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Review

The lateral prefrontal cortex and complex value-based learning and decision making

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ABSTRACT

Tremendous progress has been made in discerning the neurocognitive basis of value-based decision making and learning. Although the majority of studies to date have employed simple task paradigms, recent work has started to examine more complex aspects of value processing including: the value of engaging rule-based cognitive control; the integration of multiple pieces of information (e.g., reward magnitude and delay) to discern the best course of action; pursuing future rewards; valuation of abstract concepts (e.g., fairness); and comparing the value of executed versus imagined alternative actions. We provide a comprehensive review of functional neuroimaging, electrophysiological, and lesion evidence suggesting that the lateral prefrontal cortex (LPFC) plays a critical role in these complex aspects of value processing. In particular, we focus on the specific information that the LPFC represents, and argue that it includes both cognitive and value-based information. We also discuss how the role of the LPFC is distinct from other value-related regions. Finally, we articulate a framework for understanding the contribution of subregions along the rostro-caudal axis of the LPFC, and thereby bridge the cognitive control and decision making literatures.

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1. Introduction

In the last decade, there has been an explosion of interest in the neurocognitive basis of value-based learning and decision making. Considerable work has examined the neurocognitive mechanisms underlying the capacity to represent and update the expected value of outcomes predicted by stimuli (Gottfried et al., 2003; O'Doherty et al., 2004; Pessiglione et al., 2006; Plassmann et al., 2010; Rangel et al., 2008), the distinction between habitual (model-free) versus goal-directed (model-based) learning (Balleine and O'Doherty, 2010; Daw et al., 2005; Hampton et al., 2006; McDannald et al., 2012; Rangel et al., 2008), and the extent to which there is convergence in value-based mechanisms across species (Balleine and O'Doherty, 2010; Wallis, 2012). Additionally, this work has identified a core network of regions involved in value-based processes including the ventromedial prefrontal cortex (VMPFC), orbitofrontal cortex (OFC), ventral striatum, insula, amygdala, and several sub-regions of the cingulate cortex (Behrens et al., 2007; Gottfried et al., 2003; Kable and Glimcher, 2007; Knutson and Greer, 2008; O'Doherty et al., 2004; Plassmann et al., 2010; Preuschoff et al., 2008; Rangel et al., 2008; Rushworth et al., 2011).

Increasingly, studies have begun to examine more complex aspects of value-based processes; there is a growing appreciation that in many real world situations, optimal outcomes can only be obtained by instantiating complex cognitive operations. These studies have examined: (1) the reward-value of engaging cognitive control mechanisms (e.g., the use of explicit rules for action); (2) the integration of multiple pieces of information (e.g., reward magnitude and delay) to discern the best course of action; (3) pursuing future rewards instead of immediate gratification; (4) valuation of abstract concepts (e.g., fairness); and (5) comparing the value of executed actions and imagined alternative actions. A consistent finding across these studies is the prominent involvement of the lateral prefrontal cortex (LPFC).

The traditional perspective is that the LPFC is a "cognitive" region that does not directly represent value-based information. Based on this perspective, a reasonable argument for why the LPFC is activated during complex valuation tasks is that it supports the cognitive element of the tasks, and that the core valuation regions noted above represent the specific value-related elements. Indeed, many of these studies suggest that the LPFC supports the cognitive control (or top-down regulation) of processing occurring in other value-related brain regions (e.g., Hare et al., 2009). However, we argue that a strict "cognitive" account cannot fully explain the involvement of the LPFC, especially when considering the LPFC from a representational perspective. Specifically, we propose that the data is most consistent with the idea that the *LPFC represents both cognitive and value-based information*. For example, the LPFC may represent associations between task-rules and predicted motivational outcomes, and thereby provide an overarching context that influences more basic value processing and action selection in other regions. This idea builds upon traditional theories linking the LPFC to cognitive control (Miller and Cohen, 2001), as well as several excellent reviews of electrophysiological work demonstrating that the LPFC represents both cognitive and reward-related information (Seo and Lee, 2008; Watanabe and Sakagami, 2007). Additionally, recent human neuroimaging work is also starting to recognize that the LPFC may directly represent value information (Hutcherson et al., 2012; McClure et al., 2004; Plassmann et al., 2010; Tobler et al., 2009).

In this paper, we provide a comprehensive review of electrophysiological, functional magnetic resonance imaging (fMRI), and lesion studies demonstrating that the LPFC plays a fundamental role in complex value-based learning and decision making. We first review the anatomical connections of the LPFC to provide context

for understanding its role in valuation. We then review evidence suggesting that the LPFC represents specific reward and punishment outcomes, even during simple tasks with minimal cognitive demands. We then review the role of the LPFC and the information it represents in more complex valuation tasks. Furthermore, we describe how the role of the LPFC differs from other value-related brain regions. Finally, we articulate a preliminary framework for understanding the distinct contribution of subregions situated along the rostro-caudal axis of the LPFC to value-based learning and decision making, and thereby attempt to bridge findings from the decision making and cognitive control literatures.

2. Anatomical context for understanding the LPFC in value processing

Fig. 1 provides a schematic illustration of key anatomical connections of the LPFC. The LPFC's anatomical connections with other "cognitive" regions (e.g., lateral temporal, parietal, and premotor cortices) are often emphasized. However, the LPFC also has robust reciprocal connections with key motivation-related regions of the brain. We provide a general overview of these connections based on monkey tracing studies, acknowledging that connections differ to some extent for the ventral and dorsal LPFC, and for the architectonic subdivisions within each of these areas. The LPFC receives strong input from the OFC, especially rostral area 11 (Petrides and Pandya, 1999, 2002, 2007). This pathway may supply the LPFC with information about object-outcome associations (Gottfried et al., 2003; Wallis and Miller, 2003; Walton et al., 2010). The LPFC (especially the mid-dorsolateral prefrontal cortex; mid-DLPFC) is robustly interconnected with area 32 of the pregenual anterior cingulate cortex (Pandya et al., 1981; Petrides and Pandya, 1999, 2002, 2007), a region that plays a role in subjective emotional feeling states including happiness and embarrassment (Amemori and Graybiel, 2012; Damasio et al., 2000; Lane et al., 1997; Sturm et al., 2012). The LPFC is also well connected with the anterior mid-cingulate cortex (aMCC; often referred to as the dorsal ACC) (Pandya et al., 1981; Petrides and Pandya, 1999, 2002), a region that represents the value of actions based on the amount of required effort
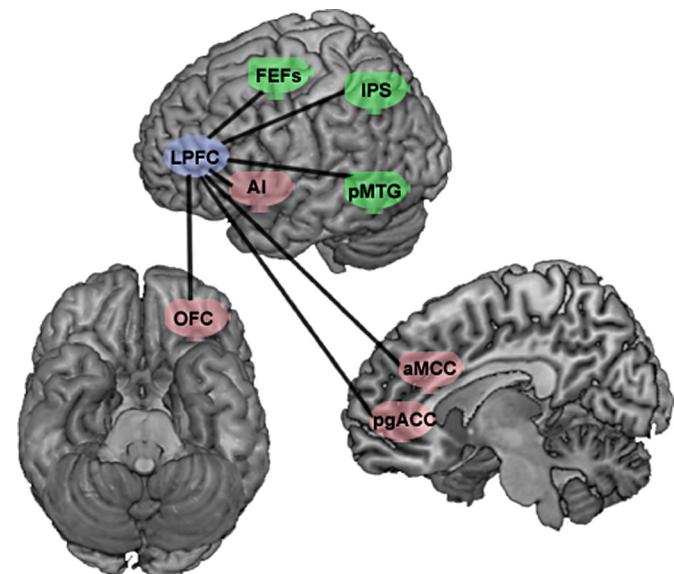
Fig. 1. Schematic Illustration of the anatomical connections of the LPFC. Connections with "cognitive" regions highlighted in green include the frontal eye fields (FEFs), intraparietal sulcus (IPS), and posterior middle temporal gyrus (pMTG). Connections with "motivation" regions highlighted in red include the pregenual anterior cingulate cortex (pgACC), anterior insula (AI), orbitofrontal cortex (OFC) and anterior mid-cingulate cortex (aMCC).

and the rewards that are expected to be obtained (Croxson et al., 2009; Kouneiher et al., 2009; Ridderinkhof et al., 2004; Rushworth et al., 2011; Shackman et al., 2011). Finally, afferent input from the insula (Petrides and Pandya, 1999, 2002) may provide the LPFC with access to feelings related to the physiological state of the body (e.g., respiration, temperature, heart rate, pain) (Craig, 2002; Critchley et al., 2004; Farb et al., 2012). To summarize, the anatomical connections of the LPFC suggest that it has the capacity to represent both cognitive and motivational (value-based) information.

3. The LPFC represents motivational outcomes

Before reviewing the role of the LPFC in complex aspects of value processing, we first consider studies of basic reward and punishment processing that have provided convincing evidence that the LPFC represents valenced outcomes. This data — which is derived from electrophysiological, functional neuroimaging, and lesion studies — provides critical evidence that the LPFC is not limited to representing cognitive information, but rather, also has the capacity to represent value-related information.

3.1. Electrophysiological evidence

The activity of single neurons in the LPFC increases in response to reward predicting cues (Matsumoto et al., 2003; Pan et al., 2008; Wallis and Miller, 2003; Watanabe et al., 2002), during delay periods when a specific reward is expected (Hikosaka and Watanabe, 2000; Watanabe, 1996; Watanabe et al., 2002), and during feedback periods when rewards are obtained (Abe and Lee, 2011; Asaad and Eskandar, 2011; Histed et al., 2009; Hosokawa and Watanabe, 2012; Kennerley and Wallis, 2009; Seo et al., 2007). For example, Watanabe and colleagues (Watanabe et al., 2002) recorded neural activity from the mid-DLPFC during a reward expectation task in which monkeys briefly saw an expected outcome (reward or no reward), and then had to wait for several seconds before they could obtain the expected outcome. They found that during the cue and delay periods, neural activity reflected the presence/absence of an expected reward and also discriminated among different food and liquid rewards (e.g., neurons exhibited a differential response for cabbage and raisons) (Watanabe et al., 2002). Thus, in this simple task with minimal cognitive demands, mid-DLPFC neurons carried information about a specific expected reward.

If LPFC reward activity simply reflected enhanced attention or arousal, similar activity should be observed for both positive and negative outcomes. However, Kobayashi and colleagues (Kobayashi et al., 2006) found that neural activity of some LPFC neurons was preferentially modulated by the presence/absence of a reward outcome (juice), whereas activity of separate LPFC neurons was preferentially modulated by the presence/absence of an aversive outcome (air puff). Similarly, another study found independent coding of prediction errors for unexpected positive and unexpected negative outcomes by LPFC neurons (Asaad and Eskandar, 2011). These findings provide strong evidence that LPFC activity reflects information about specific outcomes, and not just attentional salience or heightened arousal.

3.2. Functional neuroimaging evidence

Human fMRI studies have demonstrated that LPFC activation correlates with the value of choice options in some tasks (Hutcherson et al., 2012; Plassmann et al., 2010; Tobler et al., 2009). Recent work employing multivariate pattern analysis (MVPA) has supported this idea. MVPA examines whether the specific pattern of activation across multiple voxels (rather than the activation magnitude of individual voxels) is diagnostic of different task events

(Norman et al., 2006). Using MVPA, Vickery and colleagues (Vickery et al., 2011) sought to identify regions that represent different outcomes (wins and losses) during a matching pennies game. Three regions within the LPFC were among the top 10 regions across the entire brain from which they could most accurately decode information about such outcomes (Vickery et al., 2011). Additional analyses ensured that the findings were not related to extraneous factors such as choice, strategy, or attentional salience (Vickery et al., 2011). Finally, another study found that after subjects learned cue-reward associations, the pattern of the neural activation in the OFC and LPFC during reward prediction became similar to the pattern of activation during reward receipt, consistent with a learned representation of the predicted outcome (Kahnt et al., 2011).

3.3. Lesion evidence

Human lesion studies are consistent with the idea that disruption of the LPFC has a direct impact on the representation of motivational value. Patients with LPFC lesions often display apathy, a lack of drive, disinterest in the world, and diminished self-initiated action (Fuster, 2008; Levy and Dubois, 2006; Paradiso et al., 1999; Zamboni et al., 2008). Indeed, a rare comparison of patients with medial and lateral prefrontal damage — matched on various demographic variables — found that the lateral patients were more likely to exhibit depression, exhibit a lack of energy and under-activity, apathy, self neglect, slowness, and poverty of speech (Paradiso et al., 1999). Similarly, another study found that the severity of apathy in patients with frontotemporal dementia (assessed with items such as: "has difficulty starting an activity") correlated most strongly with atrophy of the right LPFC (Zamboni et al., 2008). Motivated behavior is fundamentally altered following LPFC lesions, consistent with a disrupted representation of value information. Supporting this interpretation, one study found that disrupting LPFC function with transcranial magnetic stimulation (TMS) altered the value that subjects assigned to food items during a choice preference task (Camus et al., 2009). To summarize, a wealth of electrophysiological, functional neuroimaging, and lesion evidence suggests that the LPFC has the capacity to represent information about value.

4. The LPFC and complex aspects of value-based learning and decision making

4.1. Representing the value of rule-based cognitive control

Adaptive human behavior often depends on using a set of rules or instructions held in working memory in order to select appropriate behaviors and suppress inappropriate habitual actions (often referred to as exerting cognitive control) (Bunge, 2004; Miller and Cohen, 2001). Rules typically specify conditional ('if-then') associations between stimuli and actions (e.g., if using a PC computer then press control + c to copy a section of text, but if using a Mac computer then press command + c to copy a section of text). In essence, rules specify which actions are correct or incorrect as a function of context. Recent work has demonstrated that individuals find effortful cognitive activity (e.g., rule-based cognitive control) aversive and tend to avoid it, except when it is expected to yield a desirable outcome that offsets the effort cost (Dixon and Christoff, 2012; Kool et al., 2010; McGuire and Botvinick, 2010). For example, in a recent study (Dixon and Christoff, 2012) we developed 'free-choice' versions of classic cognitive control tasks (Stroop, Wisconsin Card Sorting Task, Go/No-Go) in which subjects had the option of selecting an action that required effortful cognitive control, or a less demanding habitual action, and earned varying amounts of money depending on their choices. We found

clear evidence that subjects chose the action requiring cognitive control only when it was expected to yield a larger monetary payoff than the habitual action (Dixon and Christoff, 2012).

Cognitive control is often based on the use of rules that specify which actions to select and which to suppress. Thus, in order to discern the value of engaging cognitive control, it is critical to form associations between specific rules and the motivational outcomes that are expected to result from rule use. Using fMRI-adaptation we demonstrated that the LPFC represents such rule-outcome associations (Dixon and Christoff, 2012). Subjects performed a task in which they determined whether a face was male or female, or determined if a word had an abstract or concrete meaning, and had the opportunity to earn money on some trials if they responded quickly and accurately (Fig. 2A). This task required simple 'if-then' type rules to respond appropriately to the stimuli (e.g., if stimulus is a face and is male, then press button "1", if female then press button "2"). Importantly, each trial started with an instruction cue that signaled the currently relevant rule and which outcome to expect (money or no money). On some trials, a second instruction cue appeared prior to the stimulus, and across the two instruction cues, we manipulated whether there was repetition of the rules, repetition of the reward outcome, repetition of both the rules and the reward outcome, or no repetition (i.e., both the rules and outcome were novel). This allowed us to look for fMRI-adaptation — a change in the magnitude of neural activation when specific information is repeated versus novel. The results demonstrated that the right LPFC (including the inferior frontal sulcus/inferior frontal gyrus; IFS/IFG) exhibited fMRI-adaptation specifically when there was repetition of a specific rule-outcome pairing, but not when there was repetition of just the rules, or just the outcome (Fig. 2B). This finding provides evidence that the IFG/IFS *represented the association between a specific rule and an expected motivational outcome* (Dixon and Christoff, 2012). We also found sustained correlated activation between the right IFS/IFG and rule-related areas (posterior middle temporal gyrus, posterior parietal cortex, cerebellum), and between the IFS/IFG and reward-related areas (pregenual anterior cingulate cortex, nucleus accumbens, insula, OFC), consistent with a role in linking information about rules and reward outcomes (Dixon and Christoff, 2012). The LPFC has a well established role in implementing cognitive control by representing task rules (Asaad et al., 2000; Bunge, 2004; Cole et al., 2010; Miller and Cohen, 2001; Sakai and Passingham, 2006; Toni et al., 2001; Wallis et al., 2001). The findings reviewed above suggest that the LPFC is additionally involved in representing rule-outcome associations, which may play an important role in the initial decision of whether or not to engage cognitive control.

4.2. Integrating multiple pieces of information to discern the optimal course of action

The value of a particular option (e.g., buying a new home) is a function of multiple dimensions or variables: reward magnitude (how much do I like the home?), costs (e.g., what will the mortgage payments be?), probability (what is the probability that I will get the home based on my offer?), the timing of reward delivery (when is the move-in date?), and effort expenditure (how much work will I need to invest to improve my chances of getting the home?). The LPFC plays a role in representing these dimensions, especially when they need to be integrated for optimal decision making. Neuroeconomic studies have shown that LPFC activation correlates with reward magnitude (Hutcherson et al., 2012; Plassmann et al., 2007, 2010; Tobler et al., 2009), risk (Christopoulos et al., 2009; Gianotti et al., 2009; Tobler et al., 2009; Weber and Huettel, 2008), uncertainty (Huettel et al., 2005), delay discounted reward value (Kim et al., 2008), a strategy focused on reward probability (Venkatraman et al., 2009), and the cost of exerting cognitive effort

(McGuire and Botvinick, 2010). Notably, the LPFC plays a causal role in allowing this information to direct behaviors. LPFC lesions in monkeys disrupt the ability to estimate the reward-value of stimuli when the magnitude and delay until the reward are concurrently varied (Simmons et al., 2010), and altering DLPFC activation with electric current or TMS can influence decision making involving risk (Fecteau et al., 2007; Knoch et al., 2006a,b). One study of risky decision making had subjects make choices between options that varied in reward magnitude (number of points) and probability (Knoch et al., 2006a). One option (the 'risky' option) was associated with a large reward, but a low probability of winning, whereas the other option (the 'safe' option) was associated with a smaller reward, but a higher probability of winning. The difference in reward magnitude between the options varied, however, the reward was always larger for the safer option. The results demonstrated that subjects were more likely to select the risky option and earned less points earned overall following disruptive TMS to the right DLPFC as compared to sham stimulation (Knoch et al., 2006a). Notably, disrupting the right DLPFC led to more selections of the risky option regardless of the relative difference in reward magnitude between the options, suggesting a general diminished sensitivity to risk (Knoch et al., 2006a). These findings suggest that the DLPFC may be involved in combining information about reward magnitude and probability, and in promoting choices that are less alluring, but are actually more favorable.

Recent findings of Wallis and colleagues (Kennerley et al., 2009) demonstrated that the cingulate cortex rather than the LPFC represented multiple dimensions including reward magnitude, effort, and probability. However, those findings were derived from a simple task design in which the influence of each variable was examined separately (e.g., when reward magnitude was varied, effort and probability were held constant). In contrast, the LPFC appears to be particularly necessary for representing the value of choice options *when multiple dimensions are concurrently varied* (Simmons et al., 2010). Thus, as choice complexity increases and there is a greater amount of information to be integrated in order to maximize rewards, the LPFC appears to play a more prominent role. A prediction from this account is that LPFC involvement in value-based learning and decision making should be directly related to the number of dimensions that must be concurrently considered to discern the value of an option, and also the number of choice options that must be compared.

4.3. Pursuit of future rewards

Humans frequently pursue rewards that are delivered in the future, temporally separated from the actions that caused them (e.g., working to obtain a monthly paycheck). This pursuit is a great challenge, because actions directed toward future rewards often conflict with actions that could be taken to procure immediate rewards. The LPFC (in particular, mid-DLPFC) plays a crucial role in pursuit of future rewards. This is frequently examined using intertemporal choice tasks in which subjects decide between smaller monetary rewards that are available immediately and larger monetary rewards that are available after some delay (e.g., $4 now versus $10 in four weeks). The offer amounts vary, however, the immediate reward is always smaller than the future reward. Several fMRI studies employing such tasks have shown that LPFC activation is greater when subjects choose the larger delayed reward over the smaller immediate reward (Diekhof and Gruber, 2010; Hare et al., 2014; Jimura et al., 2013; Lebreton et al., 2013; McClure et al., 2004; Tanaka et al., 2004). Moreover, subjects are more likely to favor immediate over delayed rewards when the mid-DLPFC is taken "off-line" via TMS, suggesting a causal influence of the DLPFC on future reward valuation and choice (Essex et al., 2012; Figner et al., 2010). One study found that DLPFC disruption led

Fig. 2. Involvement of the LPFC in representing rule - outcome associations. Illustrated are the task paradigm and results adapted from Dixon and Christoff, 2012. (A) After a variable duration fixation cross, an instruction cue signaled the currently relevant rules (profile of faces = male/female rule; book = abstract/concrete rule) and whether or not to expect a monetary reward (blue vase = no money; bills = 25¢). This was followed by a variable duration delay period and then a word or face stimulus, during which subjects made a button response. Finally, a screen revealed whether money had been earned on that trial and cumulative winnings. On key trials, a second instruction cue appeared before the stimulus. Across the two instruction cues, there was repetition of the rules, expected reward, both, or neither (in this example, neither the rules nor the outcome is repeated). (B) Regions showing significant fMRI-adaptation ($Z > 2.57$, $p < .05$ FWE corrected for cluster extent) when there was repetition of both the rules and the expected outcome (i.e., a specific rule – outcome association) included the inferior frontal gyrus/sulcus (IFG/IFS), the inferior frontal junction/premotor cortex (IFJ/PMC), and the posterior dorsolateral prefrontal cortex (pDLPFC).

to a general shift toward immediate over delayed rewards irrespective of the difference in the offer amounts (Essex et al., 2012). This finding is most consistent with the idea that the DLPFC normally represents the value of delayed rewards, and discounts their value less steeply than other brain regions (Essex et al., 2012). Notably, the LPFC is not necessary for discerning the value of a single option, but rather, is only required when there is response conflict between future and immediate rewards (Figner et al., 2010). During such conflict, LPFC activation is negatively correlated with activation in subcortical reward areas (e.g., nucleus accumbens) that respond to immediate rewards (Diekhof and Gruber, 2010; Jimura et al., 2013). One possibility is that the LPFC is required to represent future rewards in an active state within working memory such that it results in a top-down bias on action selection (McClure et al., 2004).

Several additional findings also support the notion that the DLPFC is critical for pursuing future rewards. Individual DLPFC neurons carry information about reward magnitude and delay (Kim et al., 2008) and the long-term motivational context (i.e., what reward is expected across numerous trials) (Watanabe et al., 2002). Moreover, LPFC lesions interfere with the ability to integrate reward magnitude and timing information (Simmons et al., 2010). Finally, LPFC activation is greater when subjects choose food items based on health (a choice with future benefits) rather than taste (a choice with immediate benefits) (Hare et al., 2009).

In many real-life contexts, a series of actions that span a considerable amount of time is often necessary for obtaining a future reward (for example, a student must study regularly in order to obtain a favorable grade in a class). Thus far, empirical work has not examined this type of scenario, however, there is reason to believe that the mid-DLPFC should be especially important in these cases. Koechlin and colleagues have provided evidence that the mid-DLPFC is important for 'episodic control', the use behavior-guiding rules retrieved from memory to direct action when the environmental context does not provide sufficient information to discern the correct action (Koechlin et al., 2003; Koechlin and Summerfield, 2007; Kouneiher et al., 2009). In many cases, a future reward is not present or even cued by the environment and must be recalled from long-term memory to guide behavior. For example, while at home, a student may recall the memory of a future desired outcome (e.g., obtaining an 'A' in physics class) and this may provide an overarching context that triggers a set of studying rules that in turn guide a set of actions (e.g., pulling out the class textbook and highlighting important points). This resembles the idea of episodic control in that internally derived information from memory is used an overarching context that guides behavior. Future work is necessary to directly assess this hypothesis that the DLPFC may represent complex associations between rules and future outcomes that are retrieved from episodic memory.

4.4. Valuation of abstract concepts and beliefs

A recent development in evolutionary history is the ability to attach value to, and act in accordance with, abstract concepts and beliefs including social norms, philosophical ideals, religious values, national identity, etc. In general, these abstract beliefs do not generate immediate rewards, but do confer future benefits by regulating social interactions and promoting cooperation and reciprocation across time. Several lines of evidence suggest that the LPFC plays a critical role in representing the value of abstract concepts/beliefs.

The Ultimatum Game has been used to examine humans' valuation of fairness (a social norm). A proposer decides how to split a sum of money between herself and a partner (the responder) and a ubiquitous finding is that responders will invariably reject unfair offers (e.g., $8 for the proposer and $2 for the responder), despite the fact that the responder foregoes the $2 (Henrich et al., 2006). The idea is that responders reject unfair offers because they value and want to enforce the fairness norm, even though this means giving up an immediate reward; ensuring that partners adhere to fairness should theoretically result in long-term benefits across future encounters in naturalistic settings. Mid-DLPFC activation increases in responders when they are presented with an unfair offer (Baumgartner et al., 2011; Sanfey et al., 2003), and disrupting right DLPFC activation with TMS results in diminished rejection of unfair offers (Baumgartner et al., 2011; Knoch et al., 2006a,b). Thus, when the DLPFC is taken 'offline', individuals are less likely to enforce the fairness norm, consistent with the idea that the DLPFC provides top-down support for fairness goals and suppresses the pre-potent tendency to accept an immediate financial reward (Knoch et al., 2006b). However, to fully appreciate the role of the DLPFC, it is necessary to elucidate the information that it represents, as this is what determines the influence it will have on other brain regions. We suggest that the DLPFC represents the value of enforcing the fairness norm, and that this leads to a biasing influence on action selection in favor of rejecting unfair offers. Importantly, the DLPFC is not necessary for simple judgments about whether or not an offer is fair (Knoch et al., 2006b), likely because the financial incentive is removed (i.e., no money is lost for judging an offer to be unfair) and hence, there is no response conflict. Thus, the DLPFC is specifically needed to represent the value of fairness in situations of response conflict, when the value of fairness must be maintained in an active state within working memory in order to provide a top-down influence on action selection. Future studies

are needed to examine this hypothesis about the representational content supported by the LPFC.

Humans also value the abstract idea of a good reputation because it often results in benefits over the long-term (e.g., a restaurant with a reputation for good service and food will attract a greater number of customers over time). In an economic task known as the Trust Game, the 'investor' transfers money to a 'trustee', this amount is quadrupled, and then the trustee decides whether to keep all of the money, or to back-transfer a portion of the money. The trustee can develop a good reputation by reliably back-transferring money, and this will result in accruing more money over the long-term because future investors will be more likely transfer larger amounts of money. Thus, in each round, the temptation of an immediate reward (keeping all of the transferred money) competes with the more beneficial option of building a good reputation which will result in future rewards. A recent study found that subjects were less likely to resist the temptation of immediate monetary rewards in favor of developing a good reputation if the right DLPFC was disrupted using TMS (Knoch et al., 2009). It is currently unknown what critical information the right DLPFC normally represents that promotes reputation building during this task. One possibility is that it represents the value of reputation building, i.e., the causal association between reputation and long-term financial rewards. By actively maintaining this information in working memory, it could result in a top-down bias on action selection that allows reputation building to outcompete the desire for immediate monetary gain. Again, future work is needed to examine this hypothesis regarding the representational content supported by the LPFC.

Numerous studies have also demonstrated that LPFC activation increases when individuals process statements about religious beliefs, moral dilemmas, and other "sacred" values (e.g., national and ethnic identity) (Berns et al., 2012; Greene et al., 2004; Harris et al., 2009; Kapogiannis et al., 2009). Importantly, individual differences in ventral LPFC activation predicts religiosity (Kapogiannis et al., 2009) and subjects' everyday involvement in organizations related to sacred values (e.g., religious, political, charitable) (Berns et al., 2012). These findings are suggestive that the LPFC represents the motivational value of religious and moral beliefs, however, this idea has yet to be directly tested.

4.5. Comparing the value of executed and imagined alternative actions

When it is discovered that an action leads to a desirable outcome, it is usually good to stick with that action. However, by doing so, we may be foregoing even greater rewards associated with alternative actions. Thus, to discern the optimal strategy, the value of actions being currently executed must be constantly compared with the potential value of alternative (imagined) actions. The rostrolateral prefrontal cortex (RLPFC; BA 10) appears to have a primary role in this comparison process. Boorman et al. (2009) had subjects select one of two actions on each trial and varied the long-term probability that each action would be rewarded. Thus, subjects had to keep track of and compare the value of each action, and to periodically switch from one action to the other based on these changing values. They reported several key findings: 1) bilateral RLPFC (BA 10) activation correlated with the relative value of the imagined alternative action; 2) the magnitude of RLPFC activation predicted when a switch to the alternative action would occur; 3) switches were accompanied by increased functional connectivity between the RLPFC and the intraparietal sulcus and premotor cortex, regions that translate high-level plans into concrete actions (Boorman et al., 2009). Together, these findings provide strong evidence that the RLPFC represents the value of an alternative (imagined) action relative to the value of a currently chosen action (see also Boorman et al., 2011).

A similar study (Daw et al., 2006) employing a gambling task found that bilateral RLPFC activation ramped up during exploratory decisions, when subjects strayed from the most valuable slot machine based on recent evidence in order to determine if one of the other slot machines would yield a larger payoff. Consistent with this, Badre and Colleagues demonstrated that RLPFC activation during decision making is the strongest when there is the most uncertainty about the value of an alternative action, relative to an executed action (Badre et al., 2012). Notably, in contrast to RLPFC, VMPFC activation in these studies correlated with the value of the currently executed action (Boorman et al., 2009; Daw et al., 2006). Taken together, these studies suggest that RLPFC may represent the predicted value of an alternative action relative to a currently chosen action, and promote behavioral flexibility based on changing reinforcement contingencies. The idea that the RLPFC may represent the relationship between multiple action-value associations is a natural extension of its noted role in relational comparison during reasoning (Bunge et al., 2009; Christoff et al., 2001).

5. How is the role of the LPFC distinct from other frontal regions?

A key topic for future research is discerning how the contribution of the LPFC to value processes differ from neighboring frontal regions such as the OFC, VMPFC, and cingulate cortex. Some ideas can be gleaned from the studies reviewed here. First, in our fMRI-adaptation study described above, we found that associations between rules and reward outcomes were represented in the LPFC, but not in any other value-related region (e.g., the OFC, VMPFC, insula, or cingulate cortex) (Dixon and Christoff, 2012). Notably, there is considerable evidence that the OFC represents object-outcome associations (Gottfried et al., 2003; Kahnt et al., 2011; Kringelbach and Rolls, 2003; Rudebeck and Murray, 2011) and that the anterior mid-cingulate cortex represents action-outcome associations (Hayden and Platt, 2010; Matsumoto et al., 2003; Rushworth et al., 2007; Shima and Tanji, 1998; Williams et al., 2004). Thus, the LPFC may be distinguished from these regions by its ability to represent the value of rules (i.e., conditional stimulus-response associations), which is more complex than assigning value to a specific stimulus or action.

It is also interesting to note that the LPFC appears to be primarily necessary when there is response conflict between different options, particular when a weaker but more beneficial option (e.g., a large but delayed reward) must compete with a potent but less beneficial option (e.g., a small but immediate reward) (Baumgartner et al., 2011; Diekhof and Gruber, 2010; Figner et al., 2010; Knoch et al., 2006a,b, 2009; McClure et al., 2004). This suggests that several regions may be involved in representing choice options, however, the LPFC appears to be necessary for ensuring that the most advantageous options are *actually chosen*. One possibility is that the LPFC has a unique ability to represent weaker but more beneficial options (e.g., future rewards) in an active state within working memory in a manner that is resistant to distraction from other options, and provides a top-down bias on action selection. The LPFC is also distinguished from other value regions such as the VMPFC in that it often represents the value of alternative/exploratory choices, and may therefore have a key role in comparing multiple action-value associations and promoting behavioral flexibility when a new action may be more advantageous than a currently chosen action (Badre et al., 2012; Boorman et al., 2009; Daw et al., 2006).

Finally, the nature of the value signal supported by the LPFC may differ from that in other value regions. Unlike the VMPFC, insula, and ventral cingulate cortex, the LPFC is not well connected with subcortical regions (e.g., hypothalamus, amygdala, periacqueductal gray) that regulate the physiological state of the body. As such, the value information represented by the LPFC may be more abstract

and less grounded in the body. This may allow the LPFC to assign value flexibly to abstract information such as future rewards and concepts such as fairness, but at the cost of having less 'embodied motivational force'. This is an interesting area for future inquiry.

6. Causal evidence that the LPFC represents value information

The majority of the studies reviewed above utilized fMRI or electrophysiological recordings, and hence, only provide correlative evidence linking the LPFC to value-related information. As such, many of the findings presented here should be interpreted cautiously. However, in each section we also highlighted studies employing LPFC patients or the use of TMS to disrupt LPFC functioning, thus providing causal evidence that the LPFC contributes to value-related processes. To summarize, these studies have shown that disruption of the LPFC can result in motivational deficits including apathy (Fuster, 2008; Levy and Dubois, 2006; Paradiso et al., 1999; Zamboni et al., 2008), altered valuation of food items (Camus et al., 2009), less optimal decision making when it involves risk (Knoch et al., 2006a), difficulty integrating reward magnitude and timing information and diminished preference for delayed rewards instead of immediate gratification (Essex et al., 2012; Figner et al., 2010; Simmons et al., 2010), a greater tendency to choose immediate financial gain instead of the long-term benefits associated with fairness and reputation (Baumgartner et al., 2011; Knoch et al., 2006b, 2009), and less reliance on internal models of task structure to optimize reward acquisition (Smittenaar et al., 2013).

This work provides compelling support for the argument that the LPFC is causally involved in value-based decision making. That being said, more work is needed to corroborate the idea that this causal involvement is specifically linked to the representation of value, and not to representation of other components of the task. Essex and colleagues (2010) provided evidence along these lines, demonstrating that disrupting the DLPFC with TMS altered decision making between immediate and delayed rewards in a manner that was most consistent with a change in the value of the future rewards. It would be useful for future work to specifically explore the idea that the LPFC is causally involved in representing the reward value of rules, given the hypothesis presented above, that a distinguishing function of the LPFC may be to bridge cognitive control and value processing. For example, one prediction would be that human patients or monkeys with LPFC lesions should have difficulty learning which of two rules to use based on probabilistic reward feedback, and should exhibit problems shifting between the rules when contingencies change. To ensure that this deficit is due to difficulty representing the value of rules and not simply to difficulty representing the rules themselves, this condition could be compared against a separate condition in which the correct rule is explicitly cued.

7. Rostro-caudal organization of the LPFC: bridging the cognitive control and decision making literatures

There is now compelling evidence from the cognitive control literature suggesting that LPFC representations are organized along a roughly caudal to rostral gradient, with progressively more rostral subregions supporting increasingly complex/abstract representations (Badre and D'Esposito, 2007, 2009; Christoff and Gabrieli, 2000; Christoff and Keramatian, 2007; Christoff et al., 2009; Koechlin et al., 2003; Petrides, 2005; Sakai and Passingham, 2006). Accordingly, this information should be utilized in discerning the role of the LPFC in value processing (Coutlee and Huettel, 2012). We offer a preliminary framework based on extant data (Fig. 3). More caudal and ventral parts of the LPFC may represent associations between simple rules (i.e., fixed stimulus-response associations) and expected motivational outcomes, particularly when this information is directly signaled by the environment. Moving further dorsal and rostral, the mid-DLPFC may be called upon when the environment does not specify all pertinent information, and the individual must draw upon episodic memory or future simulation to determine desired outcomes and overarching rules for behavior. This is consistent with data showing prominent DLPFC involvement in pursuing future rewards. In short, mid-DLPFC may represent the relationship between more complex/abstract rules for action and desired outcomes. Finally, at top of the hierarchy, the RLPFC may represent the relationship between multiple action-outcome or rule-outcome associations, and in doing so, facilitate behavioral flexibility by prioritizing motivational goals, and constantly determining whether a better course of action should be taken. This partition of the LPFC and corresponding value processes is clearly simplistic, and is only meant as a starting point for organizing existing findings, and generating predictions that can be used in future studies.

8. Summarizing the role of the LPFC in value-based processing

The electrophysiological, neuroimaging, and lesion evidence reviewed here provides compelling evidence that the LPFC plays an important role in complex value-based learning and decision
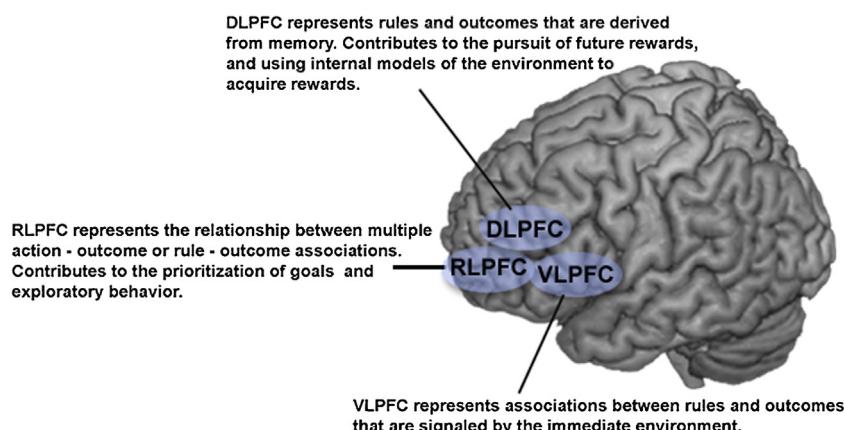

Fig. 3. Value processing along the rostro-caudal axis of the LPFC. This figure illustrates a simplistic division of labor in the LPFC, with a general increase in the complexity of value processing from ventrolateral prefrontal cortex (VLPFC; BAs 44 and 45) to mid-dorsolateral prefrontal cortex (DLPFC; BAs 9 and 46) to rostrolateral prefrontal cortex (RLPFC; BA 10).

making. We have emphasized the *information* represented by the LPFC and suggest that it includes value information in relation to cognitive information (e.g., task rules) and that this allows the LPFC to exert an adaptive top-down influence on more basic value and action processes occurring in other regions. Indeed, accumulating evidence is consistent with the idea that the LPFC supports a valuation system distinct from the VMPFC valuation system (Boorman et al., 2009; Essex et al., 2012; Hutcherson et al., 2012; Jimura et al., 2013; McClure et al., 2004; Plassmann et al., 2007). However, more work examining the precise causal contribution of the LPFC is necessary, and therefore, many of the findings and interpretations presented here should be taken cautiously. Nevertheless, some consistent patterns are emerging, and indicate that the LPFC contributes to complex value-based processes in the following ways: (1) it represents the value of choice options in demanding situations in which multiple dimensions (e.g., reward magnitude, delay, effort) vary concurrently and must be integrated to discern the optimal course of action; (2) it represents beneficial choice options in an active state within working memory when they must compete against a potent alternative (e.g., a future reward versus an immediate reward); (3) it represents the value of employing cognitive control (the use of effortful rules for behavior); and (4) it represents the value of abstract concepts/beliefs such as fairness.

Finally, it is worth noting that the LPFC certainly operates within the context of interactions with distributed cortical and subcortical regions. Indeed, the anatomical data reviewed earlier was intended to convey the message that the LPFC is ideally situated to interact with, and accumulate information from widely distributed "cognitive" and "motivational" regions. Therefore, an important avenue for future work will be to articulate the precise nature of these interactions and how they give rise to a diverse array of complex value-guide behaviors.

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