom had bilateral damage. However, in the same study, unilateral DLF damage (in 12 participants) was also found to be associated with impaired performance on the task, regardless of the involved hemisphere.

The complexity of the IGT makes it difficult to resolve these conflicting findings. At the least it seems clear that abnormal performance on the task is not a specific sign of VMF dysfunction. This has implications for interpreting the results of studies using IGT performance as a probe of VMF function in conditions including addiction, psychopathy, personality disorders, and studies of normal states such as gender differences and variations in serum testosterone (Overman, 2004; Bechara & Damasio, 2002; Best, Williams, & Coccaro, 2002; Cavedini, Riboldi, D'Annunzi, et al., 2002; Cavedini, Riboldi, Keller, et al., 2002; Grant et al., 2000; Reavis & Overman, 2001; van Honk, Hermans, Putman, Montagne, & Schutter, 2002).

A number of investigators have examined specific aspects of IGT performance in an effort to explain the impairment of VMF participants in terms of simpler underlying processes. Approaches have included cognitive modeling applied to the results of the original IGT (Busemeyer & Stout, 2002); close variants of the IGT designed to emphasize putative underlying processes (Bechara, Tranel, & Damasio, 2000; Fellows & Farah, 2005), which I will discuss further in the second half of this article; and new gambling tasks intended to examine particular component processes (Rogers, Everitt, et al., 1999; Sanfey, Hastie, Colvin, & Grafman, 2003).

Busemeyer and Stout (2002) modeled the trial-by-trial IGT behavior of normal participants with a cognitive decision model that incorporated reinforcement-expectancy learning, the relative weighting of losses over gains, and sensitivity of choices to the reinforcement expectancy (Busemeyer & Stout, 2002). Such a model approximated the performance of normal controls fairly well. According to this model, the impaired IGT performance of patients with Huntington's disease was primarily due both to impaired learning and to a gradual loss of sensitivity to reinforcement expectancy as the task progressed, perhaps reflecting nonspecific fatigue. Whether the component processes suggested by this model relate to specific functions of different frontal areas remains to be seen.

The task developed by Rogers, Everitt, et al. (1999) is intended to evaluate risk seeking using a gambling paradigm that (unlike the IGT) requires no learning. On each trial, participants choose between a high or low probability gamble and then decide how much play money to bet on the outcome. Three studies have been

published that examined the performance of participants with frontal lobe damage on this task. The first found that VMF damage ($n = 10$) was associated with a tendency to make riskier choices than either controls or participants with DLF damage ($n = 10$) but to bet smaller sums of money (Rogers, Everitt, et al., 1999). However, a larger group of participants ($n = 31$) who had suffered rupture of anterior communicating artery aneurysm (which typically results in varying degrees of VMF damage, although this was not assessed radiologically in the study) chose the riskier gamble no more often than controls but bet larger sums (Mavaddat, Kirkpatrick, Rogers, & Sahakian, 2000). Finally, Manes et al. (2002) reported that isolated damage to the OFC, DLF, or dorsomedial frontal cortex did not lead to significant impairment on this task compared to controls; damage to two or more of these regions led to poor performance, with such participants both choosing riskier gambles and placing larger bets (Manes et al., 2002). Sanfey et al. (2003) have also examined risk-taking behavior in participants with frontal damage with yet another card-based gambling task that manipulated the variance of wins and losses while keeping the overall expected value (probability \times outcome value) for each deck constant. Participants with VMF involvement ($n = 9$) did not show the normal pattern of preferring lower variance decks. A subset of this group ($n = 5$) appeared to be risk-seeking, in that they preferred the high variance decks, whereas the remaining 4 VMF participants followed a pattern similar to the control group. The risk-seeking subgroup did not differ from those who performed normally on demographic variables, IQ, or neuroanatomical grounds, except that they had more associated DLF damage. However, DLF damage in the absence of VMF injury ($n = 4$) did not lead to risk-seeking behavior in this task.

Bechara, Tranel, et al. (2000) manipulated the reward and punishment values of the original IGT deck to test whether VMF participants were hypersensitive to reward or hyposensitive to punishment and found no evidence of either as measured by task performance or the magnitude of the SCR generated in response to reinforcement.

In sum, extensive damage to the frontal lobes is associated with riskier-than-normal choices in both these tasks. However, these results taken together do not permit strong claims about the role of any particular frontal region and in fact indicate that restricted frontal damage is often not associated with risk seeking, defined as either a preference for high variance in outcomes or an increased willingness to “play the long shot.”

It is not easy to reconcile the inconsistent findings in this series of studies, in large part because of the complexity of the tasks used to measure decision making.

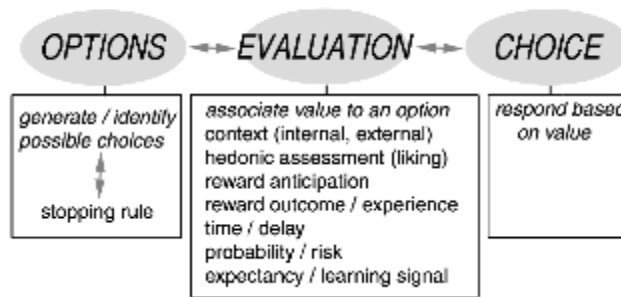


Figure 2: Schematic Summarizing a Simple Three-Stage Model of Decision Making and Listing Some of the Processes That May Be Involved at Each Stage.

One way to address this difficulty is to look at much simpler component processes of decision making.

DISSECTING DECISION MAKING

The study of decision making in normal individuals has generated a variety of frameworks for understanding the building blocks of this complex behavior. One useful (albeit certainly oversimplified) model of decision making, derived from classical decision-making theory, breaks decision making down into three interrelated processes (Baron, 1994; Herrnstein & Prelec, 1991; Lipshitz et al., 2001); these are outlined in Figure 2. Options are first identified or generated, evaluated, and finally a choice is made, as reflected in behavior. The existing decision-making literature in general, and the cognitive neuroscience literature in particular, has focused on evaluation (and, to a lesser degree, choice). However, there is no a priori reason to believe that VMF patients, or indeed others who show clinical signs of disordered decision making, are necessarily or solely impaired in the evaluative aspect of decision making. Although the distinctions between these three phases of decision making are to some extent arbitrary, such a model provides a starting point for a more systematic examination of the component processes of decision making. In the pages that follow, the discussion will be organized according to this more comprehensive framework.

IDENTIFICATION OF OPTIONS

Option identification has been little studied, even in normal participants, despite its obvious importance in real-life decision making (reviewed in Johnson & Raab, 2003). This phase of decision making is most crucial in relatively unstructured situations, often present in real

life, but less often in the laboratory (Fischhoff, 1996). Insights into this “front end” of decision making have been gleaned by having participants think aloud as they consider a difficult decision. A related approach is to provide large amounts of potentially relevant information and observe how participants go about sifting through this information in order to make a decision. The literature based on these “think aloud” and information search strategy paradigms in normal participants suggests that effective option identification requires at least two processes: first, generating or recognizing options and, second, applying a “stopping rule” when enough options have been considered (Baron, 1994; Butler & Scherer, 1997; Gigerenzer & Todd, 1999; Lipshitz et al., 2001; Saad & Russo, 1996).

Although option generation has not been evaluated using these tasks in clinical populations, one innovative think-aloud study of participants with frontal damage performing an ill-structured financial planning task found that they had more difficulty structuring the problem, pursued fewer of the (explicitly provided) goals, and were less systematic in generating options for achieving each goal than controls were (Goel, Grafman, Tajik, Gana, & Danto, 1997). Case reports of patients with frontal damage tested on other complex, real-world decision and planning tasks also support the idea that such damage may have an impact at this early stage of decision making (Grafman & Goel, 2000; Satish, Streufert, & Eslinger, 1999), and such patients often have difficulty in open-ended, unstructured task environments in general (Shallice & Burgess, 1991). One might also postulate parallels with other forms of self-initiated generation tasks, such as fluency tasks, often impaired in prefrontal patients in other domains (e.g., verbal, figural; Stuss & Benson, 1986) and associated with activations in DLF in functional imaging studies (Schlosser et al., 1998). Although patients with VMF damage are anecdotally characterized as impulsive, both clinical observations and experimental work in such patients suggest that they may spend too long contemplating decision options (Eslinger & Damasio, 1985; Rogers, Everitt, et al., 1999), raising the possibility that they are impaired in applying stopping rules (Gigerenzer & Todd, 1999). Whether or not VMF damage leads to difficulties in evaluation of options, such damage may independently affect option generation. This aspect of decision making deserves more detailed study, both to better understand whether impairments at this stage contribute to the real-life difficulties of such patients and for the light such an understanding might shed on other conditions notable for prolonged decision-making times, such as obsessive-compulsive disorder (Cavedini, Riboldi, D’Annunzi, et al., 2002).

ASSESSING VALUE

This aspect of decision making has been the most intensively studied to date. The field is very new and has been approached from a variety of interesting directions, ranging from animal learning to economics. This heterogeneity makes it difficult to summarize the existing findings; I will first provide a brief overview of the various conceptions of value and then review work that has looked at more specific aspects of value representation in the brain.

Value can be considered as a (subjective) property of a stimulus. Economists apply the term *utility* to this concept (reviewed in Glimcher & Rustichini, 2004). In animal learning terms, this property has been operationalized in terms of how hard an organism is willing to work to obtain that stimulus (reinforcement). Reinforcement value can vary along various objective dimensions, including probability, delay, and kind (Shizgal, 1997). Value can also be measured as a relative property, in preference judgment paradigms, for example.

How do humans assign value to options? This is a question that occupies researchers across many disciplines, resulting in a plethora of models. Simple in concept, it is a process that may be very complex in its instantiation. The value of a given stimulus is not fixed: It depends on external factors, such as the other available options, and it depends on internal factors, such as satiety. A banana may seem very attractive to a hungry individual but is likely to have a much lower value if that individual has just eaten a pound of bananas in one sitting. It depends on the delay before the stimulus can be obtained and, perhaps relatedly (Holt, Green, & Myerson, 2003; Rachlin, Raineri, & Cross, 1991), on the probability that it will be obtained. A dollar right now is worth more to most people than 10 dollars they will not receive for 6 months, a phenomenon known as temporal discounting. Temporal discounting has been extensively studied in normal participants and addiction research as an explanation for impulsive decision making (Ainslie, 2001; Bickel, Odum, & Madden, 1999; Coffey, Gudleski, Saladin, & Brady, 2003; Critchfield & Kollins, 2001; Kirby & Herrnstein, 1995; Kirby & Marakovic, 1996; Kirby, Petry, & Bickel, 1999; Madden, Begotka, Raiff, & Kastern, 2003), but little is known about how reinforcement and time are integrated in the brain.

Furthermore, comparing different options, or valuing a single option with both pros and cons, would seem to require a mechanism for encoding quite different factors on a common scale. This has led to the speculation that there may be a common neural “currency,” a neural mechanism for encoding value that would integrate these diverse considerations, allowing apples and

oranges (or indeed, bananas) to be compared to allow a choice to be made (Montague & Berns, 2002).

Before reviewing the evidence for this and related concepts, it is worth clarifying the relevant terminology. *Value* is a very general term. Even the more specific concepts of reward and punishment have multiple meanings, many of which are confounded in common usage but may nevertheless have different neural substrates. Reward encompasses both the incentive value of a stimulus and its hedonic properties: how hard you are willing to work for something and how much you like it. There is some evidence that liking and wanting may be mediated, at least in part, by distinct neural systems. Following near-complete dopamine depletion, rats no longer work to obtain rewards but continue to demonstrate apparently normal affective responses to pleasant and unpleasant tastes, as measured by stereotyped behavioral reactions (Berridge & Robinson, 1998). A mutant rat model with increased synaptic dopamine showed increased willingness to work for reward but again unchanged affective responses to tastes (Pecina, Cagniard, Berridge, Aldridge, & Zhuang, 2003). Studies in humans have been less conclusive but in some cases have shown that wanting or craving of drugs of abuse, but not the euphoria they induce, is reduced by pretreatment with dopamine antagonists (Brauer & de Wit, 1996; Modell, Mountz, Glaser, & Lee, 1993).

Reward may also be operationalized more generally as a guide for learning. That is, concordance between an anticipated reward and its delivery reinforces behavior, whereas a mismatch between reward expectancy and delivery leads to changes in behavior. Phasic dopamine signaling has been shown to encode such information, termed *reward expectancy error*, in monkey models (Schultz, 2002; Tremblay & Schultz, 1999), and some data from imaging studies are consistent with a similar role in humans (Aron et al., 2004; Martin-Soelch et al., 2001; O'Doherty, Dayan, Friston, Critchley, & Dolan, 2003; Pagnoni, Zink, Montague, & Berns, 2002).

There are yet other ways to operationalize reward: Reward value has been conceived of by several authors as an intrinsic stimulus property (reviewed in Baxter & Murray, 2002; Rolls, 2000). Human studies of the processing of primary rewards (such as food, pleasant odors, pleasant sounds) have shown activation, albeit variably, in the same limbic and cortical reward circuits identified in animals: midbrain, ventral striatum, medial prefrontal and orbitofrontal cortex as well as the insula and, in some cases, amygdala (Blood & Zatorre, 2001; Kringelbach, O'Doherty, Rolls, & Andrews, 2003; O'Doherty et al., 2000; O'Doherty, Deichmann, Critchley, & Dolan, 2002; Small, Zatorre, Dagher, Evans, & Jones-Gotman, 2001). Studies of other forms of reward such as beautiful paintings or beautiful faces

have shown activations in various components of the same circuitry (Aharon et al., 2001; Kawabata & Zeki, 2004; O'Doherty, Winston, et al., 2003), as has cocaine infusion in cocaine-dependent participants (Breiter & Rosen, 1999). Experiments using money as reinforcement have had more mixed results. Several studies have used simple reaction time tasks and compared activations on trials with monetary reward with unrewarded trials. Knutson and colleagues have published a series of studies using such a paradigm and have shown that activity in the nucleus accumbens increases as a function of magnitude of anticipated reward and is correlated with self-rated happiness about the possible outcome (Knutson, Adams, Fong, & Hommer, 2001). When reward anticipation is contrasted with experience of the reward outcome, activity in the ventral striatum is detected in the anticipatory phase, whereas deactivation in both ventral striatum and ventromedial prefrontal cortex occurred during the outcome phase when anticipated rewards were not obtained (Knutson, Fong, Adams, Varner, & Hommer, 2001). However, another group using a similar paradigm found little difference in the areas activated by anticipation of reward and reward delivery (Breiter, Aharon, Kahneman, Dale, & Shizgal, 2001). Finally, a study that examined the effect of monetary reward on a more difficult task (n-back) found deactivation in several areas, including the ventral striatum, when rewarded trials were compared with unrewarded trials (Pochon et al., 2002). It seems likely that a clear understanding of the interaction between reward and other cognitive processes will require both a clear definition of the aspect of reward being studied and careful attention to the time course of reward anticipation and delivery.

One of the striking properties of stimulus-reward associations is the need for flexibility. A growing body of work has examined the neural correlates of the changing reward value of a fixed stimulus. There are two basic paradigms for examining this issue: The first alters "rewardingness" by changing the internal state of the participant, such as through selective satiety. The second changes the reward value of the stimulus itself, as in the operant conditioning paradigms of reversal learning or extinction. Imaging studies of selective satiety in humans have found regions of caudal OFC in which activity relates to the current reward value of either a taste or odor, rather than unvarying features of the stimulus (Kringelbach et al., 2003; O'Doherty et al., 2000). These findings agree with single-unit recordings in monkey OFC, which have identified neurons that respond to stimuli only when these are motivationally salient (Rolls, 2000), that have firing patterns that reflect current reward value (Wallis & Miller, 2003), or that distinguish between the subjective value of different kinds of reward

as indicated by subsequent choice behavior (Tremblay & Schultz, 1999). Other work has also implicated the basolateral amygdala in similar paradigms in both rat and monkey models (Baxter & Murray, 2002). An fMRI study of classical appetitive conditioning in humans found increased activation in the amygdala for the CS+, which was modulated by selective satiety (Gottfried, O'Doherty, & Dolan, 2003). There is some evidence from disconnection experiments in the monkey (Baxter, Parker, Lindner, Izquierdo, & Murray, 2000) and rat (Schoenbaum, Setlow, Saddoris, & Gallagher, 2003) that flexible stimulus-reinforcement associations depend on the interaction between amygdala and OFC.

Further support for the hypothesis that the OFC mediates the representation of the current reinforcement value of a stimulus comes from studies of humans with VMF damage. Reversal learning and extinction, two forms of flexible stimulus-reinforcement associative learning, are impaired following VMF damage (Fellows & Farah, 2003; Hornak et al., 2004; Rolls, Hornak, Wade, & McGrath, 1994). This is selectively related to VMF damage; DLF damage does not impair simple reversal learning in monkeys (Dias, Robbins, & Roberts, 1996) or in humans (Fellows & Farah, 2003). Hornak et al. (2004) found that some participants with DLF damage had difficulty on a more complex, probabilistic reversal learning task, seemingly on the basis of inattention rather than impaired stimulus-reinforcement processing. The human studies have not detected consistent laterality effects, and at least some participants with unilateral OFC damage demonstrate normal reversal learning (Hornak et al., 2004). A lesion study in monkeys directly examined this question and found that either right or left OFC damage (in conjunction with ipsilateral amygdala damage) is sufficient to impair reversal learning (Izquierdo & Murray, 2004). An fMRI study of reversal learning with play money reward and punishment found that activity in the bilateral medial OFC was greater with the experience of reward than punishment (O'Doherty, Kringelbach, Rolls, Hornak, & Andrews, 2001).

Can this robust converging evidence for a role for the medial OFC in the flexible representation of stimulus-reinforcement associations shed light on the impaired IGT performance of human participants with damage to this area? Normal performance of the IGT appears to require reversal learning; cards are presented in a fixed order that induces an initial preference for the ultimately riskier decks that must then be overcome as losses begin to accrue. Fellows and Farah (2005) tested the hypothesis that impaired performance on the IGT of VMF participants reflected an underlying deficit in reversal learning. Nine VMF participants were abnormal on the original IGT but performed as well as normal par-

ticipants on a variant task that shuffled the card order of the original task to eliminate the reversal learning requirement. Their improvement also correlated well with how impaired they were on a simpler measure of reversal learning.

It may be the case that the IGT literature on the role of VMF in decision making is best framed as an impaired ability to flexibly update stimulus-reinforcement associations, which has the advantage of linking these findings to the larger body of work on the forms of associative learning just reviewed. An interesting, but at this point open, question is whether the real-life behavioral disturbances of these participants can also be traced to deficits in fundamental stimulus-reinforcement processing. Some preliminary correlational evidence supports this possibility (Fellows & Farah, 2003; Rolls et al., 1994).

Although the weight of evidence to date from functional imaging studies seems to support the general concept that the same regions important in reward processing in animal models are involved in reward processing in humans, and over a range of rewards, this conclusion must be regarded as very tentative. As reviewed above, the ventral striatum/nucleus accumbens and medial OFC seem to show detectable activity in response to reward compared to unrewarded baseline in most studies, and many researchers have also reported a change in amygdala activity. However, the laterality of these effects has varied, as has the more precise location of OFC activity, and even these more robust effects have not been seen in all studies. Consistent patterns of activation across reward types in at least some elements of a putative reward circuit would appear to be a minimum requirement for the hypothesis that there is a common neural currency for reward, or at least the simplest form of this hypothesis. Such a claim would be supported most compellingly by studies in which reward type (and perhaps other factors, such as delay to reward, or probability of reward) were varied within subjects and showed both common areas of activation and activity that scaled with subjective preference as indicated by the participants' choices. Finally, unconfounding salience and reward remains a challenge for such studies (Zink, Pagnoni, Martin-Skurski, Chappelow, & Berns, 2004).

The principal difficulties in interpreting the existing literature are that the way in which reward has been operationalized has varied, anticipation of reward and reward outcome have not been consistently disambiguated, and the sensitivity of individual fMRI studies for detecting signal in crucial areas of VMF susceptible to artifact has not always been specified. Certainly, questions remain about the neural bases of the incentive and hedonic aspects of reward and whether anticipation and experience of reward are mediated by distinct neural circuits.

As discussed above, the relationship between reinforcement value and time is a central concept in a variety of models of impulsiveness (see Evenden, 1999, for review) and decision making (Ariely & Zakay, 2001). Particular attention has been paid to this concept in research on addiction, using a variety of methods. These studies have found an association between shortsightedness, defined by several different measures, and pathological real-life decision making, reflected in substance abuse (Kirby et al., 1999; Monterosso, Ehrman, Napier, O'Brien, & Childress, 2001; Petry, Bickel, & Arnett, 1998). Myopia for future reinforcement has been suggested as an explanation for the impaired decision making of VMF patients, both in life and in the lab (Bechara et al., 1994; Bechara, Tranel, et al., 2000), and in rats, both the nucleus accumbens and the OFC seem to play a role in responding to delayed reward, in that lesions to either of these areas lead to a tendency to choose small, immediate over larger, delayed rewards, that is, to show steeper temporal discounting (Cardinal, Pennicott, Sugathapala, Robbins, & Everitt, 2001; Mobini et al., 2002). One recent fMRI study used an analogous design, with human participants either choosing small, immediate rewards or accepting small, immediate losses in return for an eventual large payoff. The immediate reward condition was related to activation in the OFC, whereas the trade-off choice also recruited DLF, among other areas (Tanaka et al., 2004). A broadly similar pattern was found by a second group using a different temporal discounting task (McClure, Laibson, Loewenstein, & Cohen, 2004). However, when temporal discounting was examined in participants with frontal injury using a standard discounting task (in which participants make hypothetical choices between sums of money across different delays), neither DLF nor VMF damage systematically affected the rate at which reward lost its subjective value as a function of delay (Fellows & Farah, in press).

Although this last study did not find evidence of temporal myopia for reward following frontal damage, the VMF participants did seem to think differently about the future. VMF damage (but not DLF damage or nonfrontal damage) was associated with selective foreshortening of the window of time that participants considered when thinking about the future. Another study has reported that patients with OFC damage overestimate the passage of time over short (second to minute) intervals (Berlin, Rolls, & Kischka, 2004). Interestingly, the foreshortened future time measure in the first study correlated with self-reported apathy but not impulsivity. Although the group with OFC damage reported by Berlin et al. (2004) was more impulsive than a comparison group with DLF damage, this did not correlate with performance on the time estimation task.

CHOICE: THE DECISION IN ACTION

Studies of normal decision making have documented the frequent dissociation between hypothetical preferences and actual choices (Barlas, 2003; Slovic & Lichtenstein, 1971). More extreme forms of this dissociation are often mentioned, at least as anecdotes, in studies of patients with frontal lobe damage. For example, some such patients are said to persist in making punished choices while saying "No!" (Rolls et al., 1994). This suggests the possibility that preferences and choices are also dissociable in the brain. There is some evidence from functional imaging studies and monkey neurophysiology work that associating a reward with a stimulus and choosing an action on the basis of reward are mediated, at least in part, by different neural structures, although in many tasks, these two processes are confounded. As reviewed above, the OFC appears to play a crucial role in forming flexible stimulus-reinforcement associations or what might be considered the "perceptual" side of reinforcement processing. In contrast, studies examining reward-guided response selection (the action side of reinforcement processing) have generally focused on medial prefrontal regions, although the DLF has also been implicated in representing both reward and responses, at least in monkeys (Wallis & Miller, 2003). The caudate nucleus may also play a particular role in contingently rewarded action as opposed to the passive experience of reward (Tricomi, Delgado, & Fiez, 2004), perhaps by virtue of its connections with the medial and dorsolateral prefrontal cortex (Alexander, Delong, & Strick, 1986).

There is evidence that medial prefrontal areas are involved in representing value and perhaps more so when a response is required. An fMRI study of a speeded motor response task that was either unrewarded or rewarded with small amounts of money showed greater activation of the medial prefrontal cortex in the rewarded condition. The BOLD signal in this region increased as the amount of money won increased, and deactivation was seen when no win was obtained (Knutson, Fong, Bennett, Adams, & Hommer, 2003). Interestingly, no further signal changes were detected in the "punished" condition, when money was lost. In an fMRI study of reversal learning, O'Doherty, Critchley, Deichmann, and Dolan (2003) found that activity in the medial prefrontal cortex predicted subsequent choice. That is, reduced activity in this area was more likely to be followed by a response shift on the subsequent trial. Similar reductions in activity prior to punishment-induced response switching were observed in the dorsal anterior cingulate cortex (ACC) in that study and in at least one other study (Bush et al., 2002).

There is also evidence from event-related potential studies that the medial prefrontal cortex plays a role in rapid monitoring of outcome value and that this monitoring is related to subsequent choices. A midline negative potential beginning at about 200 ms was detected in response to the outcome of a simple gambling game with monetary wins and losses. The amplitude of this potential was larger for losses than for wins and scaled with the amount of money at stake. The magnitude of the potential was systematically related to the riskiness of the decision taken on the next trial, leading the authors to argue that this potential reflected a rapid assessment of the motivational value of an outcome, which influenced subsequent decision making. Dipole modeling indicates that the source is likely in or near the anterior cingulate cortex (Gehring & Willoughby, 2002).

There are also clues from the animal literature that the medial prefrontal cortex is important in motivated behavior. Rats with lesions to the anterior cingulate choose small rewards that require little physical effort, in contrast to their prelesion willingness to work harder for larger rewards (Walton, Bannerman, Alterescu, & Rushworth, 2003). Single-unit recordings from monkey ACC have found that a relatively large proportion of neurons are sensitive to the proximity of reward delivery in a multistep task (Shidara & Richmond, 2002). Lesions to this area in monkeys impaired learning of reward–motor response associations, although stimulus–reward learning remained intact (Hadland, Rushworth, Gaffan, & Passingham, 2003).

Preference judgments are yet another way of measuring the relative value of stimuli. These have the advantage of relating clearly to everyday behavior but the disadvantage of conflating value and choice, liking and wanting. The difficulties of interpretation that arise from this are illustrated by the lack of consistency between the animal and human literatures on preference judgments. The monkey literature suggests a role for the amygdala and OFC in this process, although evidence for a role for the OFC is not consistent. Bilateral lesions of either of these structures lead to abnormal food preferences in monkeys. This was expressed both as a tendency to choose foods that are not preferred by normal monkeys in a two-choice task and by inconsistent preference ordering for unfamiliar foods (Baylis & Gaffan, 1991). In contrast, a recent study reported stable preferences for familiar, palatable foods in monkeys with bilateral OFC lesions (Izquierdo, Suda, & Murray, 2004).

The handful of fMRI studies of preference judgment in humans have generally not detected changes in activity in either the OFC or amygdala. This may be related to technical issues brought about by signal loss in the region of the OFC (see earlier), but it may also be due to

a focus on choice rather than evaluation in the tasks. When participants made preference judgments of food items (presented as pictures) compared to determinations of simple visual features of the same stimuli, activations were seen in the anterior medial frontal cortex as well as the ACC, superior parietal lobe, and insula (Paulus & Frank, 2003). Another study asked participants to make either value judgments about (famous) people, places, or activities or to recall semantic or episodic information about the same stimuli. Again, the anterior medial frontal cortex was more active for the evaluative versus either the episodic or semantic recall task (Zysset, Huber, Ferstl, & von Cramon, 2002). A study focusing on the evaluation of famous people found activations in the medial prefrontal cortex, VLF, and ACC compared to a nonevaluative baseline task involving the same stimuli (Cunningham, Johnson, Gatenby, Gore, & Banaji, 2003). A recent H_2O^{15} -PET study explicitly attempted to disambiguate value from motivated choice with a region-of-interest design that focused on the amygdala and OFC (Arana et al., 2003). Participants passively viewed descriptions of food taken from restaurant menus and were asked to either imagine the dishes or choose the dish they preferred. Both the amygdala and medial OFC were more active when participants chose between highly preferred foods than between less preferred foods, and activity in the amygdala correlated with the participants' predetermined food preferences, regardless of whether a choice was required. A similar area of the OFC was more active in the choice than no-choice condition. Interestingly, no activations were detected in the medial prefrontal regions in the exploratory whole-brain analysis in this study.

As yet, studies of the brain basis of evaluation and choice do not yield entirely consistent results. It does seem clear that the ventral and medial prefrontal cortex mediate some or many aspects of reinforcement processing in humans as in animal models. The correlational nature of functional imaging results leaves open whether the activity detected in these areas is necessary for evaluation and choice. However, it is tempting to speculate that different clinical manifestations of frontal lobe damage may relate in part to disruption of different aspects of reinforcement processing. That is, the impulsive and/or erratic choices often associated with ventral prefrontal injury might relate to impairment in associating stimuli with context-specific reinforcement. In contrast, the abulia (or "lack of will") classically related to medial prefrontal damage could reflect disruption of reinforcement-guided responding. Studies relating these symptoms to precisely defined aspects of evaluation and choice will be important in linking these basic cognitive neuroscience findings to the clinic.

CONCLUSION

Cognitive neuroscience is just beginning to provide data relevant to developing a brain-based understanding of human decision making. There have been two main approaches to this topic to date. The first of these approaches attempts to capture the key aspects of hard decisions, such as choices that pit reward magnitude against risk using laboratory tasks. Studies using these relatively complex tasks have sparked renewed interest in long-standing ideas about the relationship between emotion and cognition and have at the least shown that the frontal lobes play an important role in making tough choices. However, efforts to understand the neural processes involved in performing these tasks at a finer level of resolution have led to decidedly mixed results.

A second approach to this problem that may help to elucidate the neural bases of decision making is to examine it at the component process level. This has several advantages: First, the extensive literature on normal human decision making can be used to identify theoretically meaningful candidate processes. Such a framework also forces more clarity in defining and operationalizing these processes. Second, existing data from several areas of neuroscience, ranging from associative learning to addiction research to studies of impulsivity, can provide starting points for developing hypotheses about the neural bases of these component processes. This article has attempted to frame the existing literature in such terms.

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