The Ventromedial Frontal Lobe Contributes to Forming Effective Solutions to Real-world Problems

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Abstract

■ Although the ventromedial frontal lobe (VMF) has been implicated in several complex cognitive tasks such as decision-making and problem solving, the processes for which this region is critical remain unclear. Laboratory studies have largely focused on how the VMF contributes to decision-making when outcomes or options are provided, but in the real world generating appropriate options is likely a crucial and rate-limiting initial step. Here, we determined how VMF damage affected the option generation phase of naturalistic problem solving. A group of patients with VMF damage and two controls groups —age-matched healthy participants and patients with frontal damage sparing VMF—were asked to generate as many options as possible to five scenarios depicting open-ended, real-world problems (e.g., having lunch at a restaurant and forgetting your wallet at home). Both the number of options and the effectiveness of each option generated were examined. Damage to VMF led to a significant reduction in both the number of options produced across all problem-solving scenarios and the ability to generate effective options, most notably for scenarios that were social in nature. We discuss these findings in terms of the mechanisms by which the VMF may contribute to option generation, focusing on proposals suggesting this region is important for integrating subjective value and retrieving schematic representations. ■

INTRODUCTION

Daily life provides a steady stream of ambiguous problems, from deciding what to eat for dinner to figuring out how to deal with an obnoxious neighbor. A first step in solving such problems is to construct a set of potential options that can be evaluated with respect to how effectively each resolves the current dilemma. Much of the research investigating the neural mechanisms of problem solving has focused on the role of the pFC and specifically the ventromedial frontal lobe (VMF; here referring both to ventromedial pFC and adjacent OFC) in the later evaluation and decision stages (Gerlach, Spreng, Gilmore, & Schacter, 2011; Tom, Fox, Trepel, & Poldrack, 2007; Valentin, Dickinson, & O'Doherty, 2007; Manes et al., 2002; Bechara, Damasio, Damasio, & Lee, 1999; Baker et al., 1996; Shallice, 1982). Less is known about the neural correlates of the initial generation or identification of options, which represents a key step in real-life decision-making and problem solving (Kaiser et al., 2013; Klein, 2008; Fellows, 2006). The aim of the current study was to investigate the brain basis of this option generation phase in real-world problem solving, focusing specifically on the contributions of the VMF.

To date, the majority of problem solving studies have employed structured or well-defined tasks (e.g., Tower of Hanoi) to provide evidence that selective lesions to the pFC affect general problem-solving ability (Baker et al., 1996; Owen, Downes, Sahakian, Polkey, & Robbins, 1990; Shallice, 1982). Yet, real-world problems are often open-ended in that they are not associated with a set algorithm to reach a well-defined goal (Sheldon et al., 2015; Sheldon, McAndrews, & Moscovitch, 2011). Solving such problems requires several different cognitive stages (Kaiser et al., 2013; Smaldino & Richerson, 2012; Porcelli & Delgado, 2009; Fellows, 2004; Johnson & Raab, 2003; Klein, Wolf, Militello, & Zsambok, 1995; Keller & Ho, 1988), beginning with accessing relevant knowledge to create and evaluate multiple solutions or options (Goel, 2010; Channon, 2004; Goel & Grafman, 2000; Goel, Grafman, Tajik, Gana, & Danto, 1997) before a decision can be made.

There are suggestions that the VMF contributes to real-world open-ended problem solving. For example, a single case study described a patient where damage to the VMF resulted in striking deficits in navigating real-world problem scenarios (Eslinger & Damasio, 1985). Although this patient performed well on lab-based tasks related to choice and planning (e.g., the Wisconsin Card Sorting task) and could logically reason his way through hypothetical ethical dilemmas, he was unable to make appropriate decisions or solve simple problems in real-world open-ended settings (e.g., deciding on a restaurant for dinner). Although clinical observations, such as the case noted above, point to a general role for the VMF in open-ended problem solving, evidence that this region might contribute specifically to the option generation phase comes from the decision-making literature, which supports VMF involvement in evaluating outcomes for goal-oriented behaviors (Fellows, 2011; Grabenhorst & Rolls,

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2011; Padoa-Schioppa, 2011; Rushworth, 2008). The VMF is thought to be involved in encoding and comparing the relative value of potential problem outcomes or decision choices (for a review, see Levy & Glimcher, 2012). In support, neuroimaging reports have found that VMF activity correlates with value judgments and predicts choice behavior (Levy, Lazzaro, Rutledge, & Glimcher, 2011; Padoa-Schioppa, 2011; Rangel & Hare, 2010; Plassmann, O'Doherty, & Rangel, 2007), and neuropsychological data have shown that VMF lesions result in inconsistent choice behavior and deficits in linking value to choice options (Henri-Bhargava, Simioni, & Fellows, 2012; Camille, Griffiths, Vo, Fellows, & Kable, 2011; Tsuchida, Doll, & Fellows, 2010). One possibility is that the same VMF processes involved in evaluation of specified options are also involved in identifying potential options in ambiguous or open-ended situations. In line with this hypothesis is work demonstrating that the value of options are computed "online" as they are generated (Padoa-Schioppa, 2011), and the relative quality of these options is continuously evaluated (and updated) until the most appropriate one comes to mind and option generation is terminated (Johnson & Raab, 2003; Gigerenzer & Goldstein, 1996).

Another process plausibly important for option generation is retrieving associated scripts and schemas. In the context of problem solving, schemas can act as knowledge structures or scaffolds to direct a controlled search through memory for details related to potential options (Moscovitch & Melo, 1997). Damage to VMF has been shown to result in deficits in schema reinstatement, in memory and nonmemory tasks (Ghosh, Moscovitch, Colella, & Gilboa, 2014), and impaired information search during predecisional stages of unstructured problem solving (Eggen et al., 2015). VMF-dependent schema reinstatement may be critical for implementing an appropriate framework that can help one both construct and "test out" hypothetical solutions during option generation (Sheldon et al., 2011, 2015; Vandermorris, Sheldon, Winocur, & Moscovitch, 2013).

In short, these two literatures suggest that the VMF might contribute to option generation. To directly test this hypothesis, we presented a series of naturalistic open-ended scenarios to three groups of participants—individuals with lesions affecting the VMF, individuals with frontal damage sparing the VMF, and healthy controls—and asked them to generate as many options as possible. Our main objective was to test the prediction that VMF lesions would impair the number and quality of options generated in response to these open-ended problems. As a secondary objective, we explored whether predicted impairments were related to the nature of the problem, contrasting social and nonsocial scenarios. This was based on work that has implicated a preferential role for the VMF in self-insight as well as social and emotional processing (e.g., Beer, John, Scabini, & Knight, 2006; Channon, 2004; Damasio, Tranel, & Damasio, 1990), which we hypothesize is important for constructing appropriate options to social problems.

METHODS

Participants

Twenty-three patients with stable focal damage to the frontal lobe of at least 6 months duration were recruited from the research database of the Center for Cognitive Neuroscience at the University of Pennsylvania. The patients were further categorized into two groups, based on their most recent CT or MR imaging: Those with damage affecting the VMF, defined as the medial portion of the OFC and the adjacent ventral portion of the medial wall of the pFC (Wheeler & Fellows, 2008; Fellows, 2007), were assigned to the group of interest ($n = 12$; 7 women). Damage to the VMF was due to aneurysm rupture ($n = 8$), low-grade tumor resection ($n = 1$), or ischemic stroke ($n = 3$), and five patients were taking at least one psychoactive medication, most commonly an anticonvulsant. Of the 12 VMF patients, seven had lesions that were primarily left-lateralized, three that were primarily right-lateralized, and two that were bilateral. Three VMF patients had lesions extending into the dorsomedial frontal region (see Figure 1, slice 40); however, none of the reported results were driven by their performance on experimental tasks as their scores were well within the range for VMF group as a whole.

Patients with frontal damage sparing this region were assigned to the frontal control group ($n = 11$; 7 women). Here, damage was due to ischemic stroke ($n = 7$), hemorrhagic stroke ($n = 1$), or low-grade tumor resection ($n = 2$), and five patients were taking a psychoactive medication, again, most commonly an anticonvulsant. Lesions were manually registered to a standard template by a neurologist with experience in image analysis to allow lesion overlap images to be created (Figure 1).

Healthy control participants ($n = 22$; 17 women), age-matched to the patient groups (VMF: $t = 0.962, p > .05$; frontal control: $t = 0.369, p > .05$), were recruited from the local community by advertisement. All of the control participants indicated that they were free of neurological or psychiatric conditions. On average, all groups were educated to a high school level or beyond (Table 1), and there was no significant difference in years of education between groups ($F(2, 42) = 3.187, p > .05$). Although the difference between VMF and frontal control groups approached significance ($t = 2.399, p = .053$), variation in years of education beyond high school has been shown not to affect real-world problem solving (Burton, Strauss, Hultsch, & Hunter, 2006; Cornelius & Caspi, 1987). To test this assumption in our own sample, we have, where appropriate, included years of education as a covariate in analyses. The protocol used in this study was approved by the institutional research ethics board; all participants received an honorarium in exchange for participation and provided written informed consent.

Neuropsychological Measures

A battery of standardized measures was administered to each participant to establish general intellectual functioning,

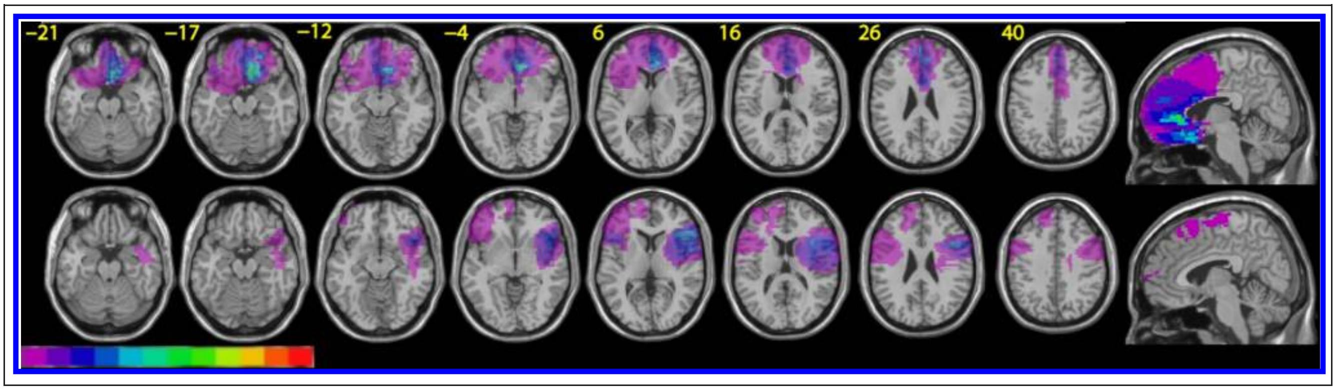

Figure 1. Lesion overlap images for VMF (top) and frontal control (bottom) groups, shown on axial (oriented so that left is right) and midsaggital slices of the MNI brain. The same slices are shown for both groups with slide numbers provided for reference. Warmer colors indicate greater degree of lesion overlap, as shown in the legends. Pale purple indicates voxel damage in only one subject.

verbal fluency, and subjective reports of mood. Crystallized intelligence was estimated using the American National Adult Reading Test (Grober, Sliwinsk, & Korey, 1991). The Beck Depression Inventory (BDI-II; Beck, Ward, & Mendelson, 1961), a 21-item self-administered measure, was used to assess symptoms associated with depression. Participants also completed two measures of verbal fluency: a semantic fluency task, which required participants to generate as many instances as possible of a particular category (animals) in 60 sec, and a phonemic fluency task, in which participants generated as many words as possible that began with a specific letter ("F", "A," and "S") in 60 sec (Bechtoldt, Benton, & Fogel, 1962; Thurstone, 1938). Mean scores for all measures are presented in Table 1.

Problem-solving Measure

Participants were given a battery of experimental tasks that included the problem-solving measure of interest: the option generation task. The experimenter administering the task was blind to the patient groups and study hypotheses, although he or she was aware of the patient to healthy control distinction.

Stimuli. Five real-world scenarios representing problems individuals could encounter in everyday life were developed for the experiment and are presented below. All of the problem scenarios were designed to be open-ended, in that there was no single solution or established script associated with resolving the problem. Because the VMF has been linked to social processing during everyday problem-solving tasks (e.g., Channon, 2004), both social and nonsocial scenarios were included. Social scenarios (Problems 1 and 2) contained an interpersonal conflict that was to be resolved, whereas nonsocial problems (Problems 3–5) did not include social confrontation as a central feature of the problem. All scenarios (listed below) were presented as a short statement, setting the scene with a description of the problem to be resolved.

Problem 1 (Social): You go to a dinner party at a friend's house. When you get there, you find that another of your friends is angry with you and won't speak to you. What can you do?

Problem 2 (Social): You are involved in a group project that requires you to work with several of your coworkers. One coworker has not been doing all of his assigned work and, as a result, you have had to take on more work to make up for this. What can you do?

Problem 3 (Nonsocial): You treat yourself to a nice lunch at a fancy restaurant. When the bill for $25 comes, you realize that you have left your wallet at home. You have no money to pay for lunch. What can you do?

Table 1. Demographic and Clinical Information, Mean (*SD*)

Group	*Age (years)*	*Education (years)*	*Estimated IQ*	*Beck Depression Inventory*	*Phonemic Fluency ("F")*	*Category Fluency ("Animal")*	*Lesion Volume (cc)*
Healthy$_{CTL}$ (n = 22)	57.7 (2.0)	14.8 (2.3)	124.1 (2.1)	4.0 (0.8)	13.9 (4.9)	21.4 (7.2)	
Frontal$_{CTL}$ (n = 11)	58.0 (3.3)	15.5 (2.7)	120.2 (3.8)	10.27 (1.4)	10.3 (3.8)	15.6 (4.4)	27.5 (18.3)
VMF (n = 12)	55.7 (3.4)	13.1 (2.2)	114.6 (2.6)	12.75 (2.6)	10.7 (5.4)	15.4 (5.4)	22.9 (21.0)

Problem 4 (Nonsocial): You are awoken at 2 a.m. by the sound of loud music. It seems that your next-door neighbors are having a big party. What can you do?

Problem 5 (Nonsocial): You usually drive your car to work each morning. One morning you get in your car to drive to work and you discover that the car won't start. What can you do?

To validate the social versus nonsocial problem classification, we collected ratings on the social content of each problem via Amazon's Mechanical Turk (MTurk) crowdsourcing platform (www.mturk.com). Eighty raters used a sliding scale ranging from 0 (*nonsocial*) to 100 (*social*) to indicate the amount of interpersonal contact they believed would be involved in the resolution of each problem. After removing one respondent for rating every problem as 0% social, we found that our social problems (Problems 1 and 2) were given a significantly higher rating of social content (average = 75) compared with our nonsocial problems (Problems 3–5; average = 57; $t = 5.714$, $p < .001$).

Procedure

The five problems were delivered verbally to participants, in the same order, alternating between social and nonsocial. For each problem, participants were instructed to generate as many options or ways to solve the problem as they could. No time limit was given; participants were allowed to speak until they felt they had exhausted all potential options, thereby eliminating some of the influence of individual differences in verbal fluency and cognitive speed. A single general prompt to "keep thinking" was given when a participant stopped generating options. The experimenter recorded all responses for scoring.

Problem-solving Scoring: Option Fluency

Before scoring, each participant was assigned a code by a separate experimenter, and files containing response data were scrambled. Only when all scoring was complete and verified by a second scorer were deidentified participants assigned back to their experimental groups. For each problem, the total number of options generated was tallied. These options were further classified as valid or nonvalid. An option was considered valid if it described an action an individual was capable of carrying out in the given situation, regardless of whether the action was practical. An option was scored as nonvalid if it was unrelated to the given problem, if it was a repetition of a previous response with minor variations (e.g., "call mom," "call dad," "call sister"), or if it was not an action but a thought (e.g., "I like the mall") or value judgment (e.g., "stealing is wrong"). We summed the number of valid options across all problem scenarios as well as for social and nonsocial problems.

Problem-solving Scoring: Option Quality

We established the quality of all of the options generated by participants by collecting independent ratings of option effectiveness from 50 unbiased raters (average age = 33.13 [±1.7] years; average education = 14.8 [±0.3] years) recruited online via MTurk. To limit MTurk rater burden, similar options that were generated to a given problem were summarized as a single, more general option. For example, "call family member or friend to bring money" is specific enough that it represents a unique option but broad enough to include multiple variations on the same option (e.g., "call my mother," "call a work colleague," "call my roommate"). The first author (S.P.) determined a maximum of 20 general option categories for each problem, which were independently verified by a second researcher. Only options previously scored as valid were included in this analysis.

MTurk respondents were presented with each of the five problems followed by a list of these general options. The order of options was randomized for each respondent. MTurk raters rank-ordered the options from most to least effective. We averaged the rank order ratings across all 50 respondents and then applied this score to each option generated by each participant. Using this method, higher-quality options were associated with lower average ratings (e.g., 1 = *most effective*, 20 = *least effective*). For the sake of clarity, we plotted the inverse of average rankings in the associated figures. In this way, higher average rankings were associated with more effective options. Outlandish options (e.g., "sell my firstborn"), which failed to fit into any of the general MTurk option categories, were given the same score as the option category with the highest average rating (indicating lowest effectiveness) within that response set. For example, for the Lunch Problem, "yell fire and run" was rated the least effective option with an average MTurk score of 15.59. The response "sell my firstborn" did not fit into any of the MTurk ranking categories so it was assigned a score of 15.59. These independent quality ratings were used to generate measures of total, social, and nonsocial problem-solving effectiveness.

Statistical Analyses

ANOVA and ANCOVA tests were performed in JASP (Version 0.7.5.5), and nonparametric chi-square tests of independence were performed in SPSS statistical software (Version 23; IBM Armonk, NY). All tests used $\alpha = 0.05$ as a cutoff for determining statistical significance, although effect size was also of interest and is reported throughout. Group comparisons were performed with ANOVA, using Group (VMF lesion, frontal control, healthy control) as the between-subject factor and Total number of options, Number of valid options, and MTurk quality scores as dependent variables. Additional comparisons were performed using ANCOVA with Group as the between-subject factor while covarying out semantic fluency scores or years to education to account for potential group differences in verbal output or education. For ANCOVA analyses, models were computed using Type I Sums of Squares. Sample sizes were unequal, and this model uses weighted marginal means and therefore is more appropriate. Furthermore, we were primarily interested in the main effect of group on option generation performance, and using Type I Sums of Squares in our model offers more power to address this interest. In all cases, group was entered into the model first, followed by category fluency scores or years of education. All post hoc comparisons were performed with Tukey's honest significant difference to control for multiple comparisons.

RESULTS

Neuropsychological Screening

Demographic information and neuropsychological test results are presented in Table 1. Participants did not differ on the measure of crystallized IQ (American National Adult Reading Test). As is typical for neurological clinical samples, scores on the Beck Depression Inventory were slightly higher for the VMF lesion group and the frontal control group compared with healthy control participants ($F(2, 39) = 8.463$, $p < .001$), although none of the participants were diagnosed with clinical depression.

Phonemic and semantic ("Animal") verbal fluency scores are presented in Table 1 (note that we report only results from the "F" trial of the phonemic fluency task as incomplete data was collected for the "A" and "S" trials). An ANOVA with Group (3; healthy control, frontal control, and VMF lesion) as a between-subject factor revealed a significant effect on Semantic fluency ($F(2, 42) = 5.110$, $p = .01$). Healthy controls generated significantly more items than both the VMF lesion group ($t = 2.703$, $p_{\text{tukey}} = .026$) and frontal control group ($t = 2.531$, $p_{\text{tukey}} = .039$), whereas the VMF lesion and frontal control groups generated a similar number of exemplars ($t = 0.085$, $p_{\text{tukey}} = .996$). There was no group difference in the number of items generated in the phonemic fluency task ($F(2, 42) = 2.824$, $p = .071$).

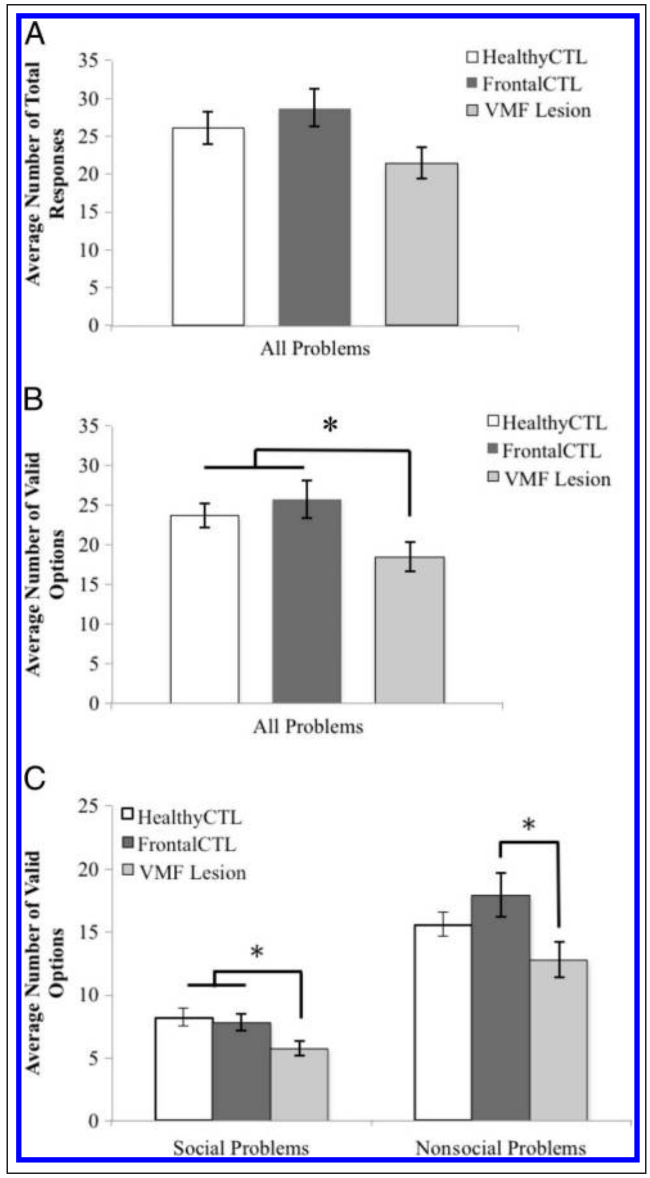

Figure 2. Option fluency in open-ended problem solving. (A) Average number of responses generated by patients with lesion to the VMF as compared with healthy and frontal controls summed across all problem types. (B) Average valid options produced by the VMF group compared with healthy and frontal control groups. (C) Average number of valid options generated by the VMF group compared with both healthy and frontal control groups for social and nonsocial problem subtypes. Standard errors bars are shown. *$p < .05$.

Problem-solving Measures

Option Fluency

On average, participants generated 25.5 (±9.3) options across all five problems. Although there were no statistical differences in total number of generated options between the three tested groups ($F(2, 42) = 1.936$, $p = .157$, $\eta^2 = 0.084$; Figure 2A), there was a statistically significant effect of Group on the Number of valid options generated ($F(2, 42) = 3.291$, $p = .047$, $\eta^2 = 0.135$). This effect remained significant when Years of education ($F(2, 41) = 5.099$, $p = .011$, $\eta^2 = 0.135$) or Semantic fluency scores ($F(2, 41) = 3.284$, $p = .048$, $\eta^2 = 0.122$) were included as covariates to control for potential differences in education or verbal output, respectively (Figure 2B).

On the basis of a priori hypotheses concerning VMF contributions to option generation, we ran select pairwise comparisons to better understand the main effect of Group on valid option fluency. First, we directly compared those with VMF damage to healthy control participants. The VMF group generated significantly fewer valid options compared with healthy controls ($F(1, 32) = 4.486$, $p = .042$, $\eta^2 = 0.123$; $M_{\text{Control}} = 23.73$ [$SD = 7.9$] vs. $M_{\text{VMF}} = 18.50$ [$SD = 6.4$]; Figure 2B). This pattern was evident for social problems ($F(1, 32) = 5.295, p = .028, \eta^2 = 0.142$; $M_{Control} = 8.35$ [$SD = 3.4$] vs. $M_{VMF} = 5.75$ [$SD = 2.1$]) but not for nonsocial problems ($F(1, 32) = 2.899, p = .098, \eta^2 = 0.083$; $M_{Control} = 15.55$ [$SD = 4.4$] vs. $M_{VMF} = 12.75$ [$SD = 4.9$]; Figure 2C). There were no differences in the number of options produced between the frontal and healthy control groups (Figure 2A–C).

Next, we directly compared the performance of the VMF group with that of the frontal control group. An ANOVA with Group (frontal controls and VMF) as a between-subject factor found a significant effect on the Number of valid options generated ($F(1, 21) = 5.833, p = .025, \eta^2 = 0.217$) with the VMF group providing significantly fewer valid options than frontal controls ($M_{frontalCTL} = 25.73$ [$SD = 7.9$] vs. $M_{VMF} = 18.50$ [$SD = 6.4$]; Figure 2B). A subsequent analysis revealed that this pattern was present for both social ($F(1, 21) = 4.962, p = .037, \eta^2 = 0.191$) and nonsocial problems ($F(1, 20) = 5.354, p = .031, \eta^2 = 0.203$; Figure 2C).

Option Quality

Option Effectiveness

To compare overall quality of the valid options, while controlling for the above-reported differences in option fluency, we averaged the effectiveness ratings gathered from the MTurk raters for each participant. An ANOVA revealed a significant effect of Group (healthy controls, frontal controls, and VMF) on the Average effectiveness ratings across all problems types ($F(2, 42) = 6.074, p = .005, \eta^2 = 0.224$; Figure 3A). These Group differences remained significant when Years of education was included as a covariate ($F(2, 41) = 5.917, p = .006, \eta^2 = 0.221$).

Follow-up analyses revealed that the VMF group produced valid options of lower overall quality across all problems relative to healthy control participants; however, this difference was not statistically significant ($F(1, 32) = 2.940, p = .096, \eta^2 = 0.084$; Figure 3A). A closer look revealed that the VMF group exhibited an impairment in providing effective options to social problems ($F(1, 32) = 14.57, p < .001, \eta^2 = 0.313$) but not to nonsocial problems ($F(1, 32) = 2.779, p = .105, \eta^2 = 0.080$) as compared with the healthy controls (Figure 3B). There was no significant difference in the quality of valid options between the VMF and frontal control groups, across all problems ($F(1, 21) = 1.643, p = .214, \eta^2 = 0.073$). Further examination revealed that the VMF group generated valid options of lower quality for social problems and relatively higher quality for nonsocial problems compared with frontal controls (Figure 3B); however, these differences were not statistically significant.

Differences were found in the quality of options generated by the frontal and healthy control groups ($F(1, 31) = 17.84, p < .001, \eta^2 = 0.365$; Figure 3A), which we report for the sake of completeness. This effect was driven almost exclusively by a deficit in nonsocial problem solving, where

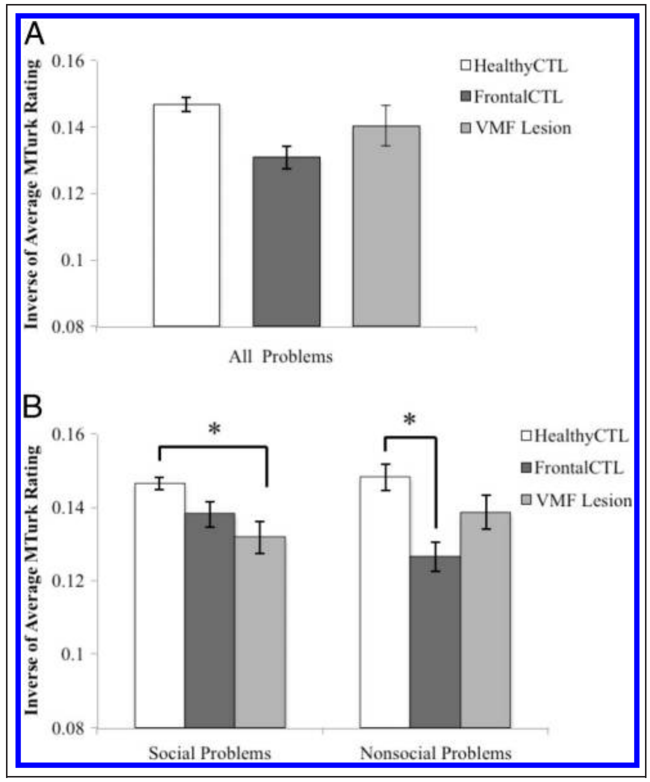

Figure 3. Effectiveness of options generated during open-ended problem solving. (A) Average quality, as determined by unbiased raters, of options generated by patients with lesion to the VMF as compared with healthy and frontal control participants across all problem types. (B) Average quality of options generated by the VMF group compared with healthy and frontal control groups to social and nonsocial problems. Standard errors bars are shown. $*p < .05$.

frontal controls produced options of significantly poorer quality compared with healthy controls ($F(1, 31) = 14.93, p < .001, \eta^2 = 0.325$; Figure 3B). The quality of valid options produced for social problems did not differ between the two control groups.

Presence of the Most Effective Option

To further investigate the quality of generated options, the most effective option was identified based on the MTurk quality ratings for each of the five problems. We searched each participant's response set to the problem scenarios for the option ranked as most effective. A problem was coded a "1" if participants included the most effective option and a "0" if they did not. We used a chi-square test of independence with Yates Continuity Correction to determine if the proportion of participants who included the best option in their response set was significantly different between groups. A 3 (Group) × 2 (Social, nonsocial) contingency table indicated that, between groups, the difference in the proportion of individuals who included the most effective option approached significance ($\chi^2_{(2)} = 5.373, p = .068$, Cramer's $V = 0.158$). Follow-up comparisons revealed a significant difference between the VMF group and healthy control group ($\chi^2_{(1)}$ = 5.386, p = .020). The VMF group was significantly less likely to generate the best option across all problems compared with healthy controls (Control: 84% vs. VMF: 68.3% of problems; Figure 4A). Subsequent analyses showed that this finding was driven by differences in options generated to social problems, with 92.5% of healthy controls compared with 66.7% of the VMF group including the most effective option in their response set ($\chi^2_{(1)}$ = 5.386, p = .008; two-tailed Fisher's exact test, p = .014, Cramer's V = 0.331; Figure 4B). There was no significant difference between the VMF and healthy control groups for the nonsocial problems (Control: 78.3% vs. VMF: 69.4%; $\chi^2_{(1)}$ = 0.948, p = .330; two-tailed Fisher's exact test, p = .342, Cramer's V = 0.099; Figure 4B).

A final set of chi-square tests of independence revealed no significant differences between VMF group and frontal control group in the probability of including the most effective option to all problem scenarios ($\chi^2_{(1)}$ = 1.551, p = .213, Cramer's V = 0.117; Figure 4A) as well as social ($\chi^2_{(1)}$ = 2.448, p = .118, Cramer's V = 0.231) and nonsocial ($\chi^2_{(1)}$ = 0.090, p = .764, Cramer's V = 0.036; Figure 4B) problems when examined separately.

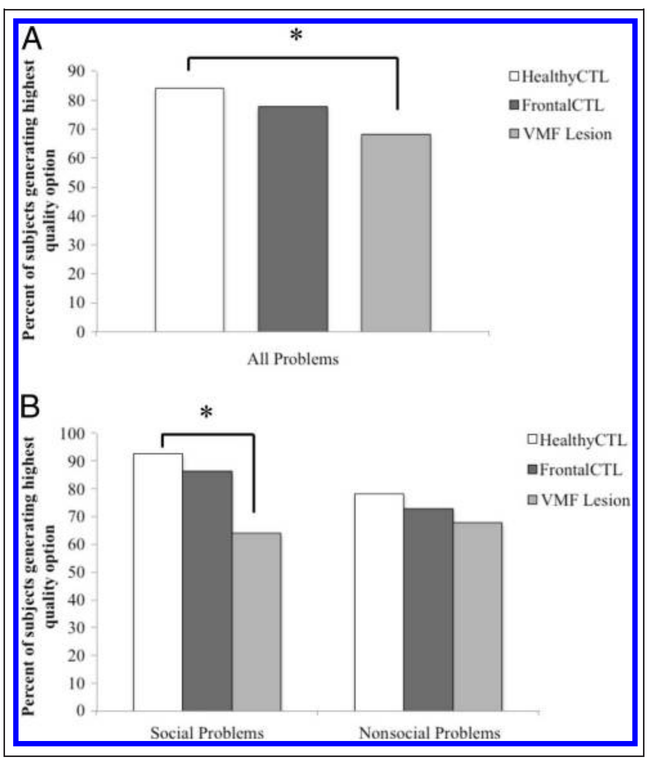

Figure 4. Presence of the most effective option in the response set generated to real-world problems. (A) Percentage of patients with damage to the VMF compared with healthy and frontal controls who included the most effective option in the response set generated across all problems. (B) Percentage of the VMF group who included the most effective option to social and nonsocial problems compared with healthy and frontal controls. Option effectiveness was determined by unbiased raters. Standard errors bars are shown. *p < .05.

DISCUSSION

The primary objective of this study was to test whether VMF, a brain region implicated in multiple aspects of complex goal-oriented behavior, is involved in the option generation phase of open-ended real-world problem solving. We measured the ability of three groups of participants—patients with VMF lesions, patients with frontal damage sparing the VMF, and healthy controls—to generate multiple potential options to open-ended problem scenarios. We observed that patients with VMF lesions produced fewer valid options for these problems than both the frontal and healthy control groups. Moreover, we found that VMF patients produced options that were significantly less effective than either control group, as judged by an independent sample of raters recruited from an online testing platform. This effect was most prominent for social problems; the quality of options produced by the VMF group to nonsocial problems appeared relatively spared. Taken together, these data expand upon the established role of the VMF by suggesting that this region also contributes to the early option generation phase of problem solving. Below we discuss potential processing contributions of the VMF to this phase.

VMF and Option Generation

The majority of the studies examining how VMF damage affects higher-order cognitive tasks (i.e., decision-making and problem solving) have reported deficits in evaluation and choice behavior when options are externally provided (for reviews, see, e.g., Fellows, 2011; Zald & Andreotti, 2010; Channon, 2004). In the decision-making literature, this deficit is often explained using an economic framework, wherein VMF lesions result in errors in computing the subjective value of presented options (e.g., Camille et al., 2011). Applying this framework to option generation during open-ended problem solving, it may be that the VMF is important for accurately assigning and integrating the value of different options as they come to mind, a process that is disrupted following damage to this region. In other words, when the VMF is compromised, potentially effective options may be discarded (i.e., not generated) before conscious deliberation and choice. Furthermore, because the influence of evaluation and option generation is likely bidirectional (Fellows, 2011), over- or undervaluing certain options could lead to prematurely terminating option generation before the most appropriate option is produced.

Another possibility is that the VMF contributes to option generation by retrieving schemas related to a given problem (i.e., thinking about a familiar life script or scenario), thereby guiding the mental search for potential options and allowing an individual to appropriately integrate relevant past information with a current context or scenario (Spalding, Jones, Duff, Tranel, & Warren, 2015; Ghosh et al., 2014). Along these lines, prior research has specifically implicated VMF in strategic search processes and response monitoring during a variety of tasks (Eggen et al., 2015; Ghosh et al., 2014; van Kesteren, Fernández, Norris, & Hermans, 2010; Zeithamova & Preston, 2010; Kumaran, Summerfield, Hassabis, & Maguire, 2009; Moscovitch & Melo, 1997). Other work has noted that the VMF is functionally connected to brain regions important for schematic knowledge processing (e.g., the dorsal medial pFC and parahippocampal cortex), and these connections are stronger when individuals are prompted to think of familiar (i.e., more schematic) as compared with novel scenarios (Benoit, Szpunar, & Schacter, 2014). It follows that if VMF lesions result in defective schema-driven strategic search processes, this would effectively reduce the number of options generated by limiting access to relevant information and/or related past events.

Although the VMF likely supports knowledge recruitment and evaluation during option generation, it still remains to be determined if this support is contingent on the type of representation being retrieved. Our findings indicate this may be case. Specifically, we found that the deficit in option generation following VMF lesion was most pronounced for social problems, particularly with respect to option quality. One possibility is that this represents a more generalized deficit in processing social or self-based information following lesions affecting the VMF (Xia, Stolle, Gidengil, & Fellows, 2015; Anderson, Damasio, Tranel, & Damasio, 2000). In line with this view are studies implicating the VMF in tasks such as theory of mind (Leopold et al., 2012; Gallagher & Frith, 2003) and those recruiting self-referential processing or "self-awareness" (Beer et al., 2006; Mitchell, Banaji, & MacRae, 2005). Alternatively, the pronounced deficits in social option generation observed in the VMF group could be a function of the nature of the problem representation. Social problems are generally thought of as more ambiguous than nonsocial problems (Vandermorris et al., 2013; Sheldon et al., 2011), and the ability to generate appropriate options is likely heavily influenced by the background knowledge and goals of the problem solver (Channon, 2004). As a result, associative processes, directed by VMF-dependent schematic frameworks (discussed above), would be especially important for drawing links between prior experiences during the construction of options in ambiguous social scenarios (Sheldon et al., 2011, 2015). However, social and nonsocial problems may differ on other dimensions, such as difficulty or novelty, which could have led to this pattern of results. A more rigorous examination of the differential contributions of the VMF to such distinct forms of problem solving is a fruitful area of future research.

A final possibility to consider is that the reported results stem from generalized deficits in cognitive flexibility. This can be operationalized as the ability to generate novel, unconventional responses, shift between generated thoughts, and/or adjust behavior in response to feedback and can be impaired after frontal lobe damage (Eslinger & Grattan, 1993). Cognitive flexibility captures several specific processes, with both VMF and more dorsal frontal regions involved. The present experiment was not designed to address this perspective. However, the fact that we observed a specific effect of VMF damage and that the VMF group seemed to have particular impairment in social problems argues against a generic flexibility account.

Limitations and Future Directions

This study represents an important first step in providing direct evidence for the involvement of the VMF in the option generation phase of problem solving. However, as with any study, there are limitations. First, the VMF is not an anatomically or functionally homogenous structure, and frontal lesions in humans are rarely confined to distinct subregions. The data presented here cannot disentangle differential ventromedial pFC and OFC contributions or the effect of white matter disconnection to open-ended problem solving. In fact, several groups have reported distinct contributions of specific subregions of the macaque OFC to goal-directed behaviors (e.g., Rudebeck & Murray, 2011; Noonan et al., 2010), highlighting the need for converging methods to provide more anatomical specificity. Second, although typical for studies of this nature, sample sizes for both VMF lesion and frontal controls were small and, as such, replication is desirable to strengthen confidence in the current findings. Third, both years of education and estimates of IQ were slightly lower for the VMF lesion group. Although these differences were not statistically different and the main findings were robust when education was included as a covariate, the possibility exists that education and IQ effects could be influencing results. That said, it is reassuring that studies in healthy subjects have found that small differences in years of education beyond high school do not influence everyday problem-solving ability (Burton et al., 2006; Cornelius & Caspi, 1987). Lastly, although we had a priori hypotheses about social versus nonsocial problem solving that were supported by the current findings, the mechanisms by which the VMF contributes to option generation in social problem solving remain to be clarified. Furthermore, our hypotheses were tested using five problems, only two of which were considered social in nature, making this distinction tentative and in need of further study. More generally, additional work is needed to specify the mechanistic contribution of the VMF to option generation. Such work should aim to reconcile value, strategic search, and schema-related perspectives on the processes supported by this region.

Another future direction of research is to situate VMF contributions to open-ended problem solving in relation to the contribution of other brain regions. Prior research has shown that medial-temporal lobe structures, particularly the hippocampus, are critical for elaborating upon chosen solutions to open-ended problems (Sheldon et al., 2011, 2015; Vandermorris et al., 2013). Given that the VMF and the medial-temporal lobe are interconnected and that both are integral regions in the default mode network, a collection of brain regions active during a number of internally directed thought processes (Schacter et al., 2012; Andrews-Hanna, Reidler, Sepulcre, Poulin, & Buckner, 2010; Addis, Wong, & Schacter, 2007), we suggest that reciprocal interactions between these structures support disparate problem-solving processes. On the basis of past work and the current study, we hypothesize that the VMF is important for evaluating and choosing outcomes to open-ended problems whereas hippocampal-dependent processes are important for supplementing a chosen solution with detail, thereby facilitating the rich mental construction of a potential outcome. Interestingly, damage to the VMF has been shown to cause dramatic deficits in some hippocampally dependent tasks, such as episodic remembering and future imagining, but the mechanisms underlying these deficits remain to be established (Bertossi, Tesini, Cappelli, & Ciaramelli, 2016; Fellows & Farah, 2005).

Conclusions

Option generation is an important stage in open-ended real-world problem solving, but little is known about its neural substrates. Understanding how high-quality options are generated can clarify how we approach ambiguous scenarios in the real world. The quality of the decision made hinges critically on the quality of options considered, making the option generation process potentially "rate limiting" in real-world decision-making. The current study demonstrates a necessary role of the VMF in the number and quality of options generated for open-ended real-world problems. These findings may provide a conceptual link between value-based and schema- or model-based views of VMF function.

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REFERENCES

Addis, D. R., Wong, A. T., & Schacter, D. L. (2007). Remembering the past and imagining the future: Common and distinct neural substrates during event construction and elaboration. *Neuropsychologia, 45,* 1363–1377.

Anderson, S. W., Damasio, H., Tranel, D., & Damasio, A. R. (2000). Long-term sequelae of prefrontal cortex damage acquired in early childhood. *Developmental Neuropsychology, 18,* 281–296.

Andrews-Hanna, J. R., Reidler, J. S., Sepulcre, J., Poulin, R., & Buckner, R. L. (2010). Functional-anatomic fractionation of the brain's default network. *Neuron, 65,* 550–562.

Baker, S., Rogers, R., Owen, A., Frith, C., Dolan, R., Frackowiak, R., et al. (1996). Neural systems engaged by planning: A PET study of the Tower of London task. *Neuropsychologia, 34,* 515–526.

Bechtoldt, H. P., Benton, A. L., & Fogel, M. L. (1962). An application of factor analysis in neuropsychology. *Psychological Record, 12,* 147.

Beck, A. T., Ward, C., & Mendelson, M. (1961). Beck Depression Inventory (BDI). *Archives of General Psychiatry, 4,* 561–571.

Bechara, A., Damasio, H., Damasio, A. R., & Lee, G. P. (1999). Different contributions of the human amygdala and ventromedial prefrontal cortex to decision-making. *Journal of Neuroscience, 19,* 5473–5481.

Beer, J. S., John, O. P., Scabini, D., & Knight, R. T. (2006). Orbitofrontal cortex and social behavior: Integrating self-monitoring and emotion-cognition interactions. *Journal of Cognitive Neuroscience, 18,* 871–879.

Benoit, R. G., Szpunar, K. K., & Schacter, D. L. (2014). Ventromedial prefrontal cortex supports affective future simulation by integrating distributed knowledge. *Proceedings of the National Academy of Sciences, U.S.A., 111,* 16550–16555.

Bertossi, E., Tesini, C., Cappelli, A., & Ciaramelli, E. (2016). Ventromedial prefrontal damage causes a pervasive impairment of episodic memory and future thinking. *Neuropsychologia, 90,* 12–24.

Burton, C. L., Strauss, E., Hultsch, D. F., & Hunter, M. A. (2006). Cognitive functioning and everyday problem solving in older adults. *The Clinical Neuropsychologist, 20,* 432–452.

Camille, N., Griffiths, C. A., Vo, K., Fellows, L. K., & Kable, J. W. (2011). Ventromedial frontal lobe damage disrupts value maximization in humans. *Journal of Neuroscience, 31,* 7527–7532.

Channon, S. (2004). Frontal lobe dysfunction and everyday problem-solving: Social and non-social contributions. *Acta Psychologica, 115,* 235–254.

Cornelius, S. W., & Caspi, A. (1987). Everyday problem solving in adulthood and old age. *Psychology and Aging, 2,* 144–153.

Damasio, A. R., Tranel, D., & Damasio, H. (1990). Individuals with sociopathic behavior caused by frontal damage fail to respond autonomically to social stimuli. *Behavioural Brain Research, 41,* 81–94.

Eggen, C., Huber, O., Bär, A., Huber, O. W., Perrig, W. J., Müri, R., et al. (2015). Impairments in an early stage of the decision-making process in patients with ventromedial prefrontal damage: Preliminary results. *Neurocase, 21,* 509–519.

Eslinger, P. J., & Damasio, A. R. (1985). Severe disturbance of higher cognition after bilateral frontal lobe ablation: Patient EVR. *Neurology, 35,* 1731–1741.

Eslinger, P. J., & Grattan, L. M. (1993). Frontal lobe and frontal-striatal substrates for different forms of human cognitive flexibility. *Neuropsychologia, 31,* 17–28.

Fellows, L. K. (2004). The cognitive neuroscience of human decision making: A review and conceptual framework. *Behavioral and Cognitive Neuroscience Reviews, 3,* 159–172.

Fellows, L. K. (2006). Deciding how to decide: Ventromedial frontal lobe damage affects information acquisition in multi-attribute decision making. *Brain, 129,* 944–952.

Fellows, L. K. (2007). Advances in understanding ventromedial prefrontal function the accountant joins the executive. *Neurology, 68,* 991–995.

Fellows, L. K. (2011). Orbitofrontal contributions to value-based decision making: Evidence from humans with frontal lobe damage. *Annals of the New York Academy of Sciences, 1239,* 51–58.

Fellows, L. K., & Farah, M. J. (2005). Dissociable elements of human foresight: A role for the ventromedial frontal lobes in framing the future, but not in discounting future rewards. *Neuropsychologia, 43,* 1214–1221.

Gallagher, H. L., & Frith, C. D. (2003). Functional imaging of 'theory of mind'. *Trends in Cognitive Sciences, 7,* 77–83.

Gerlach, K. D., Spreng, R. N., Gilmore, A. W., & Schacter, D. L. (2011). Solving future problems: Default network and executive activity associated with goal-directed mental simulations. *Neuroimage, 55,* 1816–1824.

Ghosh, V. E., Moscovitch, M., Colella, B. M., & Gilboa, A. (2014). Schema representation in patients with ventromedial PFC lesions. *Journal of Neuroscience, 34,* 12057–12070.

Gigerenzer, G., & Goldstein, D. G. (1996). Reasoning the fast and frugal way: Models of bounded rationality. *Psychological Review, 103,* 650.

Goel, V. (2010). Neural basis of thinking: Laboratory problems versus real-world problems. *Wiley Interdisciplinary Reviews: Cognitive Science, 1,* 613–621.

Goel, V., & Grafman, J. (2000). Role of the right prefrontal cortex in ill-structured planning. *Cognitive Neuropsychology, 17,* 415–436.

Goel, V., Grafman, J., Tajik, J., Gana, S., & Danto, D. (1997). A study of the performance of patients with frontal lobe lesions in a financial planning task. *Brain, 120,* 1805–1822.

Grabenhorst, F., & Rolls, E. T. (2011). Value, pleasure and choice in the ventral prefrontal cortex. *Trends in Cognitive Sciences, 15,* 56–67.

Grober, E., Sliwinsk, M., & Korey, S. R. (1991). Development and validation of a model for estimating premorbid verbal intelligence in the elderly. *Journal of Clinical and Experimental Neuropsychology, 13,* 933–949.

Henri-Bhargava, A., Simioni, A., & Fellows, L. K. (2012). Ventromedial frontal lobe damage disrupts the accuracy, but not the speed, of value-based preference judgments. *Neuropsychologia, 50,* 1536–1542.

Johnson, J. G., & Raab, M. (2003). Take the first: Option-generation and resulting choices. *Organizational Behavior and Human Decision Processes, 91,* 215–229.

Kaiser, S., Simon, J. J., Kalis, A., Schweizer, S., Tobler, P. N., & Mojzisch, A. (2013). The cognitive and neural basis of option generation and subsequent choice. *Cognitive, Affective, & Behavioral Neuroscience, 13,* 814–829.

Keller, L. R., & Ho, J. L. (1988). Decision problem structuring: Generating options. *IEEE Transactions on Systems, Man, and Cybernetics, 18,* 715–728.

Klein, G. (2008). Naturalistic decision making. *Human Factors: Journal of the Human Factors and Ergonomics Society, 50,* 456–460.

Klein, G., Wolf, S., Militello, L., & Zsambok, C. (1995). Characteristics of skilled option generation in chess. *Organizational Behavior and Human Decision Processes, 62,* 63–69.

Kumaran, D., Summerfield, J. J., Hassabis, D., & Maguire, E. A. (2009). Tracking the emergence of conceptual knowledge during human decision making. *Neuron, 63,* 889–901.

Leopold, A., Krueger, F., dal Monte, O., Pardini, M., Pulaski, S. J., Solomon, J., et al. (2012). Damage to the left ventromedial prefrontal cortex impacts affective theory of mind. *Social Cognitive and Affective Neuroscience, 7,* 871–880.

Levy, D. J., & Glimcher, P. W. (2012). The root of all value: A neural common currency for choice. *Current Opinion in Neurobiology, 22,* 1027–1038.

Levy, I., Lazzaro, S. C., Rutledge, R. B., & Glimcher, P. W.. (2011). Choice from non-choice: Predicting consumer preferences from blood oxygenation level-dependent signals obtained during passive viewing. *Journal of Neuroscience, 31,* 118–125.

Manes, F., Sahakian, B., Clark, L., Rogers, R., Antoun, N., Aitken, M., et al. (2002). Decision-making processes following damage to the prefrontal cortex. *Brain, 15,* 624–639.

Mitchell, J. P., Banaji, M. R., & MacRae, C. N. (2005). The link between social cognition and self-referential thought in the medial prefrontal cortex. *Journal of Cognitive Neuroscience, 17,* 1306–1315.

Moscovitch, M., & Melo, B. (1997). Strategic retrieval and the frontal lobes: Evidence from confabulation and amnesia. *Neuropsychologia, 35,* 1017–1034.

Noonan, M., Walton, M., Behrens, T., Sallet, J., Buckley, M., & Rushworth, M. (2010). Separate value comparison and learning mechanisms in macaque medial and lateral orbitofrontal cortex. *Proceedings of the National Academy of Sciences, U.S.A., 107,* 20547–20552.

Owen, A. M., Downes, J. J., Sahakian, B. J., Polkey, C. E., & Robbins, T. W. (1990). Planning and spatial working memory following frontal lobe lesions in man. *Neuropsychologia, 28,* 1021–1034.

Padoa-Schioppa, C. (2011). Neurobiology of economic choice: A good-based model. *Annual Review of Neuroscience, 34,* 333–359.

Plassmann, H., O'Doherty, J., & Rangel, A. (2007). Orbitofrontal cortex encodes willingness to pay in everyday economic transactions. *Journal of Neuroscience, 27,* 9984–9988.

Porcelli, A. J., & Delgado, M. R. (2009). Acute stress modulates risk taking in financial decision making. *Psychological Science, 20,* 278–283.

Rangel, A., & Hare, T. (2010). Neural computations associated with goal-directed choice. *Current Opinion in Neurobiology, 20,* 262–270.

Rudebeck, P. H., & Murray, E. A. (2011). Dissociable effects of subtotal lesions within the macaque orbital prefrontal cortex on reward-guided behavior. *Journal of Neuroscience, 31,* 10569–10578.

Rushworth, M. F. (2008). Intention, choice, and the medial frontal cortex. *Annals of the New York Academy of Sciences, 1124,* 181–207.

Schacter, D. L., Addis, D. R., Hassabis, D., Martin, V. C., Spreng, R. N., & Szpunar, K. K. (2012). The future of memory: Remembering, imagining, and the brain. *Neuron, 76,* 677–694.

Shallice, T. (1982). Specific impairments of planning. *Philosophical Transactions of the Royal Society of London, Series B, Biological Sciences, 298,* 199–209.

Sheldon, S., McAndrews, M., & Moscovitch, M. (2011). Episodic memory processes mediated by the medial temporal lobes contribute to open-ended problem solving. *Neuropsychologia, 49,* 2439–2447.

Sheldon, S., Vandermorris, S., Al-Haj, M., Cohen, S., Winocur, G., & Moscovitch, M. (2015). Ill-defined problem solving in amnestic mild cognitive impairment: Linking episodic memory to effective solution generation. *Neuropsychologia, 68,* 168–175.

Smaldino, P. E., & Richerson, P. J. (2012). The origins of options. *Frontiers in Neuroscience, 6,* 92–103.

Spalding, K. N., Jones, S. H., Duff, M. C., Tranel, D., & Warren, D. E. (2015). Investigating the neural correlates of schemas: Ventromedial prefrontal cortex is necessary for normal schematic influence on memory. *Journal of Neuroscience, 35,* 15746–15751.

Thurstone, L. L. (1938). *Primary mental abilities*. Chicago: University of Chicago Press.

Tom, S. M., Fox, C. R., Trepel, C., & Poldrack, R. A. (2007). The neural basis of loss aversion in decision-making under risk. *Science, 315,* 515–518.

Tsuchida, A., Doll, B. B., & Fellows, L. K. (2010). Beyond reversal: A critical role for human orbitofrontal cortex in flexible learning from probabilistic feedback. *Journal of Neuroscience, 30,* 16868–16875.

van Kesteren, M. T., Fernández, G., Norris, D. G., & Hermans, E. J. (2010). Persistent schema-dependent hippocampal-neocortical connectivity during memory encoding and postencoding rest in humans. *Proceedings of the National Academy of Sciences, U.S.A., 107,* 7550–7555.

Valentin, V. V., Dickinson, A., & O'Doherty, J. P. (2007). Determining the neural substrates of goal-directed learning

in the human brain. *Journal of Neuroscience, 27,* 4019–4026.
Vandermorris, S., Sheldon, S., Winocur, G., & Moscovitch, M. (2013). Differential contributions of executive and episodic memory functions to problem solving in younger and older adults. *Journal of the International Neuropsychological Society, 19,* 1087–1096.
Wheeler, E. Z., & Fellows, L. K. (2008). The human ventromedial frontal lobe is critical for learning from negative feedback. *Brain, 131,* 1323–1331.
Xia, C., Stolle, D., Gidengil, E., & Fellows, L. K. (2015). Lateral orbitofrontal cortex links social impressions to political choices. *Journal of Neuroscience, 35,* 8507–8514.
Zald, D. H., & Andreotti, C. (2010). Neuropsychological assessment of the orbital and ventromedial prefrontal cortex. *Neuropsychologia, 48,* 3377–3391.
Zeithamova, D., & Preston, A. R. (2010). Flexible memories: Differential roles for medial temporal lobe and prefrontal cortex in cross-episode binding. *Journal of Neuroscience, 30,* 14676–14684.

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