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Ventromedial frontal lobe damage disrupts the accuracy, but not the speed, of value-based preference judgments

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ABSTRACT

The ventromedial frontal lobe (VMF) plays a role in decision making, but its precise function remains unclear. Several lines of evidence suggest that VMF is involved in representing the economic value of options. A prior study from our lab has shown that patients with lesions to the VMF are less consistent than controls in making simple preference judgments between stimuli presented in pairs. Here, we followed up that observation in a larger sample, using more sensitive tasks, and examining the category-specificity of this effect. Patients with damage to VMF ($N = 15$) were compared to patients with frontal damage sparing that region ($N = 8$) and to demographically matched healthy control participants ($N = 23$). Five separate preference tasks were administered, requiring subjects to indicate their preference for 12 stimuli presented two at a time, in all possible combinations. Categories included fruits, vegetables, colors, landscapes, and puppies. Choices were analyzed for internal consistency, and decision times were measured. Three control tasks with the same format, but requiring perceptual judgments, were also administered. VMF patients were significantly more erratic than both non-VMF and healthy control participants in their preference judgments across all stimulus categories. However, decision times, and the relationship between decision time and relative value, were similar to that seen in control participants. The groups did not differ in perceptual judgment performance. These findings add further weight to the claim that VMF plays a critical role in simple value-based decision-making under conditions of certainty. This region appears to be necessary for consistent choices across a variety of stimulus categories, supporting the view that human VMF represents the (relative) value of decision options rather generally. That such damage impairs decision 'accuracy' without affecting reaction time has implications for theories of the role of VMF in decision-making, arguing that this region may be critical for linking a particular value to a particular option.

1. Introduction

The concept of subjective value has been very powerful in the formal analysis of economic behavior. The burgeoning field of neuroeconomics has built on this tradition, with perhaps the greatest progress in defining the neural substrates of decision-making coming from mapping the brain regions that carry information related to value. Functional neuroimaging in humans and electrophysiological studies in monkeys have identified value-related signals in several frontal, parietal, and subcortical regions. Current models based on these findings suggest that activity in orbitofrontal and/or ventromedial prefrontal cortex (a region here referred to together as ventromedial frontal lobe (VMF)) represents the value of goods, and may even constitute a "common currency" for comparing different kinds of value (Kable & Glimcher, 2009; Padoa-Schioppa, 2010; Rangel, Camerer, & Montague, 2008). These signals have also been shown to predict choice in a variety of paradigms, suggesting that this value information is used to make decisions (Knutson, Rick, Wimmer, Prelec, & Loewenstein, 2007; Levy, Lazzaro, Rutledge, & Glimcher, 2011; Plassmann, O'Doherty, & Rangel, 2007; Rangel & Hare, 2010; Smith et al.).

There is reason for caution, though, because subjective value is frequently correlated with other constructs, including motivation, arousal, and salience (Schoenbaum, Takahashi, Liu, & McDannald, 2011). Progress in developing neurobiologically based models of economic choice thus requires both careful efforts to disambiguate these processes in correlational designs (Litt, Plassmann, Shiv, & Rangel, 2011; Roesch & Olson, 2004), and converging evidence from loss of function methods. While there is now substantial evidence that VMF plays a key role in decision-making, based on lesion studies in both humans and non-human primates (Fellows, 2007b; Rushworth, Noonan, Boorman, Walton, & Behrens, 2011), there is still uncertainty about the specific processes for which these regions are necessary. Some of this uncertainty arises from the

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fact that much of the neuropsychological work in this area has used relatively complex tasks, engaging higher-order aspects of decision-making and learning, such as risk, ambiguity, and delay, sometimes even in combination in the same tasks (Fellows, 2007a).

However, if ventral prefrontal value signals are called upon for decision-making, damage to this region should disrupt any choice involving value comparison. Preference judgments require exactly this. When choosing between chocolate and vanilla, or chips and pretzels, there is no risk or ambiguity. The simplest forms of such choices boil down to a direct comparison of the momentary, subjective value of these options. If ventral frontal representations of value are critical for such choices, then damage to this area should disrupt even these very simple decisions. We have applied this logic in two prior studies, finding preliminary evidence that damage to this region indeed affects value-based decision making. In the most recent of these studies, we showed that VMF damage led to choices between real food items that were not consistent with maximizing subjective value (Camille, Griffiths, Vo, Fellows, & Kable, 2011). The prior experiment showed that VMF damage was associated with an increased tendency to violations of choice transitivity, at least for three categories of hypothetical choices: between famous people, between colors, and between foods. It also included a control group with frontal damage sparing VMF, arguing that this was a regionally specific effect (Fellows & Farah, 2007). However, studies using analogous tasks in non-human primates with selective lesions have yielded more mixed results (Baylis & Gaffan, 1991; Izquierdo, Suda, & Murray, 2004; Machado & Bachevalier, 2007). That work suggests that there may be important contributions of experience, habit, and memory to such choices, depending on the specific context, even in these simple paradigms. Further, the domain generality of any VMF role remains unclear: are these value signals crucial for all kinds of decisions?

To the extent the simple preference judgments isolate subjective value comparison processes, such tasks also offer the possibility of better understanding what determines the time it takes to make a decision. The effects of VMF damage on decision time, if any, have the potential to shed light on how the quality of value representations are monitored. An early case report suggested that VMF damage leads to paralyzing equivocation in real life (Eslinger & Damasio, 1985), but such damage is also linked to impulsivity. Experimental work to date in patients has not focused on this point, despite its obvious importance in developing more detailed mechanistic models of how decision-making is carried out in the brain.

Here we aimed to test the generality of ventral prefrontal contributions to value-based choice, studying patients with focal frontal lobe damage. We used an expanded preference judgment task that assessed 5 categories of goods-based choice with stimulus sets of sufficient size to minimize any memory confounds. The breadth of the required judgments was increased by adding choices that tapped appetitive, aesthetic, and quasi-social domains, and the level of difficulty of these choices was increased by avoiding stimuli about which people might have strong a priori views (i.e. political figures). We also included a frontal-damaged control group with coverage of potentially key frontopolar and dorsomedial regions. Finally, the task used here was computerized, allowing measurement of reaction times to determine the effects of the hypothesized degraded option-value representations in ventral prefrontal cortex on the speed at which decisions were taken.

2. Methods

2.1. Participants

Participants with fixed, focal injury to the frontal lobes of at least 6 months duration were recruited from the McGill Cognitive Neuroscience Research Registry ($N = 20$), and the patient database of the University of Pennsylvania ($N = 3$) (Fellows, Stark, Berg, & Chatterjee, 2008). Patients were included in the group of interest if their damage primarily affected the ventromedial frontal lobe (VMF; $N = 15$), as judged from their most recent clinical brain imaging (MRI or CT). Patients were excluded if they had extensive injury to areas outside the frontal lobes, or co-morbid conditions likely to affect cognition. Brain injury was caused by ischemic stroke, aneurysm rupture or resection of benign tumors. Three individuals in the VMF group were taking an anti-convulsant medication, and one was taking both an anti-convulsant and a low dose benzodiazepine for sleep. Four individuals in the FC group were taking an anti-convulsant, and two were taking low dose anti-depressants. Seven of the VMF subjects also participated in a study using a quite different choice task to address related questions (Camille, Griffiths et al., 2011).

Table 1
Demographic information [mean (SD)].

Group	Age	Education	Sex (M:F)	Volume of injury (cc)
VMF ($N = 15$)	58 (15)	14 (4)	3:12	49 (59)
FL ($N = 8$)	55 (11)	14 (3)	4:4	42 (35)
HC ($N = 23$)	58 (9)	15 (3)	7:16	–

For the purposes of this study, and in keeping with the existing neuropsychology literature, VMF was defined as medial orbitofrontal cortex and the adjacent ventromedial prefrontal cortex (i.e. medial frontal wall inferior to the genu of the corpus callosum) (Fellows, 2007a; Stuss & Levine, 2002). All patients included in this group have damage involving VMF so-defined, with bilateral medial OFC and adjacent ventromedial prefrontal cortex the areas of greatest lesion overlap, as intended. Of the 15 subjects, 5 had bilateral damage, 5 damage restricted to the left hemisphere, and 5 with damage restricted to the right hemisphere. In some individuals, damage extended beyond the borders of VMF proper, mainly into more dorsal frontopolar and dorsomedial areas. Patients with frontal lobe damage sparing the VMF were included as a lesioned comparison group ($N = 8$), to test the specificity of any observed effects. Some of these patients had dorsomedial or frontopolar damage, providing the opportunity to specifically address whether damage to these extra-VMF regions was contributing to the performance of the VMF group.

Lesions were traced onto the standard MNI brain by a neurologist with experience in image analysis, and blind to the patient's performance on the experimental tasks, to allow damage to be shown in a common brain space. Lesion overlap images are shown in Fig. 1. Patients completed a detailed screening evaluation at the time of their enrollment in the research registries.

In addition, healthy participants matched in age and education to the VMF group were recruited by advertisement from the local community in Montreal ($N = 23$). Healthy participants were excluded if they had a history of neurological or psychiatric illness likely to interfere with cognition, if they were taking psychoactive medications, or if they scored <28/30 on the Folstein mini-mental status examination, ≤26/30 on the Montreal Cognitive Assessment, or >15 on the Beck Depression Inventory. All participants provided written, informed consent in accordance with the Declaration of Helsinki. The protocol was approved by the Research Ethics Boards of both the Montreal Neurological Institute and the University of Pennsylvania. Demographic information is shown in Table 1; groups did not differ on these measures (all $P > 0.32$).

The results of screening neuropsychological tests are shown in Table 2. Healthy controls performed significantly better than both patient groups on a screening test covering broad cognitive domains, and on a measures of phonemic fluency and attention, and scored lower on the BDI. Importantly, the two patient groups did not differ on any of these screening measures (all $P > 0.25$).

2.2. Tasks

A computerized preference task was developed based on a simpler, briefer paper-and-pencil version used in a prior study (Fellows & Farah, 2007). Participants were required to choose between different stimuli presented two at a time. Five different categories of stimuli were used: colors, fruits, vegetables, puppy faces, and landscapes. For all five categories, 12 different stimuli were presented in all possible pair combinations (66 pairs) in a fixed, randomized order. Participants were told they would be shown items, two at a time, and were to pick the item that they preferred. They were instructed to choose as quickly as possible, without making random choices. They were further instructed to make each judgment in isolation. The instructions made no mention of internal consistency.

Three tasks employing the same format as the preference task, but requiring perceptual rather than preference judgments, were administered as control tasks. In one task, participants were shown faces of men of different ages and asked to select the man in each pair who appeared older. In a second task participants were shown lines of different lengths, presented at random angles, and asked to select the longer line. In the final control task, participants were shown different shades of blue and asked to select the color patch that was closest to "pure blue". There were 12 stimuli in each perceptual task, as in the preference tasks.

Participants were administered the five preference and three perceptual tasks in a single session, in a random sequence. Tasks were administered using E-Prime

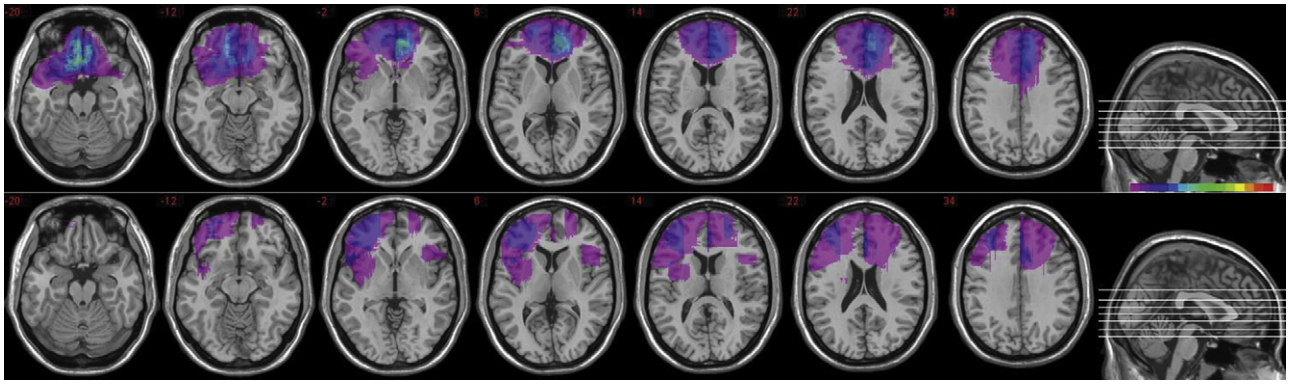

Fig. 1. Lesion overlap images shown on the same axial slices of the MNI brain (top row, VMF, bottom row, FC).

Table 2
Neuropsychological screening [mean (SD)].

Group	IQ estimate	BDI	MoCA	Backward digit span	Semantic fluency (animals)	Phonemic fluency (F + A + S)	Incidental memory (accuracy)
VMF	114 (11)	13 (13)	25.8 (3.8)	2.7 (1)	17 (6)	32 (14)	0.82 (0.13)
FL	117 (9)	17 (13)	24.8 (4.8)	3.2 (0.8)	17 (6)	27 (16)	0.72 (0.1)
HC	122 (7)	4 (3)**	28.3 (1.5)*	4.1 (0.7)**	20 (5)	43 (10)*	–

*$P < 0.05$, **$P < 0.01$ mixed ANOVA showing effect of group for each measure; where significant differences were present, post hoc pairwise contrasts showed that HC differed from the frontal groups, who did not differ from each other.

software (version 1.2, Psychology Software Tools, Inc.) on a Toshiba tablet PC running Microsoft Windows XP. The same computer with the same monitor settings was used for all study participants. Participants viewed a fixation cross on the centre of the screen, and then two stimuli appearing on either side of fixation. At the start of each category of choices, participants were instructed to "Indicate which of the following colors (or vegetables, fruits, etc.) you prefer. To select the color you prefer, press on its image". In the perceptual tasks, they were instructed to "Indicate which of the following lines is longer (or which of the following people is older, etc.). To select your choice, press on its image." Participants made their choices by touching the desired item directly on the computer screen using a stylus in all but two tasks. For technical reasons, participants used the keyboard to indicate their preference in the landscape preference task and the line length control task. Participants completed three practice trials using pairs of stimuli that were different from the task set prior to beginning each task to ensure they understood the instructions.

2.3. Analysis

The best fitting subjective preference ordering, as revealed by the choices made, was determined for each preference task and each participant. Thus, the stimulus that was chosen most often was ranked first, next most often second, and so on. This subjective value ranking was then analyzed for violations of transitivity, a concept taken from the economic and philosophical literature on decision making. Preference transitivity states that if one assigns a higher value to A than to B, and a higher value to B than to C, such that one prefers $A > B$, and $B > C$, then one should prefer $A > C$. Violations of preference transitivity (i.e., preferring $C > A$ in the preceding example) were scored as a 'preference error', i.e. they were erratic, or irrational in the economic sense. Data were analyzed with ties maintained (i.e. more than one stimulus could have the same rank order) or with ties broken by determining the option that was explicitly preferred when the tied options were presented as a pair. The overall pattern of results did not differ in these two cases; the data are therefore presented with ties maintained, a more conservative approach that allows for the existence of indifference transitivity (that is, variability in choice would be expected under normal circumstances if two options were very similar in subjective value). The total number of preference errors was the dependent measure in the main analysis.

Additionally, for each trial of each task, the 'value distance' for the trial was calculated by taking the difference in rank between the two stimuli presented in that trial. Value distance was then related to reaction time for each choice, measured from stimulus onset to selection (via touchscreen or button press).

The effect of frontal lobe injury on performance was tested with ANOVA when the dependent variables were normally distributed, and Kruskal–Wallis tests otherwise. Post hoc pairwise comparisons were made with the Student Newman Keuls test, or with Mann–Whitney U tests, as appropriate. Given the results of prior work using a similar approach, there was a strong a priori prediction that VMF damage would worsen performance; one-tailed tests of significance were therefore applied.

3. Results

The three groups differed significantly in overall performance of the preference task (Kruskal–Wallis test, $H = 6.4$, $P < 0.05$). As can be seen in Fig. 2, the VMF group made significantly more erratic choices compared to healthy subjects (Mann–Whitney U, $P < 0.05$) and to the frontal-injured control group (Mann–Whitney U, $P = 0.05$). The frontal control group's performance was statistically indistinguishable from that of the healthy controls ($P = 0.32$). In contrast, all 3 groups were similar in their perceptual judgment

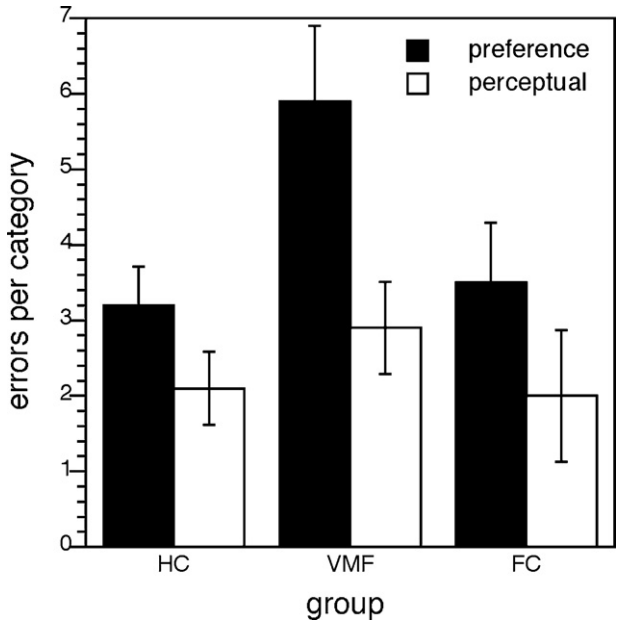

Fig. 2. Mean total errors for preference and perceptual tasks, per category tested, by group. Error bars show S.E.M. The VMF group made significantly more errors than the other two groups in the preference tasks, but did not differ from either control group in perceptual task performance. Across all groups, the preference tasks were significantly more difficult than the perceptual tasks.

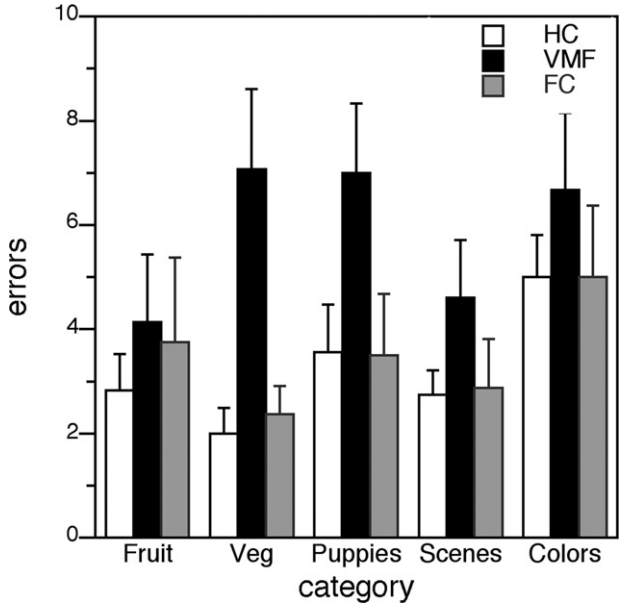

Fig. 3. Mean (±S.E.M) errors for each category, by group.

performance (Kruskal–Wallis $H = 2.3$, $P = 0.16$; Fig. 2). Nonetheless, inspection of Fig. 2 shows that the VMF group made the numerically greatest number of perceptual errors. We therefore asked if this group had disproportionately more difficulty with the preference, compared to the perceptual task. Because error counts were not normally distributed, this was done by calculating the difference between the mean errors in the preference task and in the perceptual task. This difference score analysis confirmed that VMF damage is associated with a disproportionately higher number of errors in the preference, compared to the perceptual task (mean (SD): VMF: 3 (3); FC 1.5 (1.2); HC 1.1 (1.7); Kruskal–Wallis $H = 4.7$, $P < 0.05$). Similar results were obtained with parametric analysis conducted on the total errors for each task type, adjusted for the number of categories tested in each task to take into account the fact that there were only three perceptual tasks, but 5 preferences tasks. Mixed ANOVA shows a borderline effect of group (F (2, 43) = 2.5, $P = 0.05$), an effect of task type (F (1, 43) = 28.5, $P < 0.0001$), and, critically, a group × task type interaction (F (2, 43) = 3.6, $P < 0.05$)).

There was no significant correlation in the lesion group as a whole, or in the VMF group in particular, between lesion volume and preference task performance. An exploratory analysis was undertaken to test whether the effects of VMF damage were affected by laterality. Perhaps unsurprisingly, those with bilateral damage made numerically more preference errors (mean (SD) 40 (23)) compared to those with damage affecting only the left or right hemisphere, while the latter two groups performed very similarly (left: 23.8 (15.3); right: 24.4 (20.5)). However, this pattern was not statistically significant (ANOVA, F (2,12) = 1.1, $P = 0.36$).

Three patients included in this study also participated in a previous study that provided the initial evidence for preference judgment impairment after VMF damage (Fellows & Farah, 2007). The pattern of results reported above remains the same even if these 3 patients are excluded from the analysis, therefore constituting an independent replication of the finding that VMF damage selectively disrupts the transitivity of simple preference judgments.

The VMF group showed a similar pattern of increased intransitivity of choices across all 5 categories of preference judgments tested, with the differences between VMF and HC groups greatest in the 'vegetable' and 'puppy' categories (Fig. 3). Categories were not equally difficult for healthy controls, who were more inconsistent in their color preferences than in other categories of stimuli.

This experiment provided a first opportunity to study not only the consistency of preference judgments, but also the decision time for these choices. A decades-old literature shows that, in normal subjects, the more similar in value are two options, the longer the decision time (Dashiell, 1937). We took the same approach here, examining RT as a function of "value distance". As can be seen for two representative categories, shown in Fig. 4, subjects generally showed the expected orderly value distance effect, with choices between stimuli that were more distant in the subjective value order made more quickly than choices that were more similar in value. The RT data for the color category (Fig. 4, left panel) are typical for 4 of the 5 categories, with mixed ANOVA showing a significant effect of value distance (all $P < 0.001$), but no significant effect of group (all $P > 0.19$), and no group × value distance interaction (all $P > 0.25$). The vegetable category (Fig. 4, right panel), where the VMF group made the most errors compared to controls, again showed a significant main effect of value distance ($F = 6.0$, $P < 0.001$), and no effect of group ($F = 1.5$, $P = 0.22$). However, there was a significant group × distance interaction ($F = 2.2$, $P < 0.05$). Post hoc tests showed this to be driven by the FC group, which had a flatter relationship between RT and value distance compared to the HC group (value distance × RT, F (4, 112) = 5.1, $P < 0.001$). HC and VMF, and FC and VMF groups did not show any significant group x value distance differences.

The preference task was designed to minimize memory demands: subjects were explicitly told to treat each choice as independent, were not told that the measure of interest was the internal consistency of their choices, and were exposed to a large number of stimuli in each category set. Nonetheless, there remains a possibility that they tried to be consistent by remembering their choices. If this was an explicit strategy, then memory impairment, rather than value judgment, might underlie poor performance. Two post hoc analyses were undertaken to assess this possibility. A subset of participants completed a difficult incidental memory test (for faces). As can be seen in Table 2, the FC group performed somewhat worse, on average, than the VMF group on this measure, whereas preference task performance followed the opposite pattern, arguing against this hypothesis. Further, if memory impairment is contributing to performance on the preference task, then there should be a positive correlation between errors on the memory test, and errors of preference. No such correlation was evident; in fact, the trend was in the opposite direction (Spearman rho = −0.53, $P = 0.11$). The general cognitive screening test (MoCA) we used heavily weights verbal memory. There was no relationship between scores on that test and preference task performance in the sample as a whole (Spearman rho = −0.01, $P = 0.95$), or in the VMF group specifically (rho = 0.17, $P = 0.64$).

VMF has been shown to play a critical role in reversal learning. Recent work in non-human primates has suggested that this role may be independent of the value representations that seem to underlie preference (Kazama & Bachevalier, 2009; Rushworth et al., 2011). This has yet to be addressed in humans. Although not an a priori focus of the current study, we are in a position to provide a preliminary test of this question, because a subset of the VMF patients ($N = 8$) tested here participated in a separate study examining reversal learning with a challenging probabilistic reversal learning paradigm (Tsuchida, Doll, & Fellows, 2010). There is a trend to a relationship between performance of the two tasks, but this relationship is not evident in every case: one patient is an extremely poor performer on the preference task (total errors = 59), but is near the healthy control average for reversal learning. If this outlier is excluded, the remaining 7 VMF subjects show a weak trend towards a relationship between reversal learning and preference (Spearman rho = 0.54, $P = 0.19$).

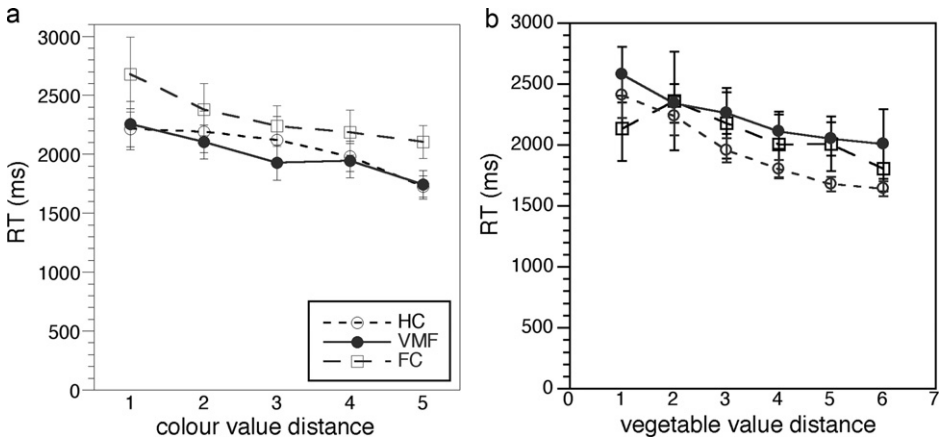

Fig. 4. Mean (±S.E.M.) decision time (in ms) as a function of the subjective 'value distance' between stimuli for two representative categories (colors, panel a; vegetables, panel b), by group. RT in the other three categories was similar to the pattern seen for colors (panel a).

4. Discussion

A growing body of work in both humans and non-human primates shows that the ventromedial PFC and adjacent medial OFC encode information about the value of decision options across a range of stimulus types including foods, consumer goods, social and aesthetic experiences. Here we show that damage to VMF disrupts the ability to make consistent value-based choices, across a similarly wide range of stimulus categories. These results argue that information encoded in VMF is indeed necessary for value-based decision-making, conceived of quite generally. Importantly, this deficit is specific to value-based choice; decisions based on perceptual information were not substantially affected by VMF damage. It is also specific to VMF: damage outside this region did not affect value-based choice. These observations confirm and extend two other studies that also used simple decision-making paradigms intended to isolate relative value judgments from other aspects of choice (Camille, Griffiths et al., 2011; Fellows & Farah, 2007). The present finding constitutes a replication of the Fellows and Farah (2007) finding in a new sample, with a more challenging version of a similar set of tasks. Importantly, here the level of difficulty of perceptual control tasks and preference tasks was better matched, the sample size larger, and the breadth of decision categories tested was greater. The task in the Camille, Griffiths et al. (2011) study is quite different, involving real choices between two snack foods varying in number. The individuals tested in that study overlapped substantially with the sample tested here; those results should thus not be considered independent replications of the present findings. However, taken together, these studies speak to the domain-generality of VMF effects on simple preference judgments. Whether real or hypothetical choices, and across a variety of categories of stimuli, such damage seems to consistently impair value-maximizing choice. As a whole, this work makes a solid case that VMF is critical for value-driven, stimulus-based decision making in humans.

Extensive neuropsychological work has shown the VMF damage disrupts more complex decision-making, ranging from financial decisions involving risk (Clark et al., 2008; Shiv, Loewenstein, Bechara, Damasio, & Damasio, 2005), delay (Sellitto, Ciaramelli, & di Pellegrino, 2010), ambiguity (Hsu, Bhatt, Adolphs, Tranel, & Camerer, 2005), regret (Camille et al., 2004), or multiple attributes (Fellows, 2006), to choices with social or moral implications (Koenigs et al., 2007). Despite the added complexity, these choices nonetheless require value comparison. It remains to be seen whether the deficits following VMF/OFC damage relate to a fundamental difficulty with value comparison, expressed in (or even amplified by) these more elaborate contexts, or whether such damage affects additional processes specific to risk or social outcomes, for example. Future work aimed at disentangling these possibilities will be important in providing a more precise understanding of the functions of this region, and of the component processes of decision-making.

While our findings argue that VMF/OFC is necessary for value-based choice in a range of contexts, they do not establish whether this region separately represents the values of distinct options, or provides a combined, relative value assessment. Functional imaging studies suggest that both such representations may be present within different VMF/OFC regions (Kahnt, Heinzle, Park, & Haynes, 2010; Smith et al., 2010). More selective lesions and electrophysiological work in non-human primates also indicate that different kinds of subjective value information may be represented within finer anatomical sub-divisions (Bouret & Richmond, 2010; Kazama & Bachevalier, 2009). The area of most lesion overlap in the patients we studied was medial OFC and adjacent (posterior) vmPFC, but the level of anatomical resolution in this sample is insufficient to address this question definitively.

Despite showing clear deviations from value-maximizing choice, patients with VMF damage were generally similar to healthy controls in the time they took to make these choices. This has implications for different theories of the VMF's role in decision making. There would seem to be at least three ways in which value-based choice might be affected in those with VMF damage. On one hand, such damage might degrade the ability to distinguish between the value of options, leading to a 'grey' value landscape in which choices are all of similar value. In such a context, intransitivity would result from indifference, as is seen in healthy subjects faced with options of near-identical subjective value. It seems likely that this would be associated with a systematic effect on RT: either global slowing (i.e. equivocation in the face of very similar values), global speeding (i.e. quick but indifferent choices), or at least a flattening of the value distance by RT relationship. None of these patterns were consistently observed in patients with VMF damage.

A second possibility is that decisions may be expressed in action when some absolute value or relative value difference threshold is exceeded (Kable & Glimcher, 2009; Padoa-Schioppa, 2010). If so, then erratic choices could result from a sub-optimal speed-accuracy tradeoff: i.e. those with VMF damage might respond "impulsively" before value comparison has been completed. However, there is no evidence that the threshold for making a choice was

systematically shifted in those with VMF damage, arguing against this view. This observation is also consistent with the finding that VMF damage does not affect value-based learning about actions in the absence of stimuli in either humans or non-human primates (Camille, Tsuchida, & Fellows, 2011; Rudebeck et al., 2008).

A final possibility is that options are assigned distinct values, but that these values are unstable, fluctuating from trial to trial in those with VMF damage. That is, VMF damage may disrupt the fidelity of the link between a specific value and a specific option (cf. (Walton, Behrens, Noonan, & Rushworth, 2011)). The decision time data seem to fit best with this account. Thus, decision times are unaffected by VMF damage because for any given decision the value comparison process is not affected, it is just that the values attached to particular options are unstable from choice to choice.

The same broad region, and perhaps specifically medial OFC, has also been shown to be critical for optimal learning from value feedback (Fellows & Farah, 2003; Hornak et al., 2004; Tsuchida et al., 2010). In principle, both learning and choice require that the value of an outcome be anticipated, providing a plausible conceptual link between these two decision contexts. The preliminary data addressing this question that we present here suggest that impaired learning and impaired preference judgments are typically related in patients with VMF/OFC damage, consistent with this hypothesis. However, one patient did not show this relationship, and selective lesion studies in monkeys raise the possibility that learning and preference judgment do not rely on a single common process, but rather on distinct, anatomically proximate processes (Kazama & Bachevalier, 2009; Rushworth et al., 2011). Further work will be needed to establish whether these abilities can be reliably dissociated in humans.

Beyond their implications for brain-based models of decision-making, these findings also provide a novel lens through which to consider clinically evident behavioral changes that may follow frontal lobe injury. Although patients with VMF damage are sometimes described as impulsive, in this experimental context their choices are more erratic, but not excessively rapid. A degraded or unstable representation of subjective value would result in poor, or at least more variable, judgment. It might also underpin some symptoms of apathy, in that pre-morbidly valuable options might be less likely to trigger behavior. It is easy to see that disturbing a person's "value system" in the formal economic sense could lead to behaviors that are out of keeping with pre-existing tendencies, thus leading to a particular kind of personality change.

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