

# Affective Judgment and Beneficial Decision Making: Ventromedial Prefrontal Activity Correlates With Performance in the Iowa Gambling Task

Georg Northoff,<sup>1,2\*</sup> Simone Grimm,<sup>1</sup> Heinz Boeker,<sup>1</sup> Conny Schmidt,<sup>3</sup> Felix Bermpohl,<sup>4</sup> Alexander Heinzl,<sup>5</sup> Daniel Hell,<sup>1</sup> and Peter Boesiger<sup>3</sup>

<sup>1</sup>Department of Psychiatry, University of Zurich, Zurich, Switzerland

<sup>2</sup>Department of Psychiatry, University of Magdeburg, Magdeburg, Germany

<sup>3</sup>Institute of Biomedical Engineering, ETH and University of Zurich, Zurich, Switzerland

<sup>4</sup>Department of Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts, USA

<sup>5</sup>Department of Nuclear Medicine Juelich, University of Duesseldorf, Duesseldorf, Germany

---

**Abstract:** Damasio proposes in his somatic marker theory that not only cognitive but also affective components are critical for decision making. Since affective judgment requires an interplay between affective and cognitive components, it might be considered a key process in decision making that has been linked to neural activity in ventromedial prefrontal cortex (VMPFC). Using functional magnetic resonance imaging (fMRI), we examined the relationship between VMPFC, emotionally (unexpected)- and cognitively (expected)-accentuated affective judgment, and beneficial decision making (Iowa Gambling Task; IGT) in healthy subjects. Neuronal activity in the VMPFC during unexpected affective judgment significantly correlated with both global and final performance in the IGT task. These findings suggest that the degree to which subjects recruit the VMPFC during affective judgment is related to beneficial performance in decision making in gambling. *Hum Brain Mapp* 27:572–587, 2006. © 2005 Wiley-Liss, Inc.

**Key words:** decision making; ventromedial prefrontal cortex; fMRI; affective judgment; high- and low-risk decisions; expectancy

---

## INTRODUCTION

One of the most persistent challenges of daily life is to make decisions about courses of action. Central to decision making is the distinction between high- and low-risk decisions, e.g., about financial matters. High-risk decisions imply the chance of great reward but also high risk to lose. By contrast, low-risk decisions are accompanied by lower reward though with less risk to lose. Despite the smaller short-term gain, low-risk decisions may lead to better long-term payoff. The ability to distinguish between financial high- and low-risk decisions and the learning effect based on the experience of losses over time can be tested in a laboratory setting using decision making tasks such as the Iowa Gambling Task [IGT; Bechera et al., 1994, 1999].

Investigation of such tasks in patients with brain lesions suggests involvement of the ventromedial prefrontal cortex (VMPFC) in beneficial decision-making [Bechara, 2004;

---

Contract grant sponsor: German Research Foundation; Contract grant number: DFG 304/4-1; Contract grant sponsor: German Academic Exchange Service; Contract grant number: DAAD D/02/46858; Contract grant sponsor: Swiss National Research Foundation; Contract grant number: 3100A0-100830; Contract grant sponsor: Research Foundation, University of Zurich, Organon Switzerland; Contract grant sponsor: ETH Zurich (SEP); Contract grant sponsor: Philips Medical Systems, Best, NL.

\*Correspondence to: Georg Northoff, MD, PhD, Dept. of Psychiatry, University of Magdeburg, Leipziger Strasse 44, 39120 Magdeburg, Germany. E-mail: georg.northoff@medizin.uni-magdeburg.de

Received 28 October 2004; Accepted 30 June 2005

DOI: 10.1002/hbm.20202

Published online 21 December 2005 in Wiley InterScience (www.interscience.wiley.com).

Clark et al., 2004; Damasio, 2004; Damasio et al., 2000; Rogers et al., 2004; Rolls, 1999, 2000]. With regard to decision-making, patients with lesions especially in the right VMPFC remain unable to develop affective reactions with appropriate affective judgment [Bolla et al., 2003; Clark et al., 2003; Hornak et al., 2003; Manes et al., 2002; Sanfey et al., 2003; Tranel et al., 2002; but see Adinoff et al., 2003]. This is reflected clinically in their preference for high-risk behavior with financial decisions that quickly squander monetary resources. Correspondingly, these patients show bad IGT performance with predominant selection of high-risk cards and absence of learning effect over time [Bolla et al., 2003; Clark et al., 2003; Hornak et al., 2003; Manes et al., 2002; Sanfey et al., 2003; Tranel et al., 2002]. The close relationship between VMPFC and decision making is underlined further by imaging studies in healthy subjects showing signal changes in the VMPFC while carrying out the IGT [Akitsuki et al., 2003; Bolla et al., 2003; Elliot et al., 1999; Patterson et al., 2002]. Finally, various psychiatric disorders with possible VMPFC involvement can be characterized by poor decision-making. For example, bad IGT performance has been demonstrated in patients with obsessive-compulsive disorder [Cavallaro et al., 2003], catatonia [Bark et al., 2005], pathological gambling [Cavedini et al., 2002], impulsive personality disorder, and substance abuse [Adinoff et al., 2003; Bechara et al., 2001; Bolla et al., 2003].

Decision making like that in the IGT presupposes the theory of somatic markers as developed by Damasio [1994]. This theory of somatic markers argues that optimal decision making is not simply the result of rationally, cognitively calculated categorization of gains and losses but is also based on good or bad affective reactions and emotionally guided evaluation [see also Bechara, 2004]. Decision-making might be influenced by a variety of cognitive and affective components including rational categorization and emotional reactions. These two components are paradigmatically reflected in affective judgment, which consists of emotional stimulation (inducing emotional reactions) and evaluation (requiring rational categorization). Affective judgment subsequently might be related to decision making.

Although the involvement of the VMPFC and affective judgment are suggested strongly by lesion studies and psychiatric patients (see above and Bechara [2004]), affective and cognitive modulation of our ability to make decisions has not yet been demonstrated in healthy subjects. The present study therefore examined the relationship between affective judgment, decision-making, and ventromedial prefrontal function in healthy subjects. Specifically, using functional magnetic resonance imaging (fMRI), we investigated neuronal activity in the VMPFC during an affective judgment task of emotional pictures and correlated it with IGT performance. Because our focus was on the effects of judgment rather than on emotions by themselves, as induced by emotional pictures, our control condition included mere emotional picture viewing without any judgment picture viewing as nonjudgmental control condition (rather than judgment about neutral pictures).

In addition to mere affective judgment, we incorporated a judgment expectancy period to shift the accent from the affective component (emotional experience and reactions) to the cognitive component (rational categorization). Although a multidimensional construct [Ploghaus et al., 2003], judgment expectancy accentuates the cognitive component by focusing and redirecting attention on the subsequent categorization and evaluation. Accordingly, affective judgment remained either unexpected, emphasizing the affective component, or was preceded by an expectancy period accentuating cognitive-attentional demands. This allowed us to explore the role of affective and cognitive-attentional components of affective judgment in relation to decision making.

Comparable to decision making, affective judgment has been associated with neuronal activity in the VMPFC [Gusnard et al., 2001; Northoff and Bermpohl, 2004]. Our findings contribute to these results by demonstrating that VMPFC signal changes during affective judgment specifically correlate with both global and final IGT performance. Moreover, we demonstrated that preceding cognitive-attentional modulation reverses signal increases into signal decreases in the VMPFC during affective judgment resulting in a differential correlation pattern with IGT. Accordingly, our results suggest that recruitment of the VMPFC during affective judgment is related to beneficial decision making in gambling. However, the exact nature of affective and cognitive processes mediating between affective judgment and beneficial decision making remains to be explored.

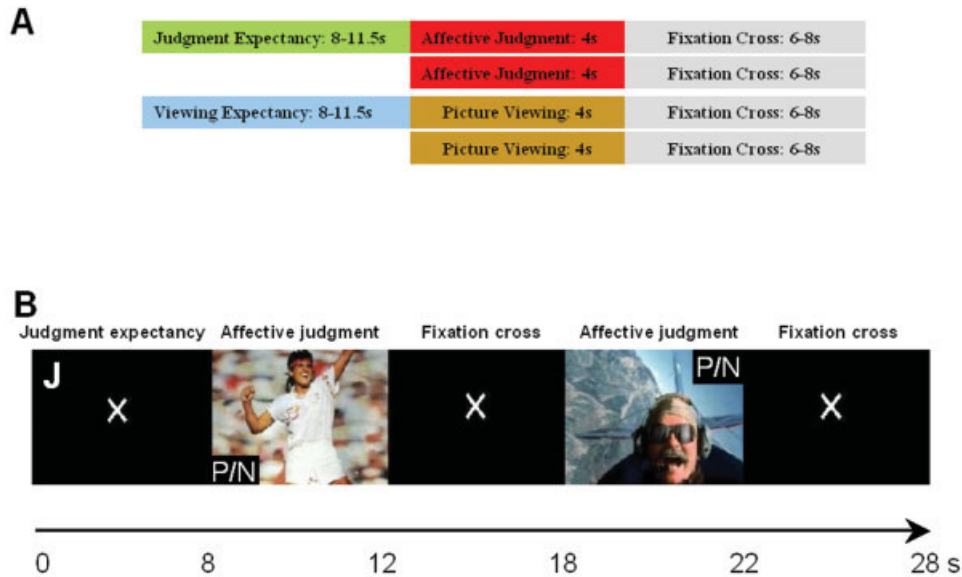
## SUBJECTS AND METHODS

### Subjects

We studied 14 healthy subjects (7 women, 7 men; average age, 28.7 years; age range, 19–34 years) without any psychiatric, neurologic, or medical disease. All were right-handed as assessed by the Edinburgh Inventory for Handedness [Oldfield, 1971]. After detailed explanation of the study design and potential risks, all subjects gave written informed consent.

### Paradigm

Subjects were asked to view photographs taken from the International Affective Picture System [IAPS; Center for Research in Psychophysiology, 1999]. Negative (valence: 1–3) and positive (valence: 7–9) pictures were presented for a duration of 4 s. Picture sets were counterbalanced across subjects as well as within each subject according to the two categories, positive and negative. In 50% of the events subjects had to judge the pictures as to whether they were positive or negative (“judgment”; see Fig. 1). This was indicated by the letters P/N in one of the four corners of the photograph. In the other 50% of the events (control condition), subjects were asked to passively view the pictures (letters A/A in the corner). The response was given by button pressing. This condition includes emotional stimulation without any judgment (picture viewing) and served to



**Figure 1.**

Activation paradigm for affective judgment with and without expectancy. **A:** Main conditions and control conditions. Affective judgment: judgment (positive/negative; P/N) of emotional pictures taken from the International Affective Picture System (IAPS) for a duration of 4 s. Response was given by button click. Affective judgment with expectancy: presentation and judgment of emotional picture were preceded by an expectancy period of 8–11.5 s (8.0, 8.5, 9.0, 9.5, 10.0, 10.5, 11.0, and 11.5 s). Fixation cross: presentation of a fixation cross for variable durations (6.0, 6.5, 7.0, 7.5, and 8.0 s), which served as baseline. Picture viewing: viewing of emotional pictures (A/B) taken from the IAPS for a duration of

4 s. Response was given by arbitrary button click. Picture viewing with expectancy: presentation and viewing of emotional picture were preceded by an expectancy period of 8–11.5 s (8.0, 8.5, 9.0, 9.5, 10.0, 10.5, 11.0, and 11.5 s). **B:** Affective judgment with and without preceding expectancy. The two main conditions affective judgment with and without preceding expectancy are schematically illustrated on a time scale. The single trials of both main conditions were randomly interspersed with trials from both control conditions, picture viewing with and without expectancy. [Color figure can be viewed in the online issue, which is available at [www.interscience.wiley.com](http://www.interscience.wiley.com).]

control for judgment but not for emotions. We included such picture viewing of emotional pictures as a nonjudgmental control condition (however, an implicit judgment cannot be excluded; see methodological limitations) because our focus was on the effects of judgment rather than on those of emotions. We therefore did not include a nonemotional condition as control such as a nonemotional, i.e., neutral judgment, which was the focus of a previous study [Northhoff et al., 2004].

In the judgment condition, a right button press was required for positive pictures, whereas the left button was pressed for negative pictures. In the control condition (picture viewing), an arbitrary button press without any judgment was required to control for movement effects. Reaction times and judgments were measured.

In both judgment and picture-viewing conditions, half of the events were started with an expectancy period (8–11.5 s) indicating the type of the task associated with the subsequently presented picture. Following Kastner et al. [1999; see also Driver and Frith, 2000 for review as well as Sakai and Passingham, 2003 for the effects of prior information], the expectancy period was indicated by presentation of a white fixation cross on a dark background and a letter in one of the four corners of the picture. The letter J indicated expectancy

of a subsequent judgment task, whereas the letter E was associated with expectancy of subsequent picture viewing (“experience”). Our paradigm did not include an ambiguous expectancy cue, which would have signaled an affective judgment and picture viewing at the same time. Such an ambiguous condition would have allowed the elimination of unspecific expectancy effects present in the comparison between expected and unexpected condition. We did not choose such ambiguous expectancy to control for expected conditions because there are indications that ambiguous cues induce effects similar to unambiguous cues [Buchel and Dolan, 2000]. Moreover, given our valence-unspecific emotional expectancy cues (subjects did not know during expectancy whether a positive or negative picture was subsequently presented) and our control condition consisting of affective judgment without preceding expectancy, we refrained from such ambiguous expectancy cues. The inclusion of ambiguous cues would have created a setting where the predictive value of the emotional expectancy cue would have differed insufficiently only from that of the fixation cross indicating the resting period. To investigate the effects of cognitive modulation on affective judgment, we therefore compared expected and unexpected affective judgment.

After the picture presentation, a fixation cross (intertrial interval) was presented for 6–8 s (6.0, 6.5, 7.0, 7.5, and 8.0 s). This allowed the subjects to recover from emotional stimulation and served as a baseline condition to distinguish between activation and deactivation [Stark and Squire, 2001]. The baseline duration was varied randomly accounting for variable stimulus onset asynchrony. In total, 240 trials were presented in eight runs. The different types of IAPS pictures and judgment tasks were pseudorandomized within and across the eight runs as well as among each other. Prior to the experimental session, subjects were familiarized with the paradigm by completing a test run with 20 trials.

During fMRI pictures were projected automatically via a computer and a forward projection system on a screen placed at the end of the subject's gurney. Subjects lay supine in the scanner and viewed the screen through a mirror positioned on the head coil. Subjects were asked to keep their eyes open and fixate the middle of the screen in front of them. They were asked not to move finger, head, or body during the judgment tasks with the exception of the button press for the response.

### Behavioral Monitoring

We measured reaction times, which were defined as the time between the onset of the picture screen (IAPS photograph) and the subsequent button press. Reaction time was calculated separately for affective judgment with and without a preceding expectancy period. Average reaction times were compared using paired *t*-tests. Response accuracy was also calculated for the two conditions.

Following the fMRI session, a surprise recognition task was carried out. In addition, the level of attention (intensity) and the valence of the emotional pictures were assessed on a visual analogue scale ranging from 1 to 9. Results of these tests will be reported in a separate article.

The psychological state before and after the fMRI investigation was assessed with the State Trait Anxiety Inventory (STAI).

### Scanning Procedures

Measurements were performed on a Philips Intera 3-T whole-body MR unit equipped with a transmit-receive body coil and a commercial eight-element head coil array (MRI Devices Corporation, Waukesha WI). A sensitivity-encoded single-shot echo-planar sequence (SENSE-sshEPI) was used for fMRI acquisition [Preibisch et al., 2003]. The following acquisition parameters were used in the fMRI protocol: echo time (TE) = 35 ms, field of view (FOV) = 22 cm, acquisition matrix =  $80 \times 80$ , interpolated to  $128 \times 128$ , voxel size  $2.75 \times 2.75 \times 4$  mm<sup>3</sup>, and SENSE acceleration factor  $R = 2.0$ . Using a midsagittal scout image, 32 contiguous axial slices were placed along the anterior–posterior commissure (AC–PC) plane covering the entire brain in less than 3 s (repetition time [TR] = 3,000 ms,  $\theta = 82$  degrees). The first three acquisitions were discarded due to T1-saturation effects. A

3-D T1-weighted anatomical scan was obtained for structural reference.

### Image Analysis

Image processing and statistical analyses were carried out using *MATLAB v. 5.3* (The Mathworks Inc., Natick, MA) and *SPM99* (SPM; Wellcome Department of Imaging Neuroscience, London, UK; online at <http://www.fil.ion.ucl.ac.uk>) [Friston et al., 1995]. The procedure is summarized below; cited articles provide more complete mathematical detail. To correct for head movement between scans, 1,276 volume images were realigned to the first image, mean-adjusted by proportional scaling, resliced, and normalized into standard stereotactic space. This spatial transformation includes both linear and nonlinear components and uses a nonlinear sampling algorithm [Friston et al., 1995]. Data were thereafter expressed in terms of standard stereotactic coordinates in the *x*-, *y*-, and *z*-axes. The resulting voxel size in standard stereotactic space was  $2 \times 2 \times 2$  mm. Transformed functional data sets from each subject were smoothed with a Gaussian kernel of 8 mm (full-width half-maximum) for the group analysis to meet the statistical requirements of the general linear model and to compensate for normal variation in individual brain size, shape, and sulcal/gyral anatomy across subjects.

Subject-specific low-frequency drifts in signal were removed by a high-pass filter of 132 s. For each subject, we defined a design matrix modeling unexpected and expected affective judgment as well as unexpected and expected picture viewing as separate events. To avoid carryover effects from the preceding picture period, the first 3 s of each baseline was discarded. We then modeled the variable duration (3.0, 3.5, 4.0, 4.5, and 5.0 s) of the baseline, making explicit use of variable intervals in the data analysis [Sakai and Passingham, 2003]. Additionally, for each experimental run, we included six parameters obtained from the realignment procedure as regressors in the design matrix. These regressors consisted of differential parameters describing rotation and translation of the subject's head during the experiment. After estimation of all model parameters, specific effects were tested by applying appropriate linear contrasts to the parameter estimates for each condition, resulting in a *t*-statistic for each voxel.

For the fMRI data group analysis, the contrast images from the analysis of the individual subjects were analyzed by one-sample *t*-tests, thereby generating a random-effects model, allowing inference to the general population. Data were analyzed with respect to affective judgment and the effects of preceding expectancy on subsequent affective judgment. In the first step, we compared unexpected affective judgment to unexpected picture viewing and baseline, respectively, to reveal and signal changes (see below for further explanation of the differentiation between and signal changes) related specifically to the judgment of one's own emotion. Affective judgement in the expected and unexpected condition were compared to reveal the effect of the preceding expectancy period on the modulation of affective

judgement. In a third step, both unexpected and expected affective judgment were compared with baseline, respectively [Gusnard and Raichle, 2001; Northhoff et al., 2004; Raichle et al., 2001]. This allowed for differentiation between “relative” signal changes (between conditions) and “true” signal changes (referring to baseline). Due to our focus on the ventral prefrontal cortex, we set the significance level to  $Z > 3.26$  ( $P < 0.001$  uncorrected, voxel level, extent threshold  $k = 5$  voxels) thereby achieving a high level of sensitivity for detection of signal increases and decreases in this region [Editorial, 2001; Gusnard et al., 2001; Gusnard and Raichle, 2001; O’Doherty et al., 2001]. The anatomic localization of local maxima was assessed by reference to the MNI brain as provided by *SPM*. The stereotactic coordinates of the voxels of local maximum significant activation were determined within regions of significant activity change. A particular focus was put on the VMPFC. The VMPFC covers the ventral part of the superior and medial frontal gyrus including the frontal pole [Ongur et al., 1998; Rajowska and Goldman-Rakic, 1995]. Laterally, it borders on the lateral prefrontal cortex (LPFC), which covers the ventral and dorsal parts of the inferior and middle frontal gyrus.

To quantify the activity in the VMPFC as the region of interest (ROI) we used *MRICro* ([www.psychology.nottingham.ac.uk](http://www.psychology.nottingham.ac.uk)), which allows one to draw 3-D ROIs and calculate the mean  $t$ -value within the ROI. An anatomical image (single-subj\_T1; provided by *SPM*) was overlaid with the *SPM(T)* of the group analysis for the contrast of interest (height threshold  $t = 3.85$ – $5.99$ , corresponding to  $P < 0.001$  uncorrected). The VMPFC as ROI was functionally defined from clusters that survived the thresholding criteria. On a subject-by-subject basis, mean  $t$ -values were extracted from the VMPFC as ROI for each experimental condition to baseline.

In a fourth step, we carried out correlation analysis between fMRI signals and scores of global IGT performance. The contrast images from the analysis of the individual subjects were analyzed by using the respective individual’s global IGT score as regressor using simple regression analysis in *SPM*. A random-effects model was generated, allowing inference to the general population. For all significant results, i.e., correlating regions, the  $r$ -value was calculated separately in a second step using Spearman correlation analysis. Here, the mean  $t$ -values of the significantly correlating (in *SPM* regression analysis) region, as obtained with *MRICro* (see above), were correlated with overall global, initial global, and final global IGT scores using Spearman correlation analysis. In a fifth step, we compared high-IGT performers with low-IGT performers in the above mentioned baseline contrasts. Data was analyzed with a two-sample  $t$ -test (using the “Basic Models” module of *SPM*). Finally, correlation analysis as described above (in fourth step) was carried out separately for global initial (block 1) and global final (block 4) IGT scores.

### Iowa Gambling Test

We used a computerized version of the IGT [Bechara, 2004] that requires 100 selections from four decks of cards

that are identical in appearance. The subjects are told that the goal of the task is to maximize profit and are given a \$2,000 loan of play money. After selecting a card, a message is displayed on the screen indicating the amount of money the subject has won or lost. Gains and losses are different for each card selected from the four decks. Decks A and B are “disadvantageous.” Although these decks pay around \$100, their penalty amounts are even higher so that they cost more in the long run and result in an overall loss. In Deck A, punishment is more frequent but of smaller magnitude than that in Deck B.

Decks C and D, in contrast, are “advantageous.” Although these decks only pay around \$50, their penalty amounts are lower so that they are associated with an overall gain in the long run. In Deck C, punishment is more frequent but of smaller magnitude than that in Deck D. In short, Decks A and B can be regarded as high-risk decks whereas decks C and D can rather be considered as low-risk decks. By choosing exclusively from the low-risk Decks C and D, a subject can make an overall gain above the original loan of \$2,000. In contrast, there is an overall loss associated with choosing primarily from the high-risk Decks A and B.

The following analyses were made. First, the difference between the total number of disadvantageous (A and B) and advantageous (C and D) cards selected was calculated. This global score ( $[C + D] - [A + B]$ ) indicates the overall or general level of performance in the IGT. This score allowed us to classify the strategy of a subject with regard to how much risk a subject decided to take. Second, the total of 100 cards selected was subdivided into four blocks of 25 cards each. The number of cards selected from the disadvantageous (A and B) and advantageous (C and D) decks was counted and compared for the first, i.e., initial ( $[C1 + D1] - [A1 + B1]$ ) and the last, i.e., final block ( $[C4 + D4] - [A4 + B4]$ ), using paired  $t$ -tests [Bechara et al., 1999]. This score allowed us to distinguish between random and deliberate decision-making performance. Third, to distinguish between high- and low-performers in the IGT, we defined a global score of 20 points as a cut-off for distinguishing between high and low performers. Subjects who had a global score below 20 were considered low performers (eight subjects) whereas those who had a score above 20 were considered high performers (six subjects).

## RESULTS

### Behavioral Results

#### Reaction time

There was no significant difference in reaction times between expected judgments (mean  $\pm$  standard deviation [SD],  $1,448 \pm 717$  ms) and unexpected judgments (mean  $\pm$  SD,  $1,393 \pm 720$  ms;  $P = 0.386$ ).

#### Response accuracy

The response accuracy of picture judgment was not modulated by expectancy. The error rate did not differ signifi-

**TABLE I. Selection of high- and low-risk cards in time course during the Iowa Gambling Task**

Block	A	B	C	D	A/B	C/D
1	4.21 ± 1.67	10.42 ± 4.27	4.00 ± 3.34	4.35 ± 2.76	15.87 ± 3.52	9.14 ± 3.52
2	4.92 ± 4.17	4.42 ± 4.43	4.00 ± 3.11	9.71 ± 7.31	8.14 ± 5.00	16.85 ± 5.00
3	2.92 ± 2.20	5.35 ± 3.49	3.28 ± 2.64	12 ± 6.52	6.57 ± 4.97	18.42 ± 4.97
4	3.14 ± 3.65	6.42 ± 5.04 <sup>a</sup>	7.50 ± 6.80	12.78 ± 7.84 <sup>a</sup>	7.85 ± 6.16 <sup>a</sup>	17.14 ± 6.16 <sup>a</sup>

Values (mean ± SD) represent the values of selected high- (A/B) and low-risk (C/D) cards within the time course (i.e., during the time blocks 1, 2, 3, and 4) during the Iowa Gambling Task. Note the significant difference between initial and final cards. This leads to reversal in relationship of high- and low-risk cards between initial and final time period that reflects the learning effect during time course of the Iowa Gambling Task.

<sup>a</sup>  $P < 0.05$  (corrected), significant difference between first (1) and last (4) block.

cantly between expected judgments (correct: 88%; wrong: 11.5%) and judgments without preceding expectancy (correct: 90.65%; wrong: 9.38%;  $P = 0.309$  for correct responses;  $P = 0.112$  for false responses).

### Psychological state

The psychological state before and after the fMRI investigation as assessed with the STAI. This test showed no significant differences in paired  $t$ -tests between the two time points.

### Performance in IGT

A paired  $t$ -test showed significant differences between initial and final choices in the IGT. Although in the beginning (block 1) subjects mainly chose cards from the disadvantageous Decks A and B (mean ± SD A/B score 15.87 ± 3.52; mean ± SD C/D score 9.14 ± 3.52), over time a learning effect occurred. In the last block (block 4), subjects mainly chose cards from the advantageous Decks C and D (mean ± SD A/B score 7.85 ± 6.16; mean ± SD C/D score 17.14 ± 6.16). Accordingly, our subjects showed the typical pattern with decreases in high risk cards (AB) and increases in low risk cards (CD) over time (see also Table I).

## Functional MRI Results

### Influence of expectancy on ventral prefrontal cortical function during affective judgment

Unexpected affective judgment induced signal increases in various areas including dorsal and ventral prefrontal cortical regions when compared to unexpected picture viewing and baseline [Grimm et al., 2005].

Affective judgment without expectancy showed signal changes in VMPFC when compared to affective judgment with expectancy (see Fig. 2). Both conditions were compared to baseline to differentiate between signal increases and decreases. The VMPFC showed signal increases in the comparison between affective judgment without expectancy and baseline (above baseline). In addition, signal decreases in VMPFC were observed in the comparison between affective judgment with expectancy and baseline (below baseline).

Signal changes in other regions included lateral and medial occipital cortex, left lateral prefrontal cortex, left poste-

rior cingulate, and precuneus (see also Fig. 2). For neither signal increases nor signal decreases could we find any significant gender difference in any of the reported regions. The following correlations thus illustrate the results for the whole group independently of gender.

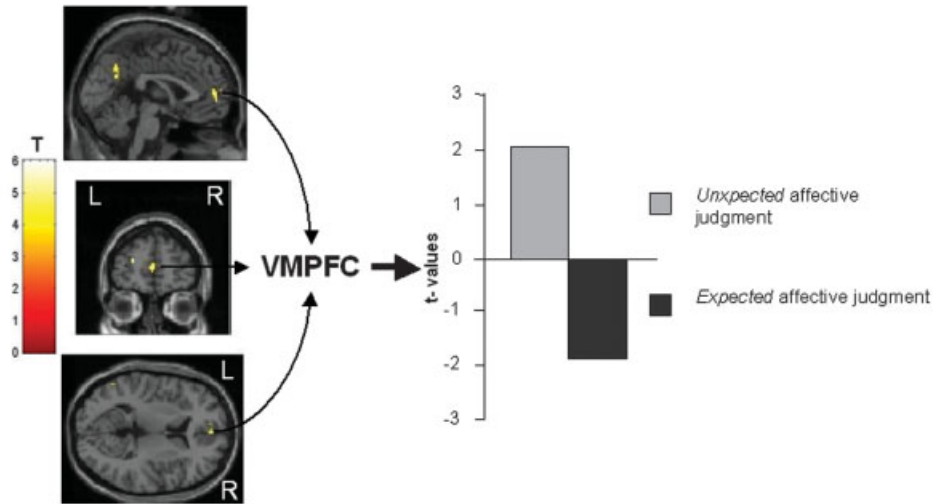
### Ventromedial prefrontal cortex and global IGT performance

Because our a priori hypothesis concerned the relationship between affective judgment, VMPFC, and beneficial decision making, we focused our analysis on correlating VMPFC involvement during affective judgment and IGT performance. Correlation with baseline contrasts allowed us to assess each condition separately. We therefore focus on correlation results with global (and initial and final; see below) IGT performance for affective judgment without and with expectancy as compared to baseline, respectively. To control for the specificity of our findings, we also correlated picture viewing as compared to baseline with global IGT performance. Because we did not obtain any significant correlation, we did not pursue further correlation analysis for picture viewing.

VMPFC signal changes during affective judgment without expectancy (versus baseline) showed a positive correlation with global IGT performance. This correlation concerned predominantly signal increases in the right VMPFC: The more signal increases were observed in the VMPFC during affective judgment without expectancy, the better was the subject's performance in the IGT (Fig. 3; Table II).

VMPFC signal changes during affective judgment with expectancy (vs. baseline) also showed positive correlation with the global IGT performance. In contrast to affective judgment without expectancy (see above), this correlation predominantly concerned signal decreases in the right VMPFC: The more signal decreases were observed in the VMPFC during affective judgment with expectancy, the worse was the subject's performance in the IGT (Fig. 3; Table II). In addition to the VMPFC, the dorsomedial prefrontal cortex (DMPFC) showed a positive correlation with signal changes during affective judgment with expectancy. Similar to the right VMPFC (see above), this positive correlation predominantly concerned signal decreases in the right DMPFC: the more signal decreases were observed in the

Affective judgment *without* expectancy > Affective judgment *with* expectancy



**Figure 2.**

Comparison between affective judgment without and with expectancy. Signal changes in the contrast affective judgment without expectancy > affective judgment with expectancy are demonstrated in the images on the left side. Signal increases are observed in the ventromedial prefrontal cortex (VMPFC;  $x = 0$ ,  $y = 54$ ,  $z = 8$ ;  $Z = 3.73$ ) and the precuneus ( $x = -8$ ,  $y = -54$ ,  $z = 28$ ;  $Z = 3.26$ ) during unexpected affective judgment compared to expected affective judgment. MNI coordinates given by  $x$ ,  $y$ ,  $z$  (in mm). All sagittal images represent the right hemisphere. Bars in the figure on the right side represent the mean  $t$ -values in VMPFC calculated for each of the two main conditions to baseline. The region of interest (ROI) was drawn

based on the contrast “affective judgment without expectancy > affective judgment with expectancy.” Accordingly, the ROI precisely reflect the blood oxygenation level-dependent (BOLD) signals reflected in the images on the left. Signal increases in VMPFC during affective judgment without expectancy are reversed to signal decreases (as compared to baseline) when the affective judgment is preceded by an expectancy period. This functional mechanism might be called modulation by reversal, which is schematically illustrated in Figure 6 in relation to high- and low-risk behavior. [Color figure can be viewed in the online issue, which is available at [www.interscience.wiley.com](http://www.interscience.wiley.com).]

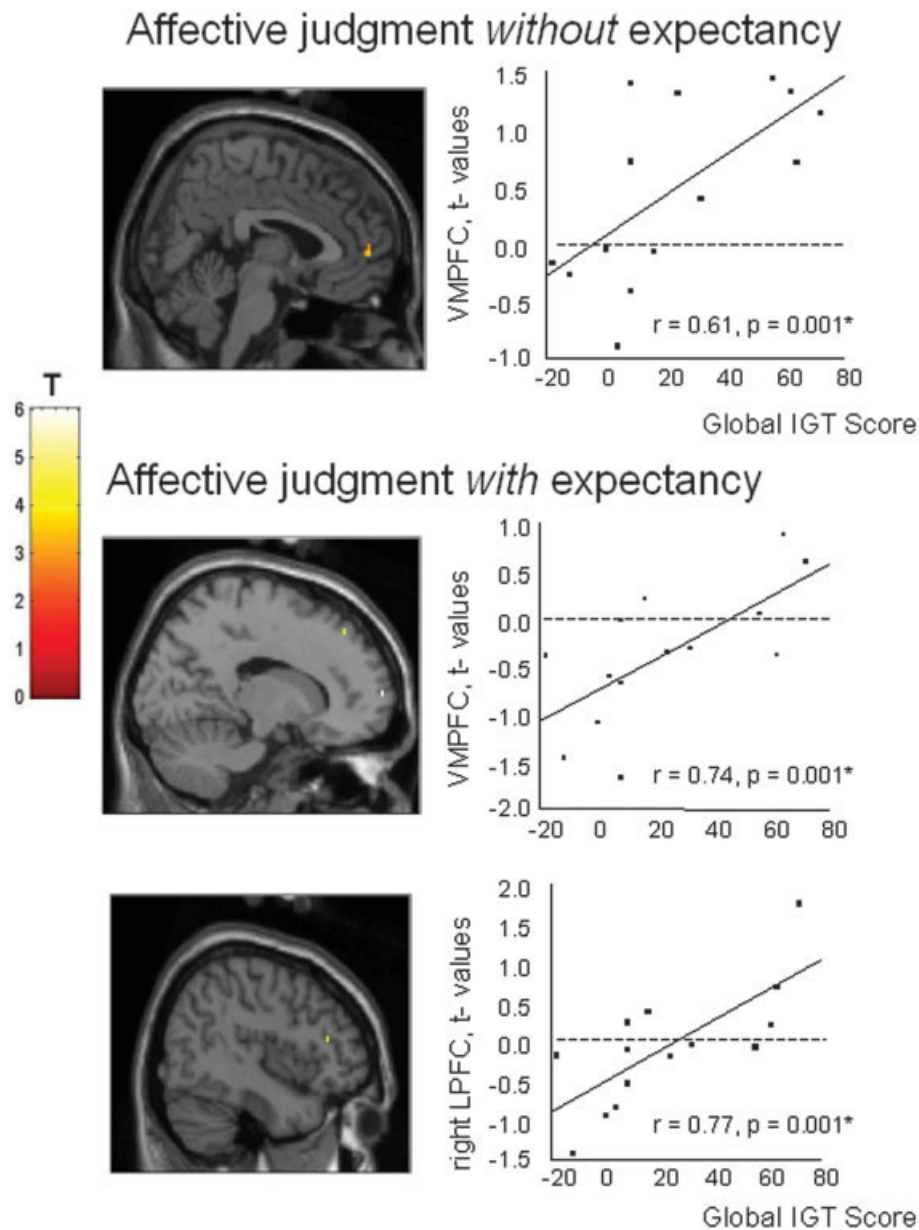
DMPFC during affective judgment with expectancy, the worse was the performance of a subject in the IGT (Fig. 3; Table II). Moreover, the same condition correlated positively with predominant signal increases in the right lateral prefrontal cortex (LPFC): the more signal increases were measured in the right LPFC during affective judgment with expectancy, the better was the subject’s IGT performance (Fig. 2; Table II).

performance. Again, we did not observe any significant correlation.

**Ventromedial prefrontal cortex and high- versus low-IGT performance**

To distinguish effects of affective judgment from those in the prejudgment phase, we analyzed prefrontal cortical signal changes observed during the preceding expectancy period. This period induced signal increases in the supracallosal anterior cingulate cortex ( $x = -3$ ,  $y = 11$ ,  $z = 33$ ;  $Z = 2.99$ ) and supplementary motor area (SMA, including pre-SMA;  $x = 5$ ,  $y = 7$ ,  $z = 53$ ;  $Z = 3.52$ ) when compared to baseline. We then correlated these signal changes to global IGT performance and did not obtain any significant correlation. Accordingly, we did not observe any signal changes or any correlation in VMPFC, DMPFC, or LPFC for the expectancy period preceding affective judgment. Finally, to exclude effects of the preceding baseline in unexpected affective judgment, we correlated the last 6 s of the baseline preceding unexpected affective judgment with global IGT

To explore further the relation between signal changes in the VMPFC during affective judgment and IGT performance, we divided our study group into two subgroups according to their global IGT performance. First, we compared high- and low-IGT performers with respect to initial cards to exclude preexisting (learning-independent) differences; neither group differed significantly in the number of initially selected high- and low-risk cards. Second, we then compared the fMRI baseline results between high- and low-IGT performers. High-IGT performers showed significantly more signal increases in the (right) VMPFC ( $x = 6.00$ ,  $y = 58.00$ ,  $z = 20.00$ ;  $Z = 3.42$ ) during affective judgment without expectancy than did low-IGT performers (Fig. 4a). In addition to that in the VMPFC, high-IGT performers showed significantly more signal increases in the right LPFC during affective judgment with expectancy ( $x = 38.00$ ,  $y$



**Figure 3.**

Correlation between signal changes during affective judgment and global score in Iowa Gambling Task (IGT). The left row shows SPM images resulting from regression between signal changes during affective judgment and global IGT scores. Because we wanted to demonstrate correlation effects for affective judgment without and with expectancy separately, we correlated the respective baseline contrasts with IGT scores. Baseline contrasts refer to affective judgment without expectancy versus baseline and affective judgment with expectancy versus baseline. Exact coordinates of correlating regions are described in Table II. The right row shows the respective curves resulting from correlation between mean  $t$ -values in the respective region of interest (ROI) and global IGT scores using Spearman correlation analysis. Quadrats in scatterplots represent relation between  $t$ -values, as obtained in functional magnetic resonance imaging (fMRI) in the respective contrast, and global IGT scores in single subjects. Positive  $t$ -values describe signal increases whereas negative  $t$ -values reflect signal decreases. Correlation coefficient and  $P$  values are presented below. Correlation of affective judgment without expectancy with IGT scores concerned predominantly signal increases in ventromedial prefrontal cortex (VMPFC). In contrast, correlation of affective judgment with expectancy with IGT scores concerned predominantly signal decreases in VMPFC and dorsomedial prefrontal cortex (DMPFC) and partially signal increases in right lateral prefrontal cortex (LPFC). Only regions with  $Z > 3.26$  ( $P < 0.001$  uncorrected, voxel level;  $P < 0.05$  corrected, cluster level) are described. All images shown represent group average. In fMRI images, areas of significant signal changes are shown as through projections onto representations of standard stereotaxic space in sagittal, coronal, and transverse projections. fMRI images represent results of group analyses for simple regression (global IGT score as regressor) depicted on standard MNI brain. All sagittal images represent the right hemisphere. Voxels shown in fMRI correlation images (simple regression), as shown on the left side, served for calculation of Spearman correlation represented in scatterplots on the right. [Color figure can be viewed in the online issue, which is available at [www.interscience.wiley.com](http://www.interscience.wiley.com).]



**TABLE II. Scores for correlation between regional signal changes and global, initial, and final IGT scores**

Score	VMPFC						Right LPFC						DMPFC					
	Affective judgement without expectancy > baseline			Affective judgement with expectancy < baseline			Affective judgement without expectancy > baseline			Affective judgement with expectancy < baseline			Affective judgement without expectancy > baseline			Affective judgement with expectancy < baseline		
	Signal increase	Spearman coefficient/ P-value (r/p)	Spearman coefficient/ P-value (r/p)	Signal decrease	Spearman coefficient/ P-value (r/p)	Spearman coefficient/ P-value (r/p)	Signal increase	Spearman coefficient/ P-value (r/p)	Spearman coefficient/ P-value (r/p)	Signal decrease	Spearman coefficient/ P-value (r/p)	Spearman coefficient/ P-value (r/p)	Signal increase	Spearman coefficient/ P-value (r/p)	Spearman coefficient/ P-value (r/p)	Signal decrease	Spearman coefficient/ P-value (r/p)	Spearman coefficient/ P-value (r/p)
Global	4, 54, 4	3.26	0.61/0.001 <sup>a</sup>	16, 66, 8	3.88	0.74/0.001 <sup>a</sup>	44, 32, 16	3.26	0.77/0.001 <sup>a</sup>	14, 40, 52	3.37	0.79/0.001 <sup>a</sup>	22, 32, 48	2.80	0.37/0.18	14, 40, 52	3.23	0.78/0.001 <sup>a</sup>
Initial	—	—	—	8, 42, -4	2.97	0.38/0.17	44, 22, 12	2.71	0.26/0.35	—	—	—	—	—	—	—	—	—
Final	2, 54, 4	3.53	0.56/0.004 <sup>a</sup>	16, 66, 8	3.50	0.72/0.003 <sup>a</sup>	42, 34, 16	3.49	0.81/0.000 <sup>a</sup>	—	—	—	—	—	—	—	—	—

Montreal Neurological Institute coordinates given by x, y, z (in mm). Coordinates describe right (+)/left (-) (x), anterior (+)/posterior (-) (y) and superior (+)/inferior (-) (z) distances. Only regions with  $Z > 3.23$  ( $P < 0.001$  uncorrected, voxel level;  $P < 0.05$  corrected, cluster level) are described. Only for correlation with initial cards, level of significance was lowered to  $Z > 2.71$  ( $P < 0.001$  uncorrected, voxel level;  $P < 0.05$  corrected, cluster level; extent threshold  $k = 5$  voxels) in order to reveal the correlation pattern. Regions of interest analysis served for calculation of the correlation coefficient using Spearman Correlation analysis. Note significant correlations between global/final IGT and regional signal changes. In contrast, correlations between initial IGT and regional signal changes were non-significant.

<sup>a</sup> Significant correlation in Spearman correlation analysis.

VMPFC, ventromedial prefrontal cortex; LPFC, lateral prefrontal cortex; DMPFC, dorsomedial prefrontal cortex.

= 42.00, z = 28.00; Z = 4.53) than did low-IGT performers (not shown).

In contrast, low-IGT performers showed significantly more signal decreases in the (right) VMPFC (x = 14.00, y = 66.00, z = 8.00; Z = 3.35) and posterior cingulate (x = 7, y = -25, z = 36; Z = 3.32) during affective judgment with expectancy than did high-IGT performers (Figure 4b).

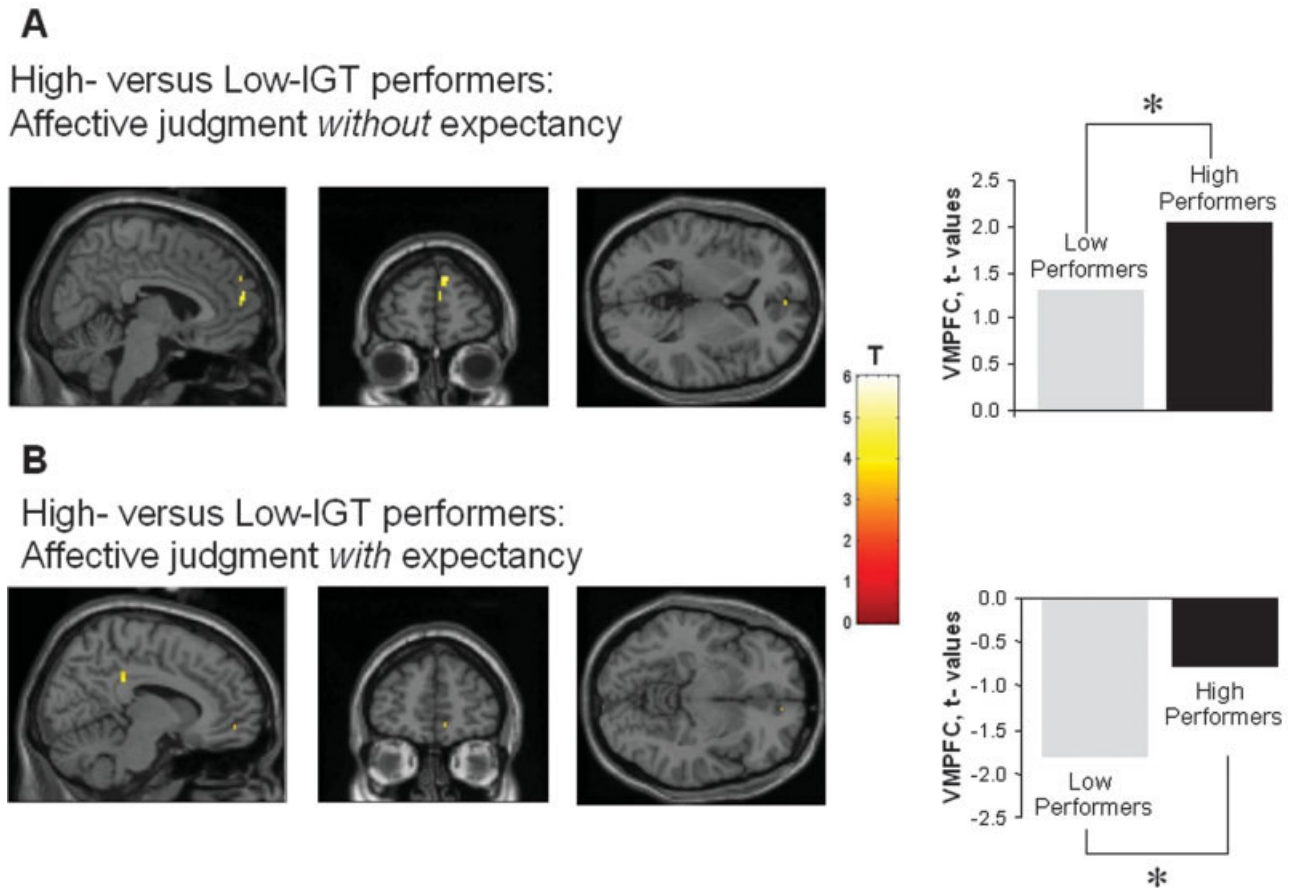
### Ventromedial prefrontal cortex and initial versus final IGT performance

To account for the learning effect over the course of the IGT, we separately correlated signal changes in the VMPFC with initial and final global IGT scores. Initial IGT performance did not correlate in any brain region with neuronal activity during unexpected affective judgment (Fig. 5a; Table II). In contrast, final IGT performance showed a positive correlation with signal changes (predominantly signal increases when compared to baseline) related to unexpected affective judgment (Fig. 5a; Table II).

An analogous correlation pattern was observed in the case of affective judgment with expectancy. For this condition, initial IGT performance did not correlate with neuronal activity in any brain region (Fig. 5b; Table II). In contrast, signal changes during affective judgment with expectancy correlated significantly with final IGT performance in the VMPFC. However, unlike that in affective judgment without expectancy this correlation concerned predominantly signal decreases (Fig. 5b; Table II). Moreover, unlike that in affective judgment without expectancy, other regions showed also significant correlations in affective judgment with expectancy including signal increases in the right VLPFC and signal decreases in the DMPFC (Table II). Finally, we also correlated the difference between initial and final IGT score with signal changes during affective judgment. We observed significant correlation of initial–final IGT difference with signal increases in VMPFC (x = 2, y = 56, z = 3; Z = 3.52; r = 0.65, P < 0.001) during unexpected affective judgment. In addition, initial–final IGT difference significantly correlated with signal decreases in VMPFC (x = 3, y = 53, z = 4; Z = 3.35; r = 0.59, P < 0.002) and signal increases in LPFC (x = 2, y = 56, z = 3; Z = 3.52; r = 0.68, P < 0.001) during expected affective judgment.

## DISCUSSION

The current study considered affective judgments to be crucial in decision-making. We distinguished between affective judgment without and with preceding expectancy period, i.e., unexpected and expected affective judgment. Blood oxygenation level-dependent (BOLD) signals related to these two types of judgment were correlated with IGT performance to investigate the relevance of VMPFC activity during affective judgment for beneficial decision-making. We discuss affective judgments in the VMPFC as key component in decision making, its cognitive modulation and its relation to our ability to learn how to make beneficial decisions (see Fig. 6 for schematic illustration).



**Figure 4.**

Comparison of signal changes during affective judgment between high- and low-performers in Iowa Gambling Task (IGT). **A:** Comparison between high and low performers in affective judgment without expectancy. SPM images are shown on the left, the bar diagrams with the respective mean  $t$ -values as obtained in region of interest (ROI) analysis are demonstrated on the right. High performers show significantly more signal increases in ventromedial prefrontal cortex (VMPFC) than do low performers during affective judgment without expectancy. **B:** Comparison between high and low performers in affective judgment with expectancy. SPM images are shown on the left, the bar diagrams with the respective mean  $t$ -values as obtained in ROI analysis are demonstrated on the right. Low performers show significantly more signal decreases in VMPFC (more orbitofrontal and thus slightly lower than in A) and

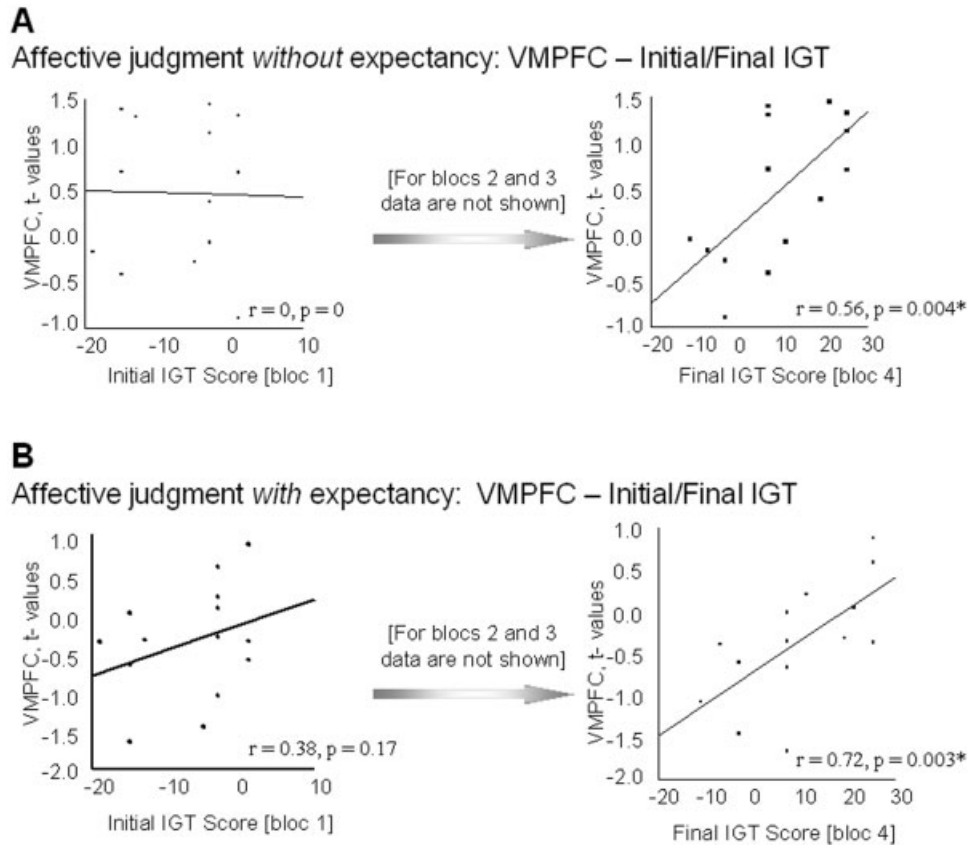
posterior cingulate (not shown in bar diagram) than do low performers during affective judgment with expectancy. Only regions with  $Z > 3.26$  ( $P < 0.001$  uncorrected, voxel level;  $P < 0.05$  corrected, cluster level) are described. All images shown represent group average. In functional magnetic resonance imaging (fMRI), areas of significant signal changes are shown as through projections onto representations of standard stereotaxic space in sagittal, coronal, and transverse projections. fMRI images represent results of group analyses for two-sample  $t$ -test depicted on standard MNI brain. All sagittal images represent the right hemisphere. Voxels shown in fMRI images served for calculation of  $t$ -values as represented in bar diagrams below. [Color figure can be viewed in the online issue, which is available at [www.interscience.wiley.com](http://www.interscience.wiley.com).]

### Affective Judgment and Decision Making

In accordance with previous studies [Gusnard et al., 2001; Northoff et al., 2004], we observed signal increases in the VMPFC during affective judgment without expectancy. These signal increases in the VMPFC seem to reflect the affective component, i.e., to judge the conveyed emotion. This is supported by recent studies [Gusnard et al., 2001; Northoff et al., 2004] showing VMPFC signal increases during affective judgment when compared to that during non-affective judgment. Furthermore, many imaging studies re-

veal analogous VMPFC activation in emotional paradigms that do not involve judgment [Northoff and Bermphohl, 2004; Phan et al., 2002]. However, because we were unable to control for the various affective and cognitive components (like valence, arousal, working memory, etc.) in affective judgment, our assumption of VMPFC representing the affective component in affective judgment remains speculative at this point.

Our results suggest that affective judgments, as accounted for by signal increases in the VMPFC, might be a key process



**Figure 5.**

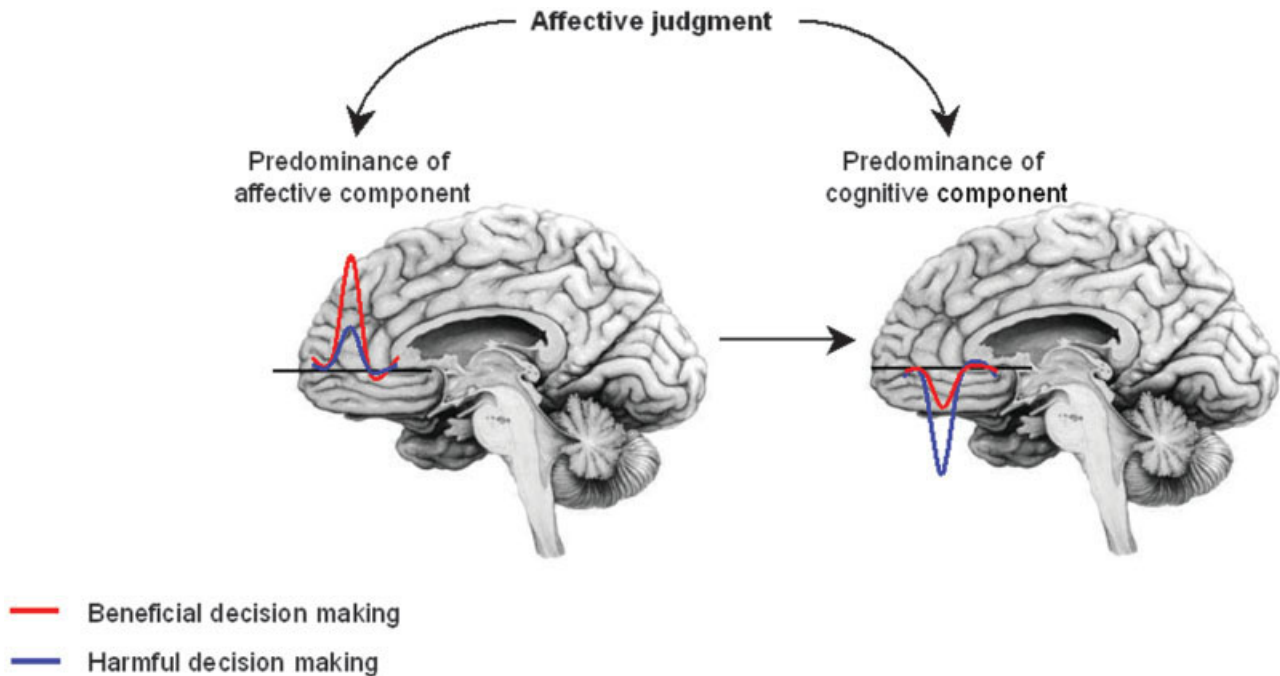
Correlation between signal changes during affective judgment and initial and final global scores in Iowa Gambling Task (IGT). The figure shows the respective curves resulting from correlation between mean *t*-values in the respective region of interest (ROI) and initial and final global IGT scores using Spearman correlation analysis. Quadrats in scatterplots represent relation between *t*-values, as obtained in functional magnetic resonance imaging (fMRI) in the respective contrast, and global IGT scores in single subjects. Positive *t*-values describe signal increases whereas negative *t*-values reflect signal decreases. Correlation coefficient and *P* values are presented below. Exact coordinates of correlating regions are described in Table II. **A:** Correlation between affective

judgment without expectancy versus baseline with initial and final global IGT scores. Correlation of affective judgment without expectancy versus baseline with initial IGT scores remained nonsignificant whereas it was significant with final IGT scores. Correlation with final IGT scores concerned predominantly signal increases in ventromedial prefrontal cortex (VMPFC). **B:** Correlation between affective judgment with expectancy versus baseline with initial and final global IGT scores. Correlation of affective judgment with expectancy versus baseline with initial IGT scores remained nonsignificant whereas it was significant with final IGT scores. Correlation with final IGT scores concerned predominantly signal decreases in VMPFC.

in decision making. More precisely, the more signal increases occur in VMPFC during affective judgment, the better subjects are able to perform in the IGT. This is underlined further and reconfirmed by our finding in high-IGT performers showed more signal increases in the VMPFC than did low-IGT performers. Subsequently, the amount of signal increases in the VMPFC during affective judgment might reflect an affective component and, at the same time, allows apparently for predicting IGT performance. This complements and extends previous imaging [Akitsuki et al., 2003; Bolla et al., 2003; Elliot et al., 1999; Patterson et al., 2002] and lesion [Clark et al., 2003, 2004; Rogers et al., 2004; Manes et al., 2002; Sanfey et al., 2003; Tranel et al., 2002] studies

showing a relationship between predominantly right-hemispheric VMPFC involvement and successful decision-making. The present study suggests that this relationship is mediated by affective judgments. However, one should be careful in overinterpreting our findings, as they do not indicate causal relationship between affective judgment, VMPFC, and decision-making. Instead, our results only suggest a correlative relationship between all three components; this makes further studies with different paradigms, such as the inclusion of an affective component into a decision task, necessary.

Our findings are in accordance with Damasio's somatic marker theory. Based on lesion studies, this theory postu-



**Figure 6.**

Schematic illustration of the interrelationship between affective judgment, cognitive modulation, ventromedial prefrontal cortex (VMPFC) activity, and decision making performance. Pronounced emotional engagement in affective judgments is associated with increased VMPFC activity. At the same time, higher VMPFC activity is associated with better decision-making performance. One might therefore conclude that beneficial decision-making depends

on how strong a person involves affective judgments as associated with VMPFC activation. This figure does not depict specific values collected in our study but rather illustrates a functional mechanism underlying decision making, as derived from our results and previous studies. [Color figure can be viewed in the online issue, which is available at [www.interscience.wiley.com](http://www.interscience.wiley.com).]

lates that emotional processing in the VMPFC is crucial to decision making. Lesions in the VMPFC interfere with the normal processing of somatic markers, leading to impairments in the decision making process. These somatic markers are supposed to be associated with emotions [Bechars, 2004]. Our results are in accordance with this assumption because they demonstrate a correlative relationship between affective judgment, VMPFC signal increases, and performance in decision making in healthy subjects. Moreover, our results specify the nature of emotional processing. Rather than involving mere emotional picture viewing, successful decision making seems to presuppose affective judgments. The following inference might be drawn, although speculatively: the higher the neuronal activity present in the VMPFC, the better subjects can make affective judgments, and the more beneficial decisions are made. Accordingly, the amount of neuronal activity in the VMPFC seems to determine our ability of making affective judgments, which in turn influences our performance in decision making.

### **Cognitive Modulation of Affective Judgment and Decision Making**

We incorporated a judgment expectancy period to shift the accent from the affective component (emotional experi-

ence and reactions) to the cognitive component (rational categorization) of affective judgment. Although a multidimensional construct [Ploghaus et al., 2003], judgment expectancy accentuates the cognitive component by focusing and redirecting attention on the subsequent categorization and evaluation. This cognitive-attentional accentuation might account for our observation of the reversal of neuronal activity during expected compared to unexpected affective judgment: Signal increases in the VMPFC during affective judgment without expectancy were reversed into signal decreases by inclusion of the preceding expectancy period, i.e., during affective judgment with expectancy. Such signal decreases during cognitive-attentional accentuation are in accordance with imaging studies that observed signal decreases in the VMPFC during cognitive tasks such as noun generation, object knowledge, and impersonal/personal word judgment [Mitchell et al., 2002; Simpson et al., 2001]. Analogous VMPFC signal decreases have been obtained in studies investigating cognitive-affective interaction [Goel and Dolan, 2003; Northoff et al., 2004]: the stronger affective involvement is associated with a cognitive task, the less signal decreases or the more signal increases occur in the VMPFC. Conversely, the less affective involvement is present in a cognitive task, the more signal decreases or the

less signal increases in the VMPFC have been observed. Accordingly, cognitive accentuation seems to be associated with the occurrence of signal decreases in the VMPFC.

Cognitive accentuation is accompanied by down-modulation of the affective component, which in turn seems to interfere with decision-making. This has been demonstrated psychologically in a recent study where the absence of affective reactions induced a decline in IGT performance [Hinson et al., 2002]. Although our experimental paradigm did not include a condition with complete absence of affective reactions, our results might nevertheless contribute by revealing VMPFC signal changes during cognitive-attentional modulation. During affective judgment with expectancy (see above), the correlation between VMPFC signals and global IGT performance predominantly concerned signal decreases. The more signal decreases were observed in the VMPFC during affective judgment with expectancy, the worse subjects performed in global IGT. Although speculative, the following inference might be drawn: The more deactivation that can be observed in the VMPFC, the more is the cognitive component emphasized within the affective judgment, and the less beneficial decisions are made (see Fig. 6 for schematic illustration). This is underlined further and reconfirmed by our finding in low-IGT performers, which showed significantly more VMPFC signal decreases than that in high-IGT performers. Accordingly, the amount of cognitively induced signal decreases in the VMPFC (i.e., during affective judgment with expectancy) might allow for predicting IGT performance. Because our focus was on the effects of an increased cognitive load rather than on emotions, we did not include a nonemotional, i.e., neutral expectancy period in our control conditions. However, this would have been necessary to distinguish between specific emotional expectancy effects and general expectancy effects, which will be the subject of future studies.

Our results contribute to the somatic marker hypothesis as established by Bechara et al. [1994, 1999] and Damasio [1994]. Although involvement of the VMPFC in decision making via somatic markers has been established (see above), modulation of neuronal activity in VMPFC by affective and cognitive processes remained unclear. Our results suggest that neural activity in the VMPFC might be related to modulation of affective and cognitive processes in decision making via signal increases and decreases, although the exact nature of affective and cognitive processes remains to be determined. Occurrence of signal decreases in VMPFC might be accompanied by suppression of somatic marker processing. This in turn might deteriorate decision-making, leading to disadvantageous decisions.

In addition to signal decreases in the VMPFC, signal increases in the right LPFC were also found to be correlated with global IGT performance. The more signal increases in the right LPFC during affective judgment with expectancy, the better subjects perform in IGT. This is supported further by the comparison between high- and low-IGT performers. High-IGT performers showed significantly more signal increases in the right LPFC than did low-IGT performers.

Involvement of the right LPFC in decision-making is in accordance with recent imaging and lesion studies. These show that changes in the right LPFC are accompanied by changes in IGT performance [Bolla et al., 2003; Clark et al., 2003; Manes et al., 2002] but Adinoff et al. [2003] found a correlation with the left DLPFC.

Psychologically, the right LPFC is often related to attention and working memory [Wood and Grafman, 2003], which have also been implicated in decision-making [Hinson et al., 2003]. One might consequently speculate that judgment expectancy includes attentional and working memory components that in turn are involved in making beneficial decisions. Our results suggest that signal increases in the right LPFC might be related to such attentional and working memory components in decision making. However, a paradigm varying the attentional or working memory loads during expectancy in relation to decision making would be necessary to lend further support to this rather speculative assumption.

### Learning Effect and the VMPFC

In real life, there might be situations where high-risk behavior is beneficial. However, in the IGT low-risk behavior implies beneficial decision-making. Such low-risk behavior can be permanent, reflecting a personality trait being either inborn or experienced-based, or transient, accounted for by a learning process over the course of the task. In our study, we observed a correlation between high performance in the global IGT and signal increases in the VMPFC during affective judgment. This finding in itself leaves open whether VMPFC signal increases are related to low-risk behavior as a permanent personality trait or as a result of a transient learning process.

How can we distinguish between these two? According to Damasio [1994], beneficial decision making presupposes the ability to learn which cards are beneficial and which ones are not, i.e., the learning effect. This is the case in the IGT, for example, where successful subjects learn to change their preferred selection of cards, i.e., from initial high- to final low-risk cards. Because Damasio assumes the VMPFC to be involved in beneficial decision-making, neuronal activity in this region should be related to the learning effect. If it is, neuronal activity in the VMPFC should only correlate with final but not initial cards in the IGT. Low-risk behavior might also be a personality trait that leads subjects to a constant avoidance of high-risk selections. In this case, subjects would be expected to select low-risk cards even in initial blocks of the IGT, which should then also correlate with neuronal activity in the VMPFC.

To distinguish between low-risk behavior as personality trait and as result of a learning effect, we correlated VMPFC activity with both initial and final IGT scores as well as with their difference score. There was no correlation of initial IGT performance with signal changes in the VMPFC during affective judgment. In contrast, we obtained a significant correlation of final IGT with predominant signal increases in the VMPFC during affective judgment without expectancy.

This is supported further by observation of significant correlation of VMPFC signal increases with the difference between initial and final IGT score.

The fact that signal increases in the VMPFC (during affective judgment) correlated only with final IGT performance but not with initial IGT might tentatively suggest that the correlation effect with VMPFC signal increases might be related to transient learning rather than being a permanent personality trait. This is in accordance with our observation that there was no significant difference between low- and high-IGT performers in initial cards, which speaks against a low-risk personality trait. One should be aware that our study does not really allow us to distinguish between personality traits and learning effects. To reveal personality traits, two groups of different persons, high- and low-risk persons, should be compared in IGT and fMRI. Learning effects require more complex approaches than does comparing initial and final IGT cards within one performance.

How could affective judgment and the learning effect be related to each other in beneficial decision making? According to Damasio's somatic marker theory, the learning effect might be mediated by somatic markers and the accompanying affective processes. The perception and experience of autonomic and somatic bodily reactions, as accounted for by somatic markers, induces emotions that, as a result of a conditioning process, guide our decisions and thus our behavior. Our results suggest a correlative relationship between potential learning effects, affective judgment, and neural activity in VMPFC during decision-making. One might subsequently speculate that affective judgment and underlying neuronal activity in VMPFC could possibly mediate between somatic marker and (potential learning effects accounting for) beneficial decision-making. However, further studies directly linking affective judgment to somatic marker processing on the one hand and to learning effects in decision making on the other are necessary to lend support to this rather speculative assumption.

### Methodological Limitation

First, the term affective judgment might describe distinct aspects of judgment in emotional processing. It might concern the judgment of the emotion conveyed by the IAPS pictures; this is the meaning that we presuppose. Alternatively, it might describe subjective or personal experience of emotions, i.e., what is called feeling [Damasio, 1994; Damasio et al., 2000]. Because the IAPS pictures are unlikely to induce strong feelings, this alternative meaning should not be applied in the present study. However, neural activity in the VMPFC has been related to feelings and emotional self-awareness and, thus, affective judgment in the alternative sense [Bar-On et al., 2003].

Second, it may be argued that the task we call picture viewing has already involved some kind of judgment. The present paradigm does not allow for excluding the possibility that subjects carried out (implicit random) judgments, before the actual explicit judgment instruction was given. Although the subjects were requested explicitly only to

judge if the judgment instruction was signaled, any kind of unconscious or preconscious judgment this cannot be excluded. Accordingly, we might be able to exclude explicit judgment while the task still comprises implicit unconscious judgment. Furthermore, our baseline condition consisted of a fixation cross that might, for example, induce visual and cognitive processing. Accordingly, our baseline condition should not be confused with a resting condition.

Third, one might argue that our significant correlations with IGT performance in VMPFC, DMPFC, and LPFC might be related to the preceding periods of uncertainty rather than to affective judgment itself. The baseline period that is preceding unexpected affective judgment as well as the expectancy period that is preceding expected affective judgment are characterized by uncertainty [Ploghaus et al., 2003] since the subjects don't know what stimuli will appear next (judgment or picture viewing in unexpected affective judgment; positive or negative judgment in expected affective judgment). This uncertainty, in turn, might be related to the ambiguous situation during gambling in the IGT.

To account for the preceding periods of uncertainty, we correlated signal changes during baseline (preceding unexpected affective judgment) and expectancy (preceding expected affective judgment) periods with global IGT performance. We here did not obtain nor any significant correlation in the VMPFC, DMPFC, or LPFC. Therefore, it seems likely that the detected significant correlations are a result of the affective judgement itself rather than that of the preceding periods of uncertainty.

Fourth, the exact psychological origin of the change in VMPFC-IGT correlation during expected affective judgment remains open. Our results show significant VMPFC-IGT correlation only with signal changes during affective judgment but not with those associated with either expectancy or mere picture viewing. Therefore, the VMPFC-IGT correlation seems to be a result of the affective-cognitive interaction during affective judgement. Introducing a cognitive-attentional component, we argue that the preceding expectancy period shifts the balance within affective-cognitive interaction during affective judgment. We assume that the cognitive-attentional component, as introduced by expectancy, emphasizes the subjects' focus (or attention) on the cognitive-evaluative component within affective-cognitive interaction during affective judgment. Whereas the affective component during affective judgment shifts into the background resulting in predominance of preparation for judgment even during emotional picture viewing. Since affective-cognitive interaction during affective judgment seems to be crucial VMPFC-IGT correlation, any changes in the mentioned interaction should also lead to an altered correlation pattern. This is exactly what we observed and is thus in accordance with our hypothesis.

Further experiments with distinct cognitive loads and isolation of different components in the expectancy period are necessary to lend further support to our hypothesis. This would allow to investigate the impact of both distinct cognitive loads and different noncognitive (emotion, motiva-

tion, etc.) components in the expectancy period on the affective judgment period and subsequently on VMPFC-IGT correlation.

Fifth, one needs to distinguish between distinct aspects of decision-making. The emerging field of neuroeconomics distinguishes between subjective utility describing preferences as subjective properties of the chooser and strategic thinking when confronted with an intelligent opponent [Glimcher and Rustichini, 2004; Ju, 2005; Mandler, 2005]. Unfortunately, we were unable to exactly distinguish between these two components of decision-making. One might speculate that they might be related to neural activity in distinct regions. For example, subjective utility represents the value of future decisions, which might be linked to neural activity in VMPFC. Although our and other results support a close relationship between affective value and decision value [Bechara, 2004; McClure et al., 2004], their exact relationship remains unclear. In contrast, strategic thinking requiring working memory, categorization, and other executive functions might rather be associated with neural activity in lateral prefrontal cortex. Although we obtained some significant correlation of IGT scores with signal changes in lateral prefrontal cortex, the exact psychological mechanisms remain to be explored.

## ACKNOWLEDGMENTS

We thank Y. Dahlem for recommending improvements and clarifications, especially the figures. The work was supported by the German Research Foundation (Heisenberg grant DFG 304/4-1 to G.N.), the German Academic Exchange Service (Postdoc-Program grant DAAD, D/02/46858 to F.B.), the Swiss National Research Foundation (3100A0-100830 to G.N. and H.B.), the Research Foundation at the University of Zurich, Organon Switzerland (to G.N. and H.B.), and by ETH Zurich (SEP) and Philips Medical Systems, Best, NL (to P.B.).

## REFERENCES

- Adinoff B, Devous MD Sr, Cooper DB, Best SE, Chandler P, Harris T, Cervin CA, Cullum CM (2003): Resting regional cerebral blood flow and gambling task performance in cocaine-dependent subjects and healthy comparison subjects. *Am J Psychiatry* 160:1892–1894.
- Akitsuki Y, Sugiura M, Watanabe J, Yamashita K, Sassa Y, Awata S, Matsuoka H, Maeda Y, Matsue Y, Fukuda H, Kawashima R (2003): Context-dependent cortical activation in response to financial reward and penalty: an event-related fMRI study. *Neuroimage* 19:1674–1685.
- Bark R, Dieckmann S, Bogerts B, Northhoff G (2005): Deficit in decision making in catatonic and paranoid schizophrenia: an exploratory study. *Psychiatric Res* 34:131–141.
- Bar-On R, Tranel D, Denburg NL, Bechara A (2003): Exploring the neurological substrate of emotional and social intelligence. *Brain* 126:1790–1800.
- Bechara A (2004): The role of emotion in decision-making: evidence from neurological patients with orbitofrontal damage. *Brain Cogn* 55:30–40.
- Bechara A, Damasio AR, Damasio H, Anderson SW (1994): Insensitivity to future consequences following damage to human prefrontal cortex. *Cognition* 50:7–15.
- Bechara A, Damasio H, Damasio AR, Lee GP (1999): Different contributions of the human amygdala and ventromedial prefrontal cortex to decision-making. *J Neurosci* 19:5473–5781.
- Bechara A, Dolan S, Denburg N, Hindes A, Anderson SW, Nathan PE (2001): Decision-making deficits, linked to a dysfunctional ventromedial prefrontal cortex, revealed in alcohol and stimulant abusers. *Neuropsychologia* 39:376–389.
- Bolla KI, Eldreth DA, London ED, Kiehl KA, Mouratidis M, Contoreggi C, Matochik JA, Kurian V, Cadet JL, Kimes AS, Funderburk FR, Ernst M (2003): Orbitofrontal cortex dysfunction in abstinent cocaine abusers performing a decision-making task. *Neuroimage* 19:1085–1094.
- Buchel C, Dolan RJ (2000): Classical fear conditioning in functional neuroimaging. *Curr Opin Neurobiol* 10:219–223.
- Cavallaro R, Cavedini P, Mistretta P, Bassi T, Angelone SM, Ubbiali A, Bellodi L (2003): Basal-cortico-frontal circuits in schizophrenia and obsessive-compulsive disorder: a controlled, double dissociation study. *Biol Psychiatry* 54:437–443.
- Cavedini P, Riboldi G, Keller R, D’Annunzi A, Bellodi L (2002): Frontal lobe dysfunction in pathological gambling patients. *Biol Psychiatry* 51:334–341.
- Clark L, Cools R, Robbins TW (2004): The neuropsychology of ventral prefrontal cortex: decision-making and reversal learning. *Brain Cogn* 55:41–53.
- Clark L, Manes F, Antoun N, Sahakian BJ, Robbins TW (2003): The contributions of lesion laterality and lesion volume to decision-making impairment following frontal lobe damage. *Neuropsychologia* 41:1474–1483.
- Damasio AR (1994): Descartes’ error and the future of human life. *Sci Am* 271:144.
- Damasio AR, Grabowski TJ, Bechara A, Damasio H, Ponto LL, Parvizi J, Hichwa RD (2000): Subcortical and cortical brain activity during the feeling of self-generated emotions. *Nat Neurosci* 3:1049–1056.
- Driver J, Frith C (2000): Shifting baselines in attention research. *Nat Rev Neurosci* 1:147–148.
- Editorial (2001): Analyzing functional imaging studies. *Nat Neurosci* 4:333.
- Elliott R, Rees G, Dolan RJ (1999): Ventromedial prefrontal cortex mediates guessing. *Neuropsychologia* 37:403–411.
- Friston KJ, Holmes AP, Worsley KF, Poline JP, Frith CD, Frackowiak RS (1995): Statistical parametric maps in functional imaging: a general linear approach. *Hum Brain Mapp* 2:189–210.
- Glimcher PW, Rustichini A (2004): Neuroeconomics: the consilience of brain and decision. *Science* 306:447–452.
- Goel V, Dolan RJ (2003): Explaining modulation of reasoning by belief. *Cognition* 87:11–22.
- Grimm S, Schmidt CF, Bermpohl F, Heinzel A, Dahlem Y, Wyss M, Hell D, Boesiger P, Boeker H, Northhoff G (2005): Segregated neural representation of distinct emotion dimensions in the prefrontal cortex—an fMRI study. *Neuroimage* (in press).
- Gusnard DA, Akbudak E, Shulman GL, Raichle ME (2001): Medial prefrontal cortex and self-referential mental activity: relation to a default mode of brain function. *Proc Natl Acad Sci U S A* 98:4259–4264.
- Gusnard DA, Raichle ME (2001): Searching for a baseline: functional imaging and the resting human brain. *Nat Rev Neurosci* 2:685–694.

- Hinson JM, Jameson TL, Whitney P (2002): Somatic markers, working memory, and decision making. *Cogn Affect Behav Neurosci* 2:341–353.
- Hornak J, Bramham J, Rolls ET, Morris RG, O’Doherty J, Bullock PR, Polkey CE (2003): Changes in emotion after circumscribed surgical lesions of the orbitofrontal and cingulate cortices. *Brain* 126:1691–1712.
- International affective picture system: digitized photographs (1999): Gainesville, Florida. The Center for Research in Psychophysiology, University of Florida.
- Ju B (2005): Strategy-proof risk sharing. *Games Economic Behav* 50:225–254.
- Kastner S, Pinsk MA, De Weerd P, Desimone R, Ungerleider LG (1999): Increased activity in human visual cortex during directed attention in the absence of visual stimulation. *Neuron* 22:751–761.
- Mandler M (2005): Incomplete preferences and rational intransitivity of choice. *Games Economic Behav* 50:255–277.
- Manes F, et al (2002): Decision-making processes following damage to the prefrontal cortex. *Brain* 125:624–639.
- McClure SM, Li J, Tomlin D, Cypert KS, Montague LM, Montague PR (2004): Neural correlates of behavioral preference for culturally familiar drinks. *Neuron* 44:379–387.
- Mitchell DG, Colledge E, Leonard A, Blair RJ (2002): Risky decisions and response reversal: is there evidence of orbitofrontal cortex dysfunction in psychopathic individuals? *Neuropsychologia* 40:2013–2022.
- Northoff G, Bermpohl F (2004): Cortical midline structures and the self. *Trends Cogn Sci* 8:102–107.
- Northoff G, Heinz A, Bermpohl F, Niese R, Pfennig A, Pascual-Leone A, Schlaug G (2004): Reciprocal modulation and attenuation in the prefrontal cortex: an fMRI study on emotional-cognitive interaction. *Hum Brain Mapp* 21:202–212.
- O’Doherty J, Kringelbach ML, Rolls ET, Hornak J, Andrews C (2001): Abstract reward and punishment representations in the human orbitofrontal cortex. *Nat Neurosci* 4:95–102.
- Oldfield RC (1971): The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia* 9:97–113.
- Ongur D, An X, Price JL (1998): Prefrontal cortical projections to the hypothalamus in macaque monkeys. *J Comp Neurol* 401:480–505.
- Patterson JC 2nd, Ungerleider LG, Bandettini PA (2002): Task-independent functional brain activity correlation with skin conductance changes: an fMRI study. *Neuroimage* 17:1797–1806.
- Phan KL, Wager T, Taylor SF, Liberzon I (2002): Functional neuroanatomy of emotion: a meta-analysis of emotion activation studies in PET and fMRI. *Neuroimage* 16:331–348.
- Ploghaus A, Becerra L, Borras C, Borsook D (2003): Neural circuitry underlying pain modulation: expectation, hypnosis, placebo. *Trends Cogn Sci* 7:197–200.
- Preibisch C, Pilatus U, Bunke J, Hoogenraad F, Zanella F, Lanfermann H (2003): Functional MRI using sensitivity-encoded echo planar imaging (SENSE-EPI). *Neuroimage* 19:412–421.
- Pruessmann KP, Weiger M, Scheidegger MB, Boesiger P (1999): SENSE: sensitivity encoding for fast MRI. *Magn Reson Med* 42:952–962.
- Raichle ME, MacLeod AM, Snyder AZ, Powers WJ, Gusnard DA, Shulman GL (2001): A default mode of brain function. *Proc Natl Acad Sci USA* 98:676–682.
- Rajkowska G, Goldman-Rakic PS (1995): Cytoarchitectonic definition of prefrontal areas in the normal human cortex: II. Variability in locations of areas 9 and 46 and relationship to the Talairach coordinate system. *Cereb Cortex* 5:323–337.
- Rogers RD, Ramnani N, Mackay C, Wilson JL, Jezzard P, Carter CS, Smith SM (2004): Distinct portions of anterior cingulate cortex and medial prefrontal cortex are activated by reward processing in separable phases of decision-making cognition. *Biol Psychiatry* 55:594–602.
- Rolls ET (1999): *The brain and emotion*. New York: Oxford University Press.
- Rolls ET (2000): The orbitofrontal cortex and reward. *Cereb Cortex* 10:284–294.
- Sakai K, Passingham RE (2003): Prefrontal interactions reflect future task operations. *Nat Neurosci* 6:75–81.
- Sanfey AG, Hastie R, Colvin MK, Grafman J (2003): Phineas gauged: decision-making and the human prefrontal cortex. *Neuropsychologia* 41:1218–1229.
- Simpson JR Jr, Drevets WC, Snyder AZ, Gusnard DA, Raichle ME (2001): Emotion-induced changes in human medial prefrontal cortex: II. During anticipatory anxiety. *Proc Natl Acad Sci USA* 98:688–693.
- Stark CE, Squire LR (2001): When zero is not zero: the problem of ambiguous baseline conditions in fMRI. *Proc Natl Acad Sci USA* 98:12760–12766.
- Tranel D, Bechara A, Denburg NL (2002): Asymmetric functional roles of right and left ventromedial prefrontal cortices in social conduct, decision-making, and emotional processing. *Cortex* 38:589–612.
- Wood JN, Grafman J (2003): Human prefrontal cortex: processing and representational perspectives. *Nat Rev Neurosci* 4:139–147.