

Supporting on line Material

Methods

Subjects: We tested three groups of subjects: (1) healthy normal control subjects (N = 18, 13 females, 5 males, mean age 43.7; mean education level, 14.2, range 7-22) without neurological history; (2) orbital prefrontal patients (N = 5) with focal lesions in the orbitofrontal cortex (Figure 3); (3) three control patients with lesions located in the posterior part of the cingulate cortex (BA, 23) in one case, in the dorsolateral prefrontal cortex (BA 8) in another case, and in the frontal operculum and part of the median prefrontal region (BA 44, 45, 9) in a third case. All 8 patients performed in the normal range in global cognitive test (Mattis Scale and WAIS-III) and all of them (orbitofrontal and control patients) showed impairments in tasks sensitive to frontal lobe dysfunction (see Table S1).

Task procedure: Financially motivated subjects played two sequences of thirty trials, the first sequence with partial feedback, and the second sequence with complete feedback. Subjects knew in advance the type of feedback they were going to receive. In order to facilitate the comparison between the first and the second condition we maintained the same sequence of outcomes (outcomes $\in \{-200; -50; +50; +200\}$ and probabilities (prob. $\in \{.2; .5; .8\}$) for the two sequences of thirty trials. Subjects were paid according to the outcome of the chosen gamble at the end of each trial with stacks of coins in order to maintain a high motivation level.

Skin conductance: SCR was recorded using a ProComp/ FlexPro™ system. Electrodes were placed in the non-dominant hand as proposed by Boucsein (SI). Subject sat in front of a computer screen where the two wheels were presented. Skin conductance response (SCR) was recorded using a second computer. Each trial was segmented into three time periods: (1) *choice*, when the pair of gambles appeared on the screen, (2) *waiting*, when the subject

observed the rotating arrow, (3) *feedback*, when the subject viewed the outcome. For each subject and for each condition, we obtained 90 time periods. SCRs were stored on a computer for an off-line analysis. SCR analysis was conducted using the method described by Lim *et al.* (S2). Signal amplitude having a threshold above $0.05\mu\text{S}$ was considered as a response. We measured the area under the curve (AUC). The SCR baseline was the lowest value in the inter-trial period.

Statistical Analysis

Direct statistical comparison among the two groups: normal subjects and OFC patients. We ran a repeated measures ANOVA with group (normal subjects vs. patients) as a between subjects factor and obtained outcome (4 categories, -200, -50, 50, 200) and the outcome of the unchosen gamble (5 categories -200, -50, 50, 200 and 0 representing the value of the other gamble in the partial feedback condition), as within subjects factors. The results show that there is: (1) a main effect of the “obtained outcome”, i.e. the higher the amount, the higher the evaluation, $F_{3,21} = 615.50, P < .0001$; (2) a main effect of the “unobtained outcome”, $F_{4,21} = 4.77, P < .001$, meaning that the higher the unobtained outcome, the lower the evaluation; (3) an interaction effect condition *per* group where patients’ performance was significantly different from normal subjects for the unobtained outcome, $F_{4,21} = 9.90, P < .0001$, but not for the obtained outcome, $F_{3,21} = 1.86, P = .13$. We additionally ran Kruskal-Wallis tests whose results are shown in Table S4.

Description of the choice model

The process of minimising the anticipated disappointment (denoted as d) choosing g_1 is equal to the difference between the distance of the lowest and the highest outcome, in g_2 and g_1 , respectively. These distances in absolute value are weighted by the probability of the lowest outcome, assuming that subjects attempt to avoid highly possible losses. The process of

minimizing the anticipated regret choosing g_1 (denoted as r) is equal to the difference between the lowest outcome of g_2 and the highest outcome of g_1 , and the lowest outcome of g_1 and the highest outcome of g_2 . If the subject maximizes the expected value (denoted as e), he/she will choose g_1 if its expected value is higher than the expected value of g_2 . The probability of choosing g_1 , the advantageous gamble, is a positive function of d , r , and e : $\Pr(g_1) = F [d, r, e]$ where F is a logistic function.

Orbitofrontal patients

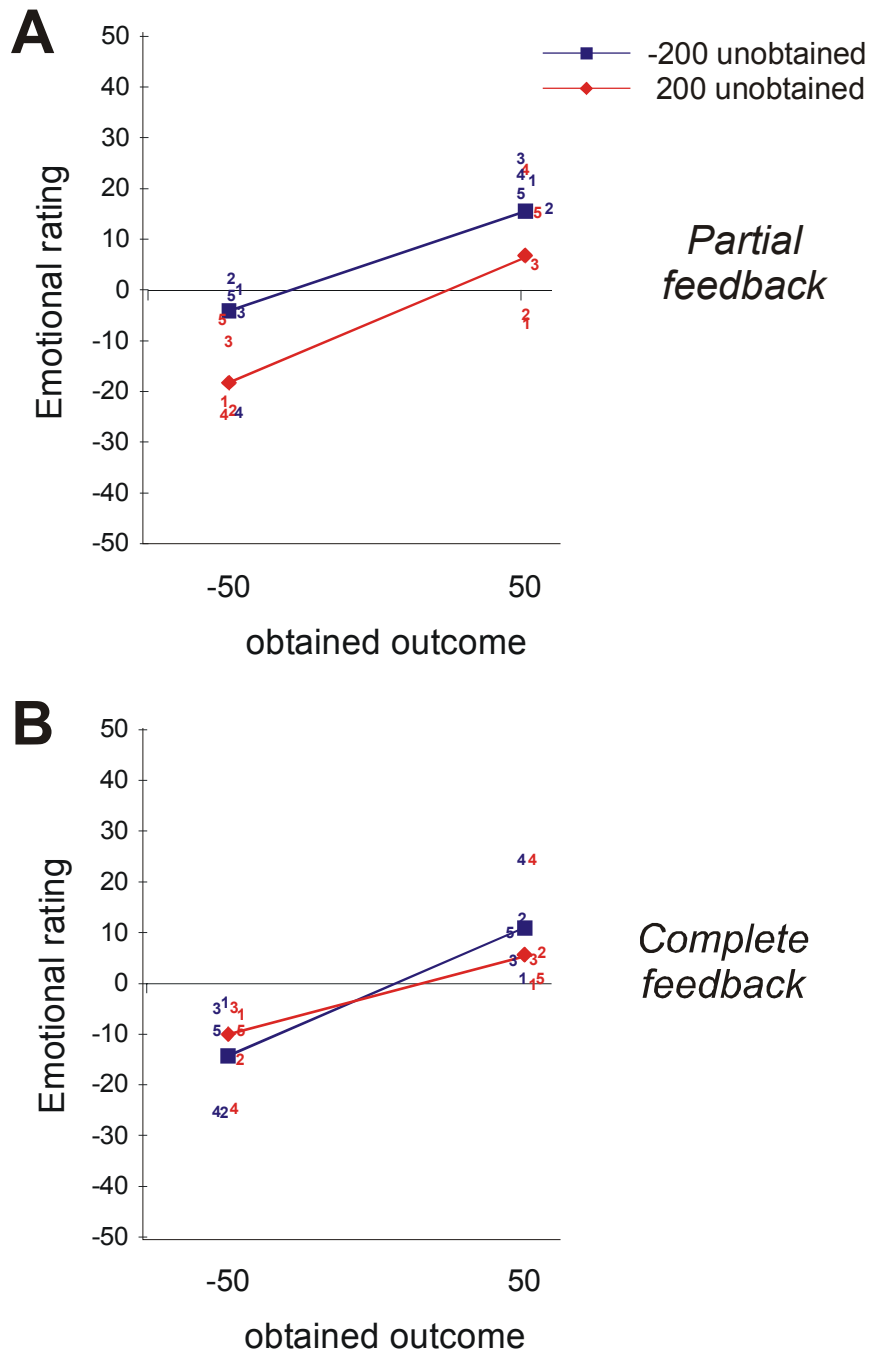


Fig. S1. Individual performance of the orbitofrontal patients group for the partial and complete feedback conditions.

Effect of [-200 200] obtained outcome

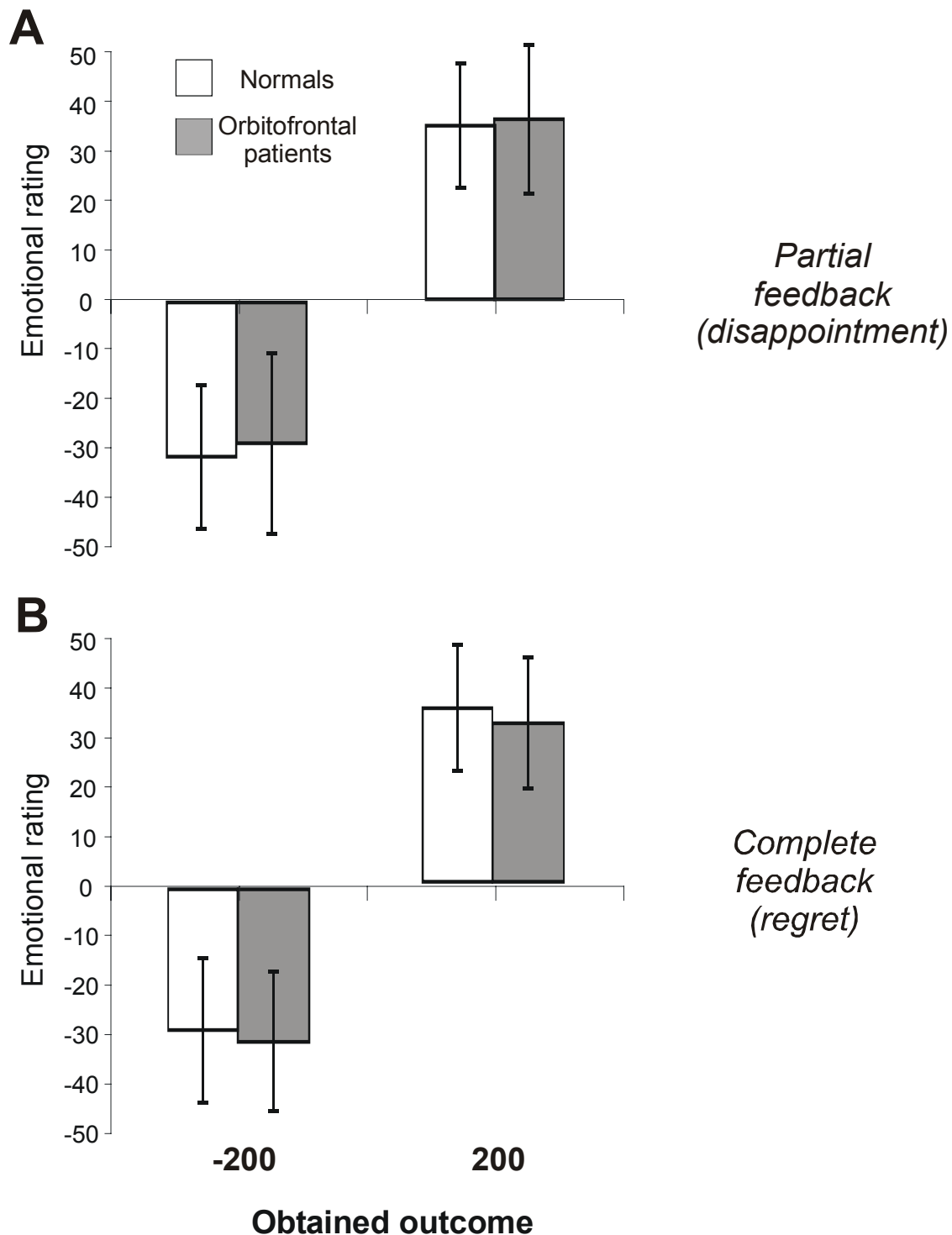


Fig. S2 Emotional rating as a function of the obtained outcome for +200 and -200, regardless of the unobtained outcome for normal control subjects and orbitofrontal patients for the partial and complete feedback condition. These data show that orbitofrontal patients used the full extent of the rating scale and experienced the same emotional intensity as normal subjects when winning or losing a large sum. Disappointment and regret effects were not investigated with these two outcomes because each one was associated with only one possible alternative: more advantageous in the losing case and more disadvantageous in the winning case.

Mesial and dorsolateral frontal patients (N=3)

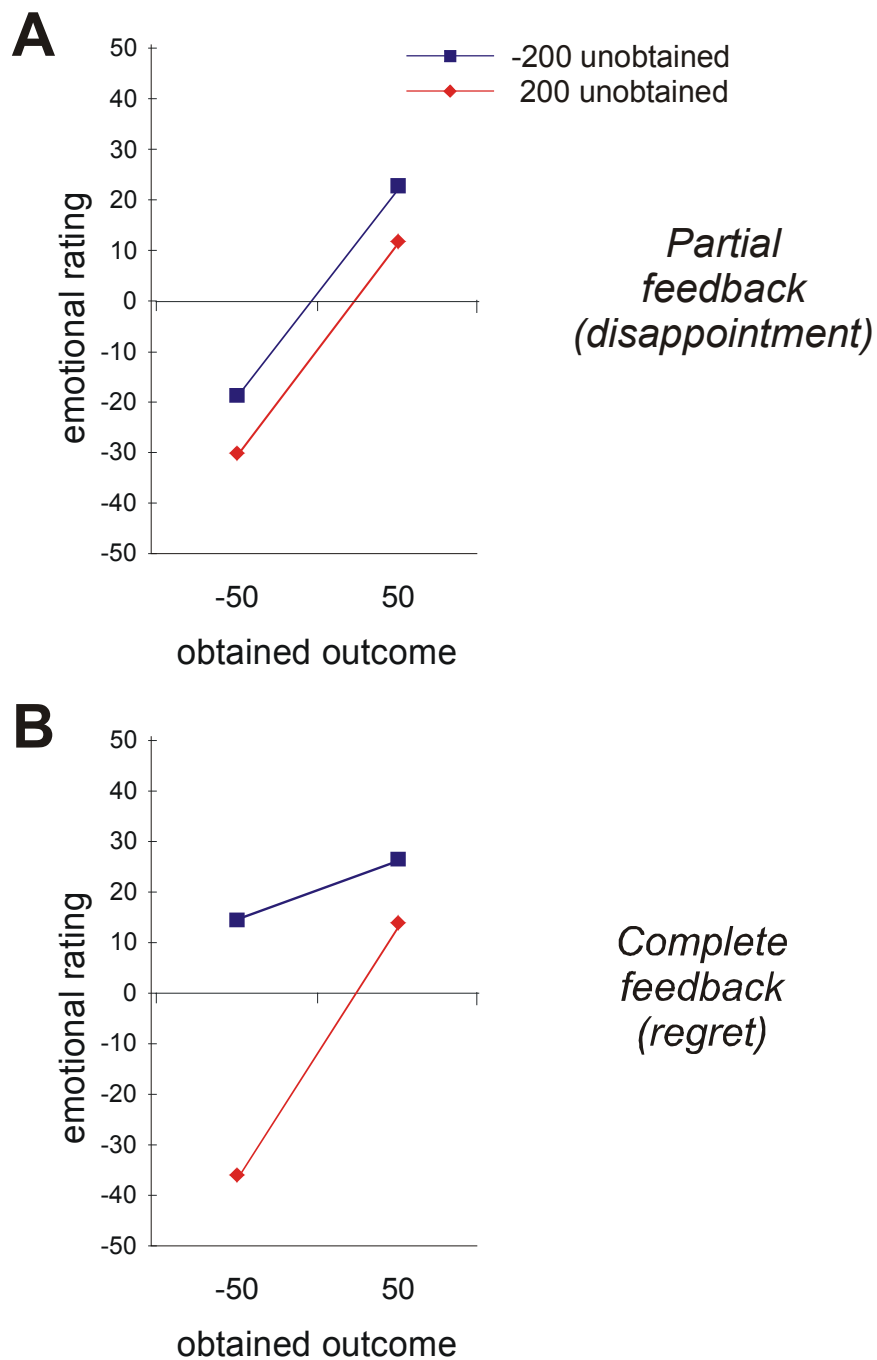


Fig. S3. Effect of unobtained outcome of the gamble in partial and complete feedback condition for three control patients with frontal lesions sparing the orbital region. **A.** Mean affective ratings for two obtained outcomes (-50 or 50) as a function of the unobtained outcome (-200 or 200) of the chosen wheel in the partial feedback condition. **B.** Mean affective ratings for two obtained outcomes (-50 or 50) as a function of the outcome (-200 or 200) of the non-chosen wheel in the complete feedback condition.

Complete feedback

Effect of unobtained outcome of chosen gamble

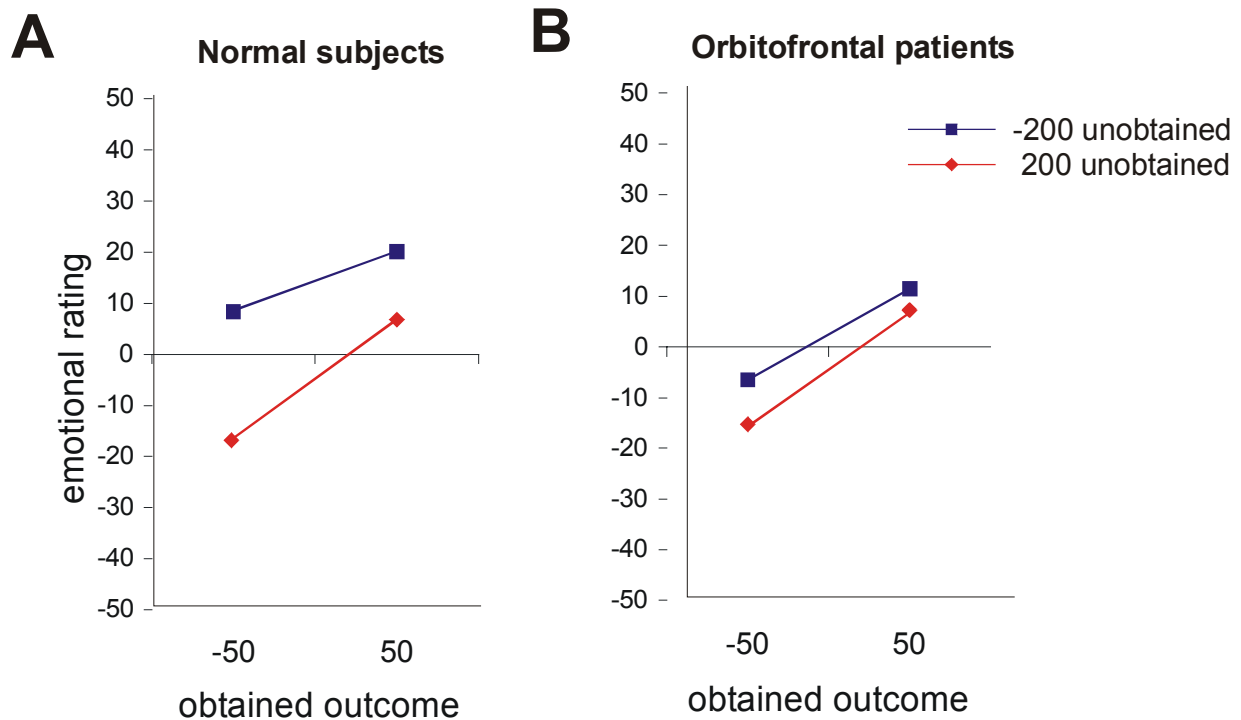


Fig. S4. Effect of the unobtained outcome of the chosen gamble in the complete feedback condition (*disappointment in regret*) for normal subjects (**A**) and orbitofrontal patients (**B**). The figure shows mean emotional rating for two obtained outcomes (-50 or 50) as a function of the unobtained outcome (-200, 200). Affective ratings in normal subjects for a given outcome obtained in the face of a more favorable outcome of 200 for the unchosen gamble are more negative than in the face of an unobtained outcome of 200 for the chosen gamble (Wilcoxon signed-rank tests, $Z = -1.931$, $P = .05$, for -50 obtained, and $Z = -3.464$, $P < .001$, for +50 obtained outcome). These results indicate that emotional ratings in the complete feedback condition are dominated by the comparison between the values associated to the positions where the two arrows stopped. These effects are absent in patients (Wilcoxon signed-rank tests, $Z = .535$, $P = .59$, for -50 obtained, and $Z = -.544$, $P = .58$, for +50 obtained outcome).

Table S1. Clinical and neuropsychological data on orbitofrontal (OFC 1-5) and control patients (AT, FG, CN). The ¹Stroop is a test of attention and susceptibility to interference. The subject has to read 100 color words (red, blue, green) printed in black as quickly as possible (A), to name the color of 100 colored dots (B), to name the color in which of color words are printed (e.g. the word « red » is written in blue) (C). The ²Trail Making Test measures movement speed, psychomotor coordination, response inhibition and interference. Subjects have to connect as fast as they can randomly arrayed numbers in ascending order (part A) or numbers and letters in alternate order (1-a-2-b-3-c...) (part B). ³Verbal fluency is a test which involves sustained attention and semantic memory abilities. The patient is required to verbally produce in 120s as many words as possible starting with a given letter, or belonging to a semantic category. ⁴Wisconsin Card Sorting Test requires subjects to sort cards based on color, shape and quantity. It measures abstract concept acquisition and mental shifting .

	OFC 1	OFC 2	OFC 3	OFC 4	OFC 5	AT	FG	CN
Sex	F	M	M	M	M	F	F	M
Age	40	45	57	54	49	61	59	37
Education in years	11	14	20	18	10	14	11	12
Lesion location	Orbitofrontal left	Orbitofrontal bilateral	Orbitofrontal right	Orbitofrontal left	Orbitofrontal bilateral	Dorsolateral prefrontal bilateral	Mesial prefrontal left	Dorsolateral prefrontal right
Etiology	Infarct	Head injury	Infarct	Infarct	Aneurysm	Méningioma	Cavernous angioma	Aneurysm
Lesion age at testing	10 years	1 year	1 year	1 year	8 years	1 year	8 years	1 year
Global intellectual efficiency	Mattis : 143	Mattis : 143	WAIS = 106	WAIS=98	Mattis : 144	Mattis : 140	Mattis : 139	Mattis : 143
¹ Stroop	95	37*	90	75*	60*	71*	40*	80
- part A	57*	28*	59*	53*	41*	45*	35*	52*
- part B	41	36	30	36	15*	20*	20*	24*
² Trail Making Test (percentile range)								
- part A	50-75/100	<10/100	10-25/100	<10/100	10-25/100	25-50/100	<10/100	10-25/100
- part B	25-50/100	<10/100	10-25/100	<10/100	<10/100	10-25/100	10-25/100	25-50/100
³ Verbal fluency								
- Letters	18	10*	6*	19	16	8*	19*	19*
- Animals	16*	15*	15*	17*	14*	13*	27*	14*
⁴ Wisconsin Card Sorting Test								
- Categories completed	6	6	4	6	6	6	6	4*
- Perseverative responses	0	6	43*	10	8	1	2	5

* below normal range

Table S2. Average emotional rating for all possible combination of obtained/unobtained outcome in partial feedback condition for normal subjects and orbitofrontal patients.

Obtained	Unobtained	Normal subjects N=18		OFC N=5	
		mean	sd	mean	sd
-200	-50	-30,41	15,29	-27,50	22,22
-200	50	-31,26	15,07	-28,83	16,93
-50	-200	3,23	6,73	-5,85	11,01
-50	50	-12,40	10,66	-14,25	15,45
-50	200	-18,13	9,60	-19,93	8,36
50	-200	22,43	10,31	16,47	6,72
50	-50	16,70	8,22	17,00	7,04
50	200	6,81	10,88	6,77	13,37
200	-50	35,09	12,44	36,00	17,37
200	50	35,68	13,04	36,00	14,24

Table S3. Average affective rating for all possible combination of obtained/unobtained outcome in complete feedback condition for normal subjects and orbitofrontal patients.

Obtained	Unobtained	Normal subjects N=18		OFC N=5	
		mean	sd	mean	sd
-200	-200	-22,22	18,63	-33,50	14,85
-200	-50	-29,47	14,75	-31,60	15,29
-200	50	-39,38	14,44	-30,00	34,64
-200	200	-39,17	11,27	-7,50	10,61
-50	-200	0,38	9,75	-13,83	10,96
-50	-50	-10,56	14,64	-17,00	21,61
-50	50	-11,65	12,54	-10,92	11,55
-50	200	-29,42	19,10	-10,56	4,19
50	-200	22,85	12,33	11,08	9,05
50	-50	19,09	8,64	16,58	6,13
50	50	10,56	15,39	11,75	11,54
50	200	-7,41	23,80	7,58	10,11
200	-200	36,25	14,99	26,75	20,49
200	-50	35,61	14,76	31,94	18,34
200	50	33,17	15,70	31,25	14,90
200	200	33,97	15,48	42,00	15,25

Table S4. Kruskal-Wallis tests (chi-square with 4 d.f.) for obtained outcome vs. the outcome of the unchosen gamble. Factor 1 was represented by the obtained outcome (4 categories: -200, -50, +50, +200) while factor 2 by the outcome of the unchosen gamble (5 categories, -200, -50, with 0 representing the partial feedback condition, +50, +200). The results show that the emotional rating for -50 and +50 is modulated by the unobtained outcome in normal subjects. No significant differences among all possible comparisons were found in patients with orbitofrontal lesions.

Obtained outcome	Normal subjects		OFC	
	$\chi^2(4)$	<i>P</i>	$\chi^2(4)$	<i>P</i>
-200	7.593	.11	2.64	.61
-50	26.89	<.001	.68	.95
+50	26.06	<.001	4.168	.33
+200	.37	.98	2.99	.55

Supporting References

S1. Boucsein, W. *Electrodermal Activity*. (New York : Plenum Press,1992).

S2. Lim C.L., et al. *Int. J. Psychophysiol.* 25, 97 (1997).