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COGNITIVE NEUROSCIENCE

Preference judgements involve a network of structures within frontal, cingulate and insula cortices

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Abstract

Environmental stimuli constantly compete for human attention and in many cases decisions are made based on the affective meaning they convey. Although the network of structures involved in processing affective value has been well described, the specific contribution of these structures to the process by which affective value guides decision making is less well understood and is the focus of the present study. Thus, subjects read descriptions of individually tailored holidays, varying in incentive value and then made preference judgements, cognitive judgements or no decision. Choices made from an affective perspective, compared with those made from a cognitive perspective, activated a region of the anterior insula/operculum and also the anterior cingulate cortex. Furthermore, activity in perigenual, anterior cingulate cortex was correlated with subjective ratings of incentive value. In contrast, medial orbitofrontal cortex (OFC) and a region of posterior ventrolateral prefrontal cortex (PFC), bordering on the insula, were found to be more active when affective stimuli guided response selection than when no selection was made. However, only the activity in the ventrolateral PFC was specific to response selection based on affective compared with cognitive judgements. It is proposed that the necessary introspection required to make subjective preference judgements is provided by the insula and cingulate cortices, while the medial OFC and posterior ventrolateral PFC/insula cortices contribute to stimulus evaluation and motivational aspects of response selection, respectively.

Introduction

Everyday stimuli in the environment compete for attention and invariably carry some form of affective significance, from a tasty-looking beverage (Paulus & Frank, 2003) to an attractive face (O'Doherty *et al.*, 2003). In many cases it is necessary to make choices based on these stimuli and the affective content may play a role, consciously or not, regardless of whether it is required for the decision. Recent neuroimaging studies have begun to define the network of structures that underlie the processing of positive affective stimuli in healthy adults, including primary reinforcers such as positive odours, tastes and flavours (Anderson *et al.*, 2003; de Araujo *et al.*, 2003b; Small & Prescott, 2005) and socially conditioned reinforcers, but still with a strong biological relevance, e.g. imagining pleasant foods (Arana *et al.*, 2003) and viewing attractive faces (Aharon *et al.*, 2001). These studies have shown activity in similar regions of the brain, regardless of the particular stimuli used to elicit positive states, including the amygdala, orbitofrontal cortex (OFC), insula and anterior cingulate. In the few studies that have examined positive emotional processing using more abstract rewarding stimuli, namely viewing images of sports cars (Erk *et al.*, 2002) and listening to pleasant music (Blood & Zatorre, 2001; Panksepp & Bernatzky, 2002; Koelsch *et al.*, 2006), some of the regions involved in processing biologically relevant stimuli also appear to be involved in processing more abstract rewarding stimuli. In particular, a region of the medial OFC that showed increased activity to sports cars compared with small cars (Erk *et al.*, 2002) was relatively near to a region of OFC activated when people read from menus comprised of high-incentive foods compared with low-incentive foods (Arana *et al.*, 2003).

In contrast to the above, few imaging studies have investigated the neural networks involved when the affective content of presented stimuli is necessary to guide response selection. In one study, involving choices based on food menus (Arana *et al.*, 2003), it was shown that whilst both the amygdala and a region of the OFC were differentially activated by incentive only, the OFC was also activated specifically when subjects made a selection, regardless of incentive value. In a further study, preference judgements differentially activated the medial prefrontal cortex (PFC), OFC, insula and anterior cingulate cortices, when subjects were asked to select their preferred beverage, although here the effects of incentive, independent of response selection, were not differentiated (Paulus & Frank, 2003). Thus, the

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present study sought to determine the network of neural structures specifically involved in making decisions based on preference judgements for abstract rewarding stimuli, while controlling for any general effects of incentive processing and response selection *per se*.

A decision that many people are familiar with, which is guided by positive affective experience, is choosing one's holiday destination and both the expected as well as the remembered pleasantness of a holiday influence the choice of subsequent holidays (Wirtz *et al.*, 2003). Therefore, the task that was designed consisted of individually tailored descriptions of high- or low-incentive holidays that subjects had to consider and in some cases select their preferred holiday.

Materials and methods

Subjects

Nineteen, healthy right-handed, male volunteers participated in this study and had no history of psychiatric intervention or neurological illness, as assessed by self-report questionnaire. Females were excluded from the study due to ethical considerations relating to the scanning technique. Subjects were aged between 21 and 38 years (mean ± SD, 25 ± 5 years). Each subject underwent structural magnetic resonance imaging (MRI) scans and positron emission tomography (PET) scans on the same day. All subjects gave written informed consent. The study was approved by Cambridge Research Ethics Committee and the Administration of Radioactive Substances Advisory Committee, UK, which apply the principles of the Declaration of Helsinki.

Experimental design and psychological task

All 19 subjects underwent 12 PET scans at 8-min intervals in an environment with low background noise and dimmed ambient lighting. All scans took place in the same session on the same day. The task the subjects had to undertake while in the scanner was presented on a touch-sensitive screen, controlled by a personal computer outside the scanning environment. The screen was oriented such that the subject could touch any location with their right index finger while maintaining a comfortable viewing distance. An instruction was displayed, 2 min 15 s prior to commencement of each scan, indicating the condition for that scan and reminding subjects how to proceed. Subjects began the task 15 s before PET scans began to ensure that subjects were fully engaged in the task during the acquisitions.

Before scanning took place all subjects completed a questionnaire to determine their individual holiday preferences (see details on questionnaire below). Subjects took part in a task called 'The Holiday Store', where they imagined they were looking through holiday options in a brochure or online. Each subject was presented with a series of 'menus' each consisting of a set of three individually tailored holidays, created from the results of their preference questionnaire, with three such menus for each PET scan. The items on these holiday menus were matched across conditions for word count and sentence length. The menus varied in incentive value (either high or low) and whether or not a choice was required. Examples of a high- and a low-incentive menu item for one individual are as follows.

High: 'White Water Rafting in British Columbia: face a thrilling experience on white foaming waters while taking in the amazing mountain scenery of this unique region'.

Low: 'Wildlife Watching in Antarctica: explore the most exceptional wilderness on earth and see inhabitants ranging from nesting penguins to the newborn seal pups'.

For the 'affective emphasis' scans, subjects were asked to read and imagine each holiday item and then select their preferred option by touching its position on the screen. In other scans, subjects were asked to select the item they thought was the most popular holiday of the three displayed, in a random survey of 100 people. These formed the 'cognitive emphasis' scans. It is important to note that, unknown to the subjects, the survey was fictional and they were not informed if their subsequent choice was correct or incorrect. In a final set of scans, subjects were not required to make any choices. Instead, they were presented with three distinct holidays and were asked to 'Read and imagine what it would be like to go on this package holiday. Then touch the third item to continue' (to match the motor response during choice conditions) in order to continue to the next screen. These formed the 'affective no choice' scans. In order to discourage subjects from making covert choices in the 'affective no choice' scans, the three holiday items were described as a 'package holiday'. The three holiday items comprising each 'package holiday' were all geographically related (e.g. all taking place in South America) and did not contain repetitions of related activities (e.g. a swimming activity was not presented on the same screen as a diving activity).

In summary, there were six types of condition in the present study, 'affective no choice', 'affective emphasis choice' and 'cognitive emphasis choice', each of which could be either high or low in incentive value. For reasons of brevity, the latter two are referred to as 'affective emphasis' and 'cognitive emphasis', respectively. Subjects were presented with each type of scan twice, such that each subject underwent 12 scans. Subjects were not informed of the incentive value manipulations at any time. The menus presented (and the order of menu presentation) during the 'cognitive emphasis' conditions were identical to those presented during the 'affective emphasis' conditions; the only difference being the task instructions given to the subject. Thus, during the 'affective emphasis' condition, the affective valence of the holidays was necessary to guide the subject's choice, while in the 'cognitive emphasis' condition the valence information was incidental to the choice being made. Scans were counterbalanced such that for half the 'cognitive' and 'affective emphasis' scans, subjects were presented with menus they were seeing for the first time. For the remaining half, subjects were presented with menus that had been seen previously in the other condition. Scans involving previously seen menus were presented in the latter half of the session, with a minimum of four scans between repeated menus. Overall, subjects experienced each condition once within the first six scans and a repeat of each condition occurred within the latter six scans, in a counterbalanced manner.

The presentation of all conditions was fully counterbalanced across subjects and all subjects performed a practice session, with a standard set of holidays, before PET scans began.

The PET images obtained from the 'affective emphasis' and 'cognitive emphasis' conditions were used to differentiate between those regions involved in making choices based on affective vs. cognitive evaluation. Comparisons between 'affective emphasis' and 'affective no choice' conditions were used to elucidate the brain regions involved in goal selection and choice behaviour (Fig. 1).

Pre-scan holiday preference questionnaire

Completion of a computer-based preference questionnaire was undertaken at least 1 week before each subject underwent their PET scans. The questionnaire consisted of a screen that displayed a holiday title (e.g. 'Skiing in the French Alps') above a visual analogue scale (VAS) that was approximately 15 cm in length and anchored at three points; 'Would never do this' on the left, 'Would not mind doing this'

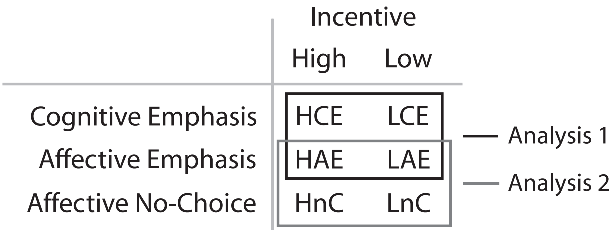

FIG. 1. Task design. The experiment was designed such that the first analysis investigated those regions involved specifically in making affectively-driven, as opposed to cognitively-driven, judgements. The second analysis was used to determine which regions were involved specifically in using the incentive value of stimuli to guide response selection.

in the centre and 'Would really like to do this' on the right. Subjects were asked to rate the holiday by moving the mouse-pointer over the scale and pressing the left mouse-button, at which point a small cursor appeared at the location of the click. After a short delay (0.5 s) the mouse-pointer was reset to the centre of the screen, below the VAS and the next holiday was presented. In total, subjects completed approximately 280 such ratings, which took approximately 25–30 min. Results were normalized to the length of the scale and, thus, are presented within the range (0, 1), where 0 is the extreme left of the scale and 1 is the extreme right. For subsequent use in the scanner, a subject's preferred holidays, defined as those rated between 0.8 and 1, were used as high-incentive items and those holidays that were not the most preferred but still acceptable, rated between 0.3 and 0.5, were used as low-incentive items. Holidays that the subjects did not like, rated from 0 to 0.2, were avoided.

Post-scan debriefing

After scanning, subjects were asked to complete a further, paper-based questionnaire that consisted of each menu screen they had seen during scanning. For the 'affective emphasis' trials subjects were asked to rate each of the three holidays for their incentive value and also how difficult they found the decision. For the 'affective no choice' trials, subjects were asked to rate the overall incentive value of the package holiday; no choice was made in this condition. For the 'cognitive emphasis' condition, subjects were asked to rate how difficult they found the decision. Incentive ratings were not required for these choices as these holidays were identical to those seen during the 'affective emphasis' trials. All ratings were made on VAS, situated adjacent to the holiday items and with anchor points identical to the holiday preference questionnaire. The scale for difficulty was anchored on the left as 'Easy' and on the right as 'Difficult'. All scales were approximately 7 cm in length.

Image acquisition and analysis

Structural MRI images were obtained for each subject using a Bruker 3T Magnet at the Wolfson Brain Imaging Centre based at Addenbrookes Hospital, Cambridge, UK. Structural MRI images were solely used for medical diagnostic purposes. PET scans were performed using a General Electric Advance system (General Electric, Milwaukee, WI, USA). Using the bolus H2-15O method, regional cerebral blood flow (rCBF) was measured during two separate scans for each of the six conditions in the design, making a total of 12 PET scans for each subject. However, a total of four scans from different subjects were discarded due to outside disturbances that may have affected attentiveness to the task. In addition, one subject underwent six PET scans, instead of 12, due to problems with equipment. In total, 218 PET images were obtained for analysis from 19 subjects. For each PET scan, the subject received a 20-s dose of H2-15O through a cannula in their left forearm, at a concentration of 300 Mbq/mL and flow rate of 10 mL/min. Each complete PET scan is an image integrated over a period of 90 s from the time at which the tracer enters the cerebral circulation. Each subjects' scans were individually preprocessed, and the preprocessed scans for all subjects were entered into a collective statistical analysis. Preprocessing and analyses were performed using the Statistical Parametric Mapping 2 (SPM2) package, provided by the Wellcome Department of Imaging Neuroscience, London, UK. Preprocessing involved: (i) realigning each subjects' scans, using their first scan as a reference; (ii) normalizing each scan for global cerebral blood flow and spatially normalizing the brain to conform to the standard MRI template produced by the Montreal Neurological Institute; and (iii) spatially smoothing using a Gaussian kernel of 12 mm full-width at half-maximum.

The general linear model, as implemented by SPM2, was used to estimate blood flow changes between conditions. To remove movement artefacts and effects due to scan order, six movement parameters and scan order were entered into the analysis as co-variates of no interest. Regions of interest (ROIs) around the amygdala and OFC were taken from previous work (Arana *et al.*, 2003), where the calculated volumes were 4435 mm^3 for the amygdala and 21 486 mm^3 for the entire OFC, leading to intensity thresholds for significance of $t > 3.28$ and $t > 3.6$ for these regions, respectively. ROIs for the anterior cingulate and insula cortices, taken from standard MNI templates, gave significance thresholds of $t > 3.6$ (21 000 mm^3) and $t > 3.72$ (28 320 mm^3), respectively.

Behavioural assessment and analysis

Behavioural measures of the latency to respond and the subjective ratings of incentive value and choice-difficulty were analysed using analysis of variance (ANOVA). Main effects were subsequently analysed using paired *t*-tests, which were uncorrected as only three paired tests were required.

Results

Behavioural analysis

The subjective ratings of the incentive value of the holidays in the post-scan debriefing validated the assignment of menus as either low or high incentive. Thus, the individually tailored holidays were judged to be of the appropriate incentive value by each subject (Fig. 2A). A repeated-measures ANOVA of both 'choice' and 'no-choice' conditions revealed a main effect of incentive value ($F_{1,18} = 264.98$, $P < 0.0005$) and no main effect of choice ($F_{1,18} < 1$), indicating that subjects rated the high-incentive conditions as having a greater incentive value than the low-incentive conditions, whilst no difference was seen between the 'affective emphasis' and 'affective no choice' conditions. However, there was an interaction between incentive and choice ($F_{1,18} = 15.88$, $P = 0.001$), such that incentive ratings for high-incentive menus were lower in the 'choice' condition compared with the 'no choice' condition, and the converse was the case for the low-incentive menus. This effect could have been due to the subject becoming more discerning when having to make choices from the high-incentive items but being far less discerning when making choices from low-incentive menus. For the trials that involved making a choice, subjects rated the difficulty of the choice equivalently for those based on personal preference ('affective emphasis') and those

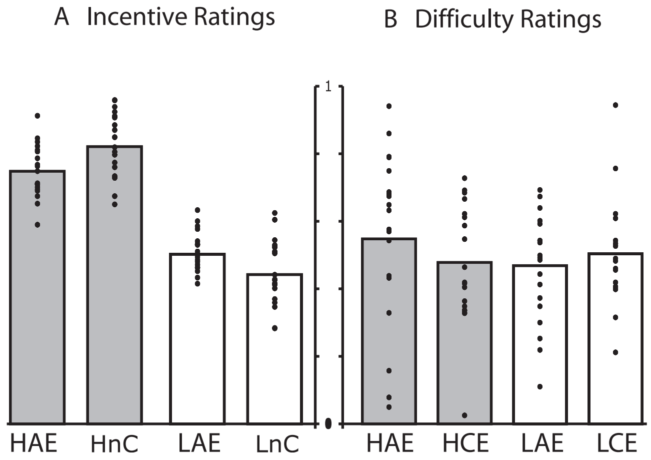

FIG. 2. Behavioural measures. (A) Normalized subjective ratings of the incentive value of holiday items. The high-incentive items (H) were considered significantly higher in incentive value than the low-incentive items (L) for both ‘affective-emphasis’ choice trials (AE) and ‘affective no choice’ trials (nC). (B) Normalized subjective difficulty of making a choice. Difficulty ratings were not significantly affected by either incentive ratings or the type of choice being made, i.e. affective emphasis (AE) or cognitive emphasis (CE). Individual points represent the mean ratings of individual subjects for each scan.

based on cognitive judgements (‘cognitive emphasis’), with no main effects of incentive ($F_{1,18} < 1$) or choice-type ($F_{1,18} < 1$; Fig. 2B).

Response latencies within the scanner were also recorded and, although no significant differences in latency were observed across incentive conditions ($F_{1,18} < 1$), an effect of choice on latency measures was found ($F_{2,36} = 19.18$, $P < 0.0005$). Response latencies were collapsed across incentive value and paired *t*-tests were performed. Subjects responded quicker during ‘cognitive emphasis’ trials compared with both ‘affective emphasis’ trials ($t_{18} = 3.246$, $P < 0.005$) and ‘affective no choice’ trials ($t_{18} = 6.313$, $P < 0.0005$). Subjects were also faster on ‘affective emphasis’ trials than on ‘affective no choice’ trials ($t_{18} = 2.814$, $P < 0.05$). Response latencies of subjects in ‘affective no choice’ trials may have been the longest because they were likely to spend more time imagining the package holidays as no choice was required. This element of reflection may also explain why response latencies in the ‘choice’ conditions did not correlate with subjective difficulty measures in the majority of subjects. Correlational analyses of the response latencies and subjective difficulty ratings for each subject (meaned across the set of menus within each scan) revealed that only three out of 18 subjects showed significant correlations (15 out of 18 subjects $r^2 < 0.24$, two subjects $r^2 \sim 0.23$ and one subject $r^2 = 0.72$). The most likely explanation for a lack of correlation is that response latencies were not only determined by the time taken to make a decision but also how long a time subjects spent ‘reflecting’ on the holidays. Consequently, subsequent analyses investigating brain regions in which activity was correlated with difficulty used ratings of subjective difficulty only.

A separate ANOVA comparing response latencies in the ‘affective’ and ‘cognitive emphasis’ conditions only (choice type), taking into account whether the condition was in the first six scans or last six scans (stage), revealed a significant effect of choice type ($F_{1,17} = 14.02$, $P = 0.002$) and a significant effect of stage ($F_{1,17} = 10.02$, $P = 0.006$), but no interaction ($F < 1$). Because subjects showed an overall reduction in response latencies in the last six scans, this may indicate either that subjects became more proficient at making their choices or that they were quicker to respond when making choices from menus they had seen previously.

Given that subjects were making choices based on the same set of stimuli for both the ‘affective emphasis’ and ‘cognitive emphasis’ conditions, it was important to determine if performing one type of choice could later influence the other type of choice when the holidays were presented for the second time. If choices were independent between the two conditions then it could reasonably be expected that only a third of selections would be the same across both conditions. When presented with the same set of holiday options but under a different experimental condition, subjects selected the same holiday only 34 ± 1% (mean ± SEM) of the time. This is a good indicator that choices were independent.

From the post-scan ratings of the holiday menus, the high-incentive condition covered ratings from 0.57 (relatively neutral) to 0.97 (highly positive). The intended range of low-incentive holiday items was between 0.3 and 0.5; however, the actual spread of these was greater, covering the range from 0.16 to 0.65, therefore including holidays that would normally be avoided and that may be considered aversive, rather than neutral. For this reason, the subsequent correlation analysis between rCBF and positive incentive value only included menus from the high-incentive condition.

Neuroimaging analysis

For all the analyses, regions of interest included the amygdala, OFC and ventromedial PFC, anterior cingulate cortex and insula. The full list of activations and correlations can be seen in Table 1.

Choices with an affective, compared with cognitive, emphasis activate insula and anterior cingulate

The inclusion of a condition in which a choice was made, with a ‘cognitive emphasis’, enabled the identification of the neural substrates underlying choice based on differing perspectives. This is highlighted as ‘Analysis 1’ in Fig. 1. In both ‘affective’ and ‘cognitive emphasis’ conditions, the stimuli presented convey affective information but only in the former condition was this information necessary to make a choice. In the latter condition, the affective information was incidental as the judgement required subjects to take a primarily

TABLE 1. Activations

	Laterality	*x*	*y*	*z*	*t*-Score
Affective choice vs. affective no choice					
Insula/VLPFC	Left	−22	24	−4	4.51
OFC	Left	−24	56	−14	3.6
OFC	Right	26	62	4	3.4
Affective choice vs. cognitive choice					
Insula/operculum	Right	42	10	10	3.72
ACC	–	0	30	14	3.72
Cognitive choice vs. affective choice					
DLPFC	Right	34	26	50	4.01 (n.s.)
Correlations					
Difficulty of affective choices					
OFC	Left	−20	42	−16	4.29
Difficulty of cognitive choices					
OFC	Left	−16	50	−22	4.16
VMPFC	–	0	26	−20	4.25
High incentive values					
ACC	Right	2	34	2	4.14

ACC, anterior cingulate cortex; DLPFC, dorsolateral prefrontal cortex; OFC, orbitofrontal cortex; VLPFC, ventrolateral prefrontal cortex; VMPFC, ventromedial prefrontal cortex.

cognitive perspective. By subtracting scans from the two perspectives, those regions involved in using 'affect' to guide choice behaviour are highlighted, whilst the reverse subtraction identifies regions involved in cognitively guided judgements. When making this comparison, it was found that both a region of the anterior cingulate (0, 30, 14; $t_{18} = 3.72$; Fig. 3A) and the right insula/operculum (42, 10, 10; $t_{18} = 3.72$; Fig. 3B) were differentially activated when making judgements based on affective preference. The opposite comparison, revealing areas involved in cognitive processing, identified activity in the right dorsolateral PFC (34, 26, 50; $t_{18} = 4.01$; Fig. 3C), though this did not survive the corrections for the whole brain.

To determine whether the activations seen in the anterior cingulate and insula/operculum in the 'affective emphasis' condition were related to the affective processing of the stimulus material, *per se*, an additional analysis compared the 'affective no choice' condition with the 'cognitive emphasis' condition. Despite these two conditions differing in many ways, regions involved in affective appraisal should show enhanced activity in the former compared with the latter condition. However, there were no such activations in the vicinity of the anterior cingulate cortex, and the region of activation in the insula (42, 10, −18; $t_{18} = 4.37$) was considerably more ventral than that seen when comparing 'affective emphasis' with 'cognitive emphasis' conditions (42, 10, 10).

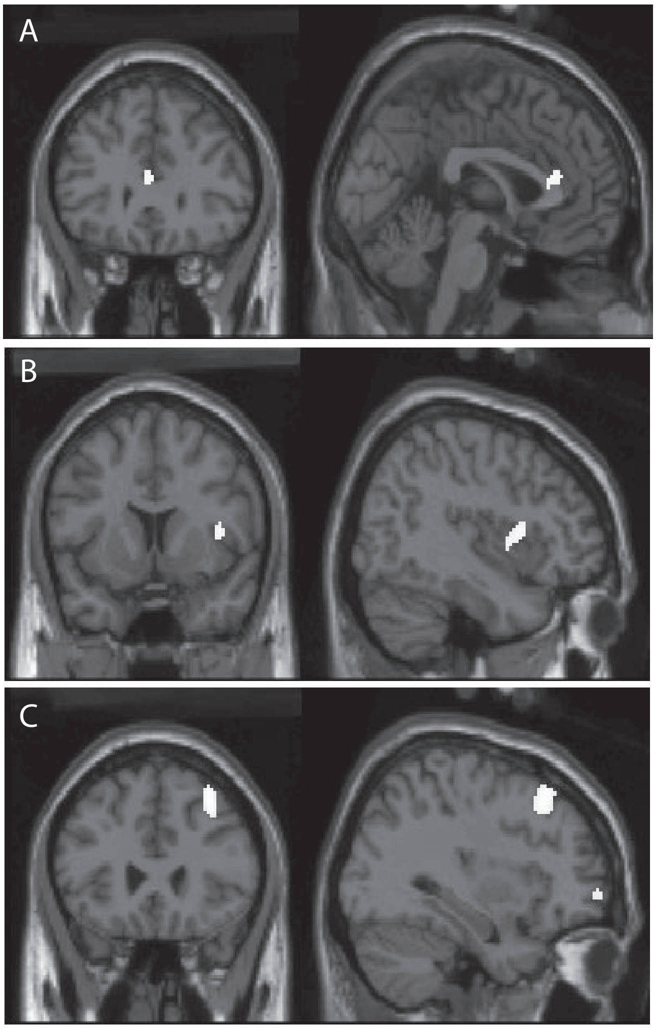

FIG. 3. Affective choice vs. cognitive choice. (A) The anterior cingulate cortex (0, 30, 14) and (B) insula/operculum (42, 10, 10), show increased rCBF when subjects made choices with an 'affective emphasis' compared with when making choices with a 'cognitive emphasis'. (C) The dorsolateral prefrontal cortex, which is known to be involved in many diverse cognitive tasks, showed increased activity when making choices with a 'cognitive emphasis' (34, 26, 50–n.s.).

Stimulus selection guided by incentive information activates OFC and posterior ventrolateral PFC

In order to examine the neural correlates of affectively driven choice behaviour, the 'affective emphasis' conditions were compared with the 'affective no choice' conditions, irrespective of incentive value. This main effect of choice represented 'Analysis 2', which is highlighted in Fig. 1. In both these conditions, subjects are required to attend to the affective value of the stimuli, but only in the choice condition are subjects required to select according to their preference. In this analysis, increased activity was observed in the left OFC (−24, 56, −14; $t_{18} = 3.60$; Fig. 4A), and also on the border between the left insula and left ventrolateral PFC (−22, 24, −4; $t_{18} = 4.51$; Fig. 4B). There was no significant interaction between incentive and choice.

To determine whether the activations seen in the OFC and insula/ventrolateral PFC were specific to stimulus selection guided by incentive information, an additional analysis compared the 'cognitive emphasis' condition with the 'affective no choice' condition. An almost identical region of activation (−22, 54, −14; $t_{18} = 4.69$) was seen within the left OFC of this contrast to that seen in the previous contrast, suggesting that this region was involved in stimulus selection in general. However, no such activation was seen in the insula/ventrolateral PFC. The nearest activation peak was seen far more ventrally (−18, 22, −22; $t_{18} = 4.03$). This would suggest that the insula/ventrolateral BOLD response seen when contrasting 'affective emphasis' with 'affective no choice' conditions was related more specifically to stimulus selection guided by the incentive value of the reward.

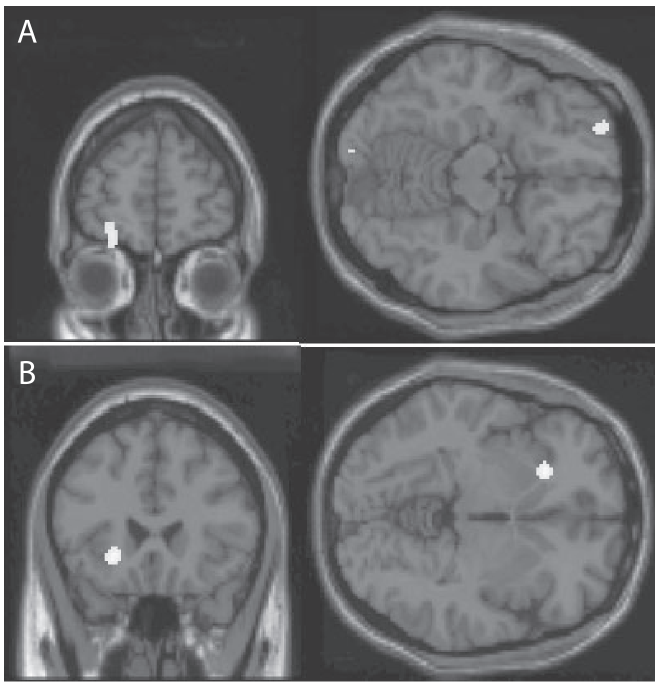

FIG. 4. Affective choice vs. affective no choice. Region of (A) the left OFC (−24, 56, −14) and (B) insula/VLPFC (−22, 24, −4) that show increased rCBF when viewing affective material and making a choice ('affective emphasis' condition) when compared with viewing affective material but not making a choice ('affective no-choice' condition).

Subjective incentive value is correlated with activity in the perigenual anterior cingulate cortex

Comparisons for the main effect of incentive value (high vs. low incentive), irrespective of choice, showed no significant activations in any of the regions of interest. Also, no activations were seen in the reverse contrast (low vs. high incentive). However, activity within a region of the perigenual anterior cingulate (2, 34, 2; $t_{18} = 4.14$; Fig. 5) was significantly correlated with subjective ratings of incentive value, showing greater levels of activity when subjects were viewing holiday menus of higher incentive value. As noted earlier, only ratings from the high-incentive condition (incentive range: 0.57–0.97) were included in this correlation as the low-incentive condition may have included items that could have been considered aversive.

Subjective difficulty of a choice correlated with activity in the OFC

Given that activity in a number of regions within the frontal lobe was associated with making selections from an affective perspective, it was determined whether regional changes in rCBF were correlated with the actual difficulty of the choices. A region of the OFC was found to correlate with the subjective difficulty of choices with an 'affective emphasis' (−20, 42, −16; $t_{18} = 4.29$; Fig. 6A), and a similar region (−16, 50, −22; $t_{18} = 4.16$; Fig. 6B) was correlated with the subjective difficulty of choices with a 'cognitive emphasis'. An additional region of the subcallosal medial PFC (0, 26, −20; $t_{18} = 4.25$; Fig. 6C) was also found to correlate with difficulty of the cognitive emphasis trials.

Discussion

This study examined the neural substrates of processing abstract rewarding stimuli whilst making choices from affective and cognitive perspectives. The stimuli employed in this study were unique in that the rewarding properties were dependent on subjects using their imagination and past experience of hedonically charged events in order to determine the anticipated value of a presented event. A number of interesting results emerge from this study. First, the opercula/insula cortex and the postgenual, anterior cingulate cortex were active when subjects were making use of affective information to guide response selection, while the dorsolateral PFC was more active, though not significantly, when making judgements from a cognitive standpoint. Because the 'affective emphasis' condition necessarily involved self-referential processing, these results suggest a role for the insula and cingulate cortices in introspective processing, while the 'cognitive emphasis' choices hinted at activity in a region involved in cognitive processing. Second, activity in the perigenual region of the anterior cingulate cortex was correlated with subjective ratings of incentive value which, together with the adjacent postgenual activity related to making affective choices, suggests a role for this region in motivational evaluation. Ventrolateral PFC and an anterolateral region of the OFC were more active during response selection, with additional regions of the OFC correlating with the subjective difficulty of the choices. These results indicate a role for these structures in goal selection and response selection.

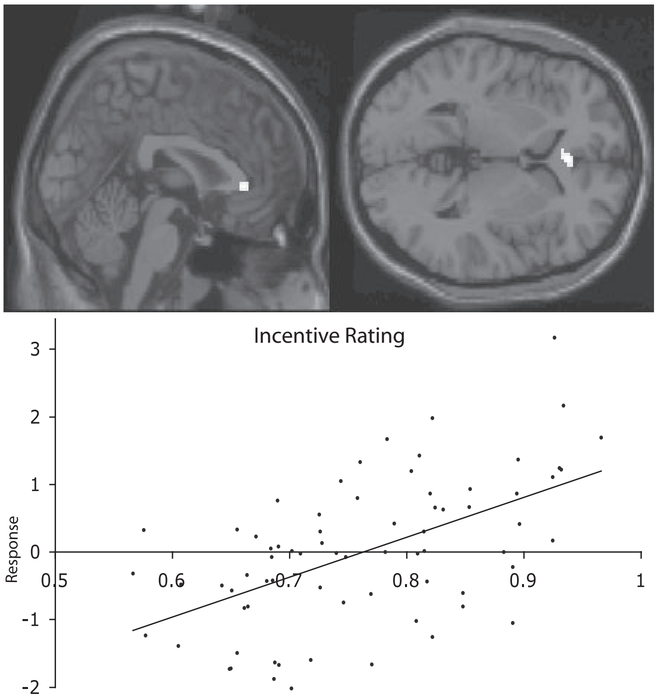

FIG. 5. Co-variation of activity in ACC with high incentive value. Activation in a region of the right ACC (2, 34, 2) was found to co-vary with subjective ratings of incentive value for the high-incentive trials.

Neural circuitry underlying the use of affective information to guide response selection

Three regions of activity were associated with positive affective processing in this study. The anterior cingulate at the level of the genu of the corpus callosum was positively correlated with incentive value, whilst a postgenu region of the anterior cingulate and an anterior region of the insula/operculum were differentially activated when response selection was guided primarily by incentive judgements rather than cognitive judgements. It could be argued that asking subjects to judge which holiday was most popular ('cognitive emphasis') may have involved affective processing that influenced the choices they made. However, the task instruction for the 'cognitive emphasis' condition was carefully worded such that subjects would be less likely to make a judgement based on their own affective appraisal of the stimuli. During debriefing, several subjects stated voluntarily that they attempted to imagine a prototypical person and make judgements based on their beliefs about such a prototype. This process is in agreement with other psychological studies, which have demonstrated that subjects tend to use 'prototype heuristics' (Kahneman & Frederick, 2002) when required to make judgements using statistical data. Moreover, it has been shown that subjects are far less likely to let affect guide their decision making when groups of people are considered as a whole, rather than as individuals. For example, subjects are less likely to donate financial aid to a group of individuals than to an identified individual from the same group, an effect thought to be due to the reduced emotional reaction of subjects when considering groups of 'victims' (Kogut & Ritov, 2005).

Therefore, it is unlikely that the 'cognitive emphasis' condition described in the present study, which presents the question in the form of a statistic, involves the subject using affective information to guide responses. In addition, because the 'cognitive' and 'affective emphasis' conditions were being directly compared, any significant differences in the affective vs. cognitive comparison would be over and above any incidental affect generated in the 'cognitive emphasis' condition. Moreover, both conditions involved retrieval of information from semantic memory, so this was not sufficient to explain differences in the neuroimaging data. Finally, evidence to suggest

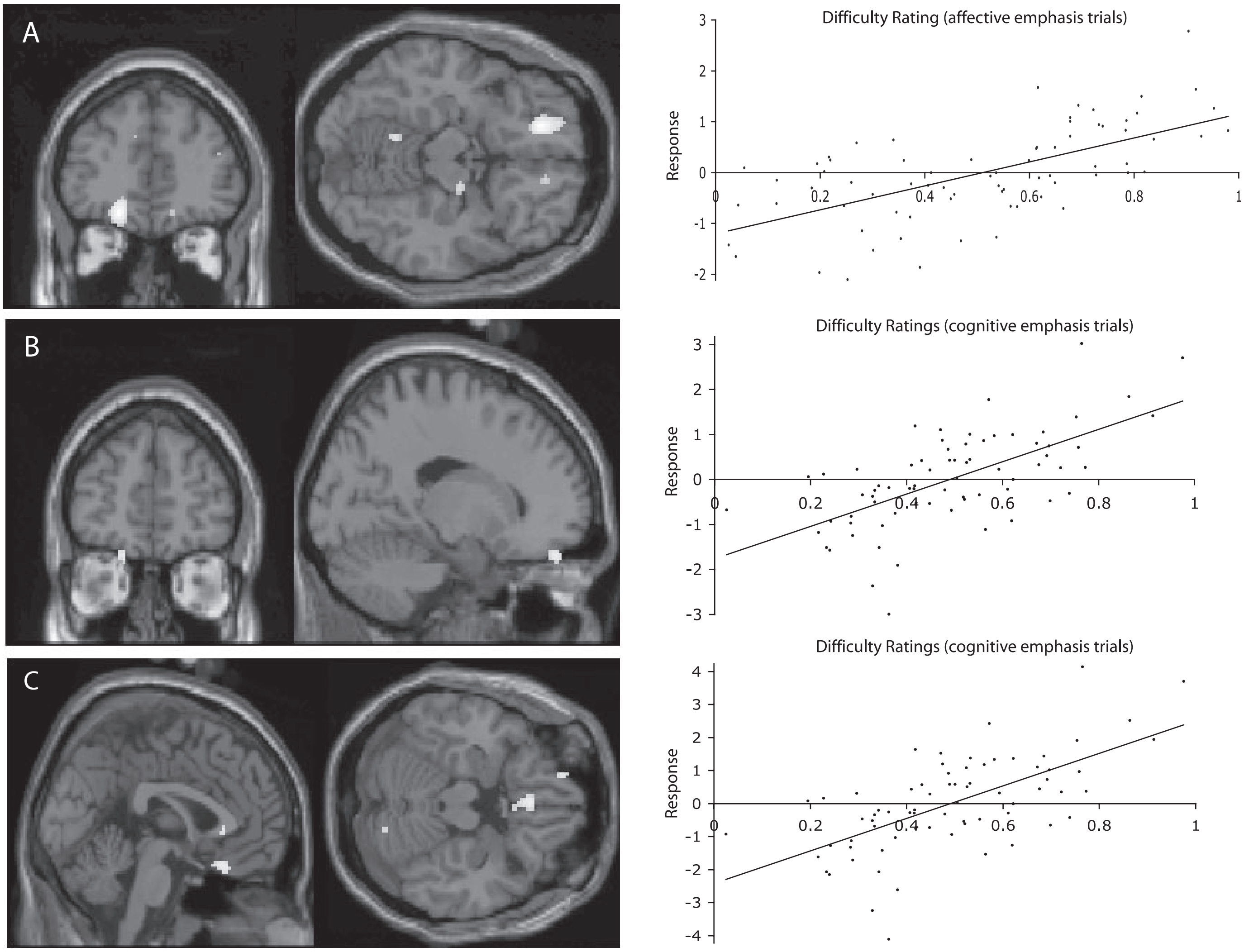

FIG. 6. Correlation with subjective difficulty of choice. (A) Choice difficulty in the 'affective emphasis' condition showed significant co-variation in a region of the OFC (−20, 42, −16). (B) Choice difficulty in the 'cognitive emphasis' condition also showed co-variation in a similar region (−16, 50, −22). (C) The subcallosal ventromedial PFC (0, 26, −20) was also found to co-vary with subjective difficulty of choices with a cognitive emphasis.

that the 'cognitive emphasis' condition involved making a cognitive judgement can be found by comparing that condition with the 'affective emphasis' condition. This represents the reverse analysis to that which examined the processing of affect and indicated enhanced (although not significant) activity in a region of the right dorsolateral PFC, which is known to be recruited by many diverse cognitive tasks (Duncan & Owen, 2000).

A functional MRI study that examined preference judgements based on biologically relevant stimuli has also found activity in both the insula and anterior cingulate cortex (Paulus & Frank, 2003), similar to that seen in the present study for abstract stimuli. In this earlier experiment, subjects viewed pictures of two drinks on a screen and were asked to select their preferred option or to identify which drink was in a bottle. Only one comparison was performed, that of the preference condition with the identification condition, which revealed activity in the left insula and also in the anterior cingulate cortex. However, because the preference and identification conditions differed with respect to the uncertainty of the choice, 'level of uncertainty' could have been responsible for the differences in brain activity observed. In contrast, the present study, and that of a colour preference study by Johnson *et al.* (2005), show that activation in these regions survives when uncertainty is controlled for, strengthening the conclusion that activity in the medial PFC and rostral regions of the anterior cingulate cortex is associated with subjective preference judgements.

Other work that bears similarities to the present study include 'hot' and 'cold' reasoning (Goel & Dolan, 2003; Schaefer *et al.*, 2003), where 'hot' reasoning refers to emotional processing and 'cold' reasoning is considered more cognitive. These studies have indicated that emotional processing, as compared with more cognitive processing, activates ventral regions of the medial PFC. However, it is important to note that in these studies the affective nature of the stimuli was incidental to the task requirements, in comparison to the present study where subjects were required to attend to the affective nature of the stimuli and to use this information to guide response selection. A more closely related task, in that subjects were required to use affective information in order to make a judgement, involved selecting between morphed faces based on either their emotional expression (an 'affective emphasis choice') or on their masculinity (a 'cognitive emphasis choice'; Winston *et al.*, 2003). The results of this study revealed activity in the anterior cingulate cortex, though in a slightly more lateral location than either of the activations in the current study. The insula cortices also showed some level of activity, although this was below significance threshold and much more posterior than the current insula activation.

The insula and anterior cingulate regions of the brain activated in the present study have been implicated in the representation and awareness of internal bodily states (Craig, 2002, 2003; Bechara & Naqvi, 2004; Wiens, 2005). Specifically, studies have shown that activity of the right insula/opercular cortex is correlated with increased accuracy on a heartbeat-detection task (Critchley *et al.*, 2004) and occurs in response to stimulation with primary reinforcers such as tastes (de Araujo *et al.*, 2003a) and flavour (Small & Prescott, 2005). Anterior cingulate activity has been shown to correlate with changes in skin conductance, a measure of peripheral arousal (Critchley *et al.*, 2002; Nagai *et al.*, 2004), and there have also been indications of its involvement in motivational processing (de Araujo *et al.*, 2003a). Numerous studies have also linked activity within dorsal cingulate and medial PFC regions with processing of information related to the self (Phan *et al.*, 2004; Gusnard, 2005; Moran *et al.*, 2006; Northoff *et al.*, 2006), whilst neighbouring ventral regions of anterior cingulate cortex are associated specifically with the processing of affective information (Moran *et al.*, 2006).

Enhanced activity was only seen in the present study in postgenual anterior cingulate cortex and anterior insula when selecting holidays based on affective preference compared with selecting holidays using a more cognitive approach. This cannot reflect specifically the use of affective information in decision making, as a similar increase in activity was not seen when viewing affective material and making an affective choice (as in the 'affective emphasis' condition) compared with viewing affective material and not making an affective choice (as in the 'affective no choice' condition). Instead, the enhanced activity may reflect either affective processing *per se* or the processes involved specifically in self-referential processing. It is unlikely that the activity in the postgenual anterior cingulate cortex reflects affective processing *per se*, as a *post hoc* comparison of the 'affective no choice' condition with the 'cognitive emphasis' condition revealed no evidence of enhanced activity in this region. Thus, the most likely explanation of the enhanced activity in the anterior cingulate, when making a preference judgement as compared with a cognitive judgement, is recruitment during self-referential processing. In contrast, although there was anterior insula activation when contrasting the 'affective no choice' condition with the 'cognitive emphasis' condition, this was far more ventral than in the comparison of the 'affective emphasis' condition with the 'cognitive emphasis' condition. Thus, the anterior insula activation in the latter most likely reflects the representation and awareness of subjective feelings/bodily states that may be used to guide preference judgements. Finally, the positive correlation of perigenual cingulate activity with incentive value may reflect the motivational desire to embark on the high-incentive holidays that subjects were imagining. Future studies should include measures of autonomic activity to address this issue.

Prefrontal circuitry involved in response selection and decision making

The ventrolateral activity reported in this study was similar to a region that was activated during the switch in a reversal learning task (Cools *et al.*, 2002). In the latter, the activity was greatest when subjects were required to inhibit responses that were no longer appropriate, specifically when subjects switched from selecting one stimulus to selecting the other upon reversal of the reward contingencies. In the present study, subjects were making selections from three items presented together, and in order to select one of the options responses to the other two would have to be suppressed. This activation was specifically seen in the comparison between 'choice' and 'no choice' trials, where affective processing was involved. A *post hoc* contrast performed between the 'cognitive emphasis' and 'affective no choice' trials, solely to examine any contribution of the ventrolateral area to making cognitive choices, failed to show any significant activity. Firstly, this rules out any alternative interpretation of the ventrolateral activation as being due to 'familiarity' due to half the menus in the 'affective emphasis' condition being novel compared with all the menus in the 'affective no choice' condition. Only half of the menus in the 'cognitive emphasis' condition were novel too, but in this case ventrolateral PFC was not activated. Secondly, and more importantly, this would imply that the activity seen in the comparison between 'affective emphasis' choice and 'affective no choice' was related to choices where affect and incentive motivation may play a role.

The OFC also showed differential activity between the 'affective emphasis' and 'affective no choice' trials. Furthermore, a very similar region showed a correlation with the difficulty of the choice being made in the affective condition. These results are in agreement with a related study that examined incentive processing and preference judgements using food-based rewards (Arana *et al.*, 2003). This latter study also found a region of OFC, similar in location to that found in the present study, which was differentially activated during trials that required a 'choice' compared with those that required 'no-choice'; it too also correlated with the subjective difficulty of the choice that subjects made. Because all menus were novel in this latter study, differences in the level of familiarity of the stimuli between the 'affective emphasis' and 'affective no choice' conditions in the present study are unlikely to contribute to the OFC activation. Because the neurons in this area of OFC have been shown to code relative reward value in monkeys (Tremblay & Schultz, 1999), the enhanced activity in humans associated with making preference judgements may reflect the role of the OFC in evaluating different rewards and thereby contributing to the process of goal selection. However, in contrast to the ventrolateral activation described above, this OFC region also showed increased activity in the 'cognitive emphasis' condition compared with the 'affective no choice' condition; moreover, an adjacent region correlated with the difficulty of the cognitive judgements. Together these findings implicate the OFC in other, non-affective aspects of subjective decision making, such as the evaluation of multiple stimulus alternatives.

Summary and conclusions

In the present study a number of regions within the frontal, cingulate and insular cortices were shown to be activated in a task requiring positive affective processing of abstract, behaviourally relevant stimuli and the subsequent use of such processing to guide response selection. It has been possible to dissect out the relative contributions of these regions to the different aspects of making preference judgements by comparing it with two other conditions using identical stimuli, one requiring a judgement with a cognitive emphasis and the other in which no judgement was required. In particular, the anterior insula/frontal operculum and postgenual, anterior cingulate cortex were differentially activated when making choices based on affectively driven judgements compared with those that were more cognitively driven. Given that the former has already been shown to be involved in the representation of internal bodily states (Critchley *et al.*, 2001, 2003, 2004), and in the generation and monitoring of peripheral arousal (Critchley *et al.*, 2000), and the latter has been implicated in the allocation of attention to such subjective emotional responses (Lane *et al.*, 1997) and in self-referential processing in general (Gusnard, 2005), the current findings suggest that these regions provide the necessary introspection required to make such preference judgements. In contrast, there was differential activity in the OFC and the posterior region of the ventrolateral PFC bordering on the insula, specifically in the condition where affective information has to guide response selection, compared with when it does not. The finding that activity in a similar region of the OFC was also present when cognitive information guided response selection suggests that this region may be involved in more general aspects of subjective decision making whenever multiple stimulus options need to be evaluated. On the other hand, the activity in the posterior ventrolateral PFC/insula was not present when cognitive information guided response selection, suggesting that it was related to choices that consider how motivated one is towards the reward.

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Abbreviations

MRI, magnetic resonance imaging; OFC, orbitofrontal cortex; PET, positron emission tomography; PFC, prefrontal cortex; rCBF, regional cerebral blood flow; ROI, region of interest; VAS, visual analogue scale.

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