Response to Comment on "The Involvement of the Orbitofrontal Cortex in the Experience of Regret"
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Standard economic theory can account for human choices in a variety of situations. It predicts that rational decision-makers will base their choice on the probability that a particular outcome will be favorable (i.e., its expected utility). However, many deviations from this prediction are observed, because humans are often anything but rational. For example, people often prefer getting \$450 with 100% certainty than \$1000 with 50% probability, even though the expected value of the second option (\$500) is higher than the first one (*1*). In the Netherlands, the "postal code" lottery is immensely popular even though playing the game is quite irrational (*2*). Its success has been explained by the possibility that people figure how bad they would feel if, not having bought a ticket, their postal code is drawn and their next-door neighbor wins the lottery. Such counterfactual reasoning is what allows us to anticipate future regret. Whether this is ultimately useful probably depends on what is at stake, for example, money, reputation, or the well-being of loved ones. When gambling, a purely rational mind fast at computing the expected value of the different options is most certainly one's best asset. However, human beings do not necessarily operate in a purely rational fashion.

Patients with orbitofrontal cortex lesions (OFC) can elaborate plans and options and even recognize the incongruence between how they should behave and how they actually behave (*3*), yet in real life their choices are inadequate in a manner suggesting a missing sense of responsibility for the consequences of their own decisions. This common clinical observation predicts that such patients should not feel regret and that their choices should not be weighted by possible future regrets. Camille *et al*. (*4*) explicitly tested this prediction. The comment by Eagleman (*5*) challenges two aspects of our study and argues that we did not describe the task properly and, more important, that a confound in the task parameters calls for another interpretation of the results.

Figure 1 in (*4*) shows an example of the gamble pairs that can be constructed from the combinations of outcome pairs from the set –200, –50, 50, and 200 and associated outcome probabilities (0.2, 0.5, or 0.8). We used only a subset of those combinations to generate the trial structure of the experiment shown (see table S2). This is a perfectly legitimate procedure and in itself is not a source of bias. The simulation shown in figure 1A in (*5*) wrongly assumes that all possible combinations were used (see fig. S1B for a correct simulation). A more critical point is that the real outcome of the gambles did not conform exactly to what would be expected based on the depicted probabilities. This is explained in the original text (*4*) and was done so that better net gains could be obtained by anticipating regret.

This manipulation is the focus of Eagleman's critique, namely, that the parameters we have used may have provoked frustration rather than regret, because the actual outcomes experienced by subjects were less favorable than they expected. Normal subjects becoming increasingly suspicious about the depicted probabilities would have somehow altered their choice strategy (although this frustration model does not clearly predict in what way), whereas OFC patients might have been insensitive to this mismatch and performed the task solely according to expected values. Unfortunately, Eagleman's argument fails to account for several findings.

Eagleman neglected one key aspect of the experiment: the comparison between partial and complete feedback. The mismatch between the expected and actual outcomes was present in both conditions because they were made from the same gamble pairs. If patients were insensitive to this mismatch, and experienced no frustration, why were their choices not significantly different from those of normal subjects in the partial feedback condition? A model that would factor in frustration should account for choice behavior whether or not feedback on the outcome of the rejected gamble is provided.

This logic also applies to emotional ratings, a dependent variable that should be particularly sensitive to feelings of frustration. Normal subjects and OFC patients exhibited similar, graded emotional responses in the partial feedback [see figure 2, A and B, in

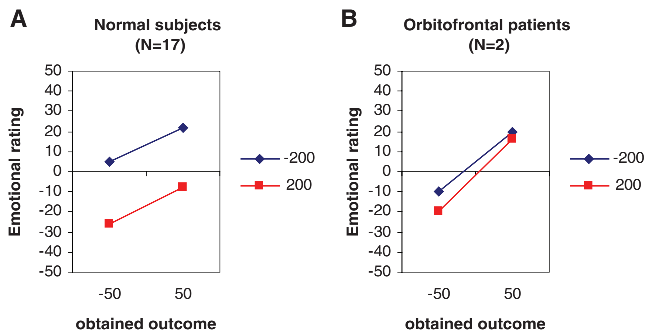

Fig. 1. Emotional ratings in a replication of the task used in (*4*), with actual outcomes matching depicted probabilities. Ratings were made by 17 normal control subjects (**A**) and 2 orbitofrontal patients (**B**) for two obtained outcomes (–50 or 50) as a function of the outcome (blue line and symbols, –200; red line and symbols, 200) of the unchosen gamble in the complete feedback condition [data from (*6*)]. The outcome of the alternative gamble strongly modulates the emotional rating (regret effect) of normal subjects but not that of OFC patients.

Table 1. Model of choice applied in a replication of the task used in (*4*), with actual outcomes matching depicted probabilities. Panel logit regression procedure with individual random effects. Dependent variable is "choice." With *d* = anticipated (minimization) disappointment, *r* = anticipated (minimization) regret, and e = maximization of expected value [data from (*6*)]. Results show that normal subjects chose maximizing expected values and minimizing regret, whereas OFC patients did not anticipate regret. Therefore, we found the same pattern of choice behavior observed in (*4*).

Variable name	Coefficient	Standard error	*z*	*P*
		Normal subjects		
Constant	.2251687	.1541618	1.46	0.144
d	–.0015986	.0018395	–0.87	0.385
r	.0068114	.0013719	4.97	0.000
e	.0304755	.0038502	7.92	0.000
		OFC patients		
Constant	–.3838773	.5012885	–0.77	0.444
d	–.023136	.0100615	–2.3	0.021
r	.0047578	.0043964	1.08	0.279
e	.0669018	.0223844	2.99	0.003

(*4*)] and to the contrast between what they hoped to obtain and what they actually obtained [figure S2 in (*4*)]. If only normal subjects, but not patients, reacted with frustration to the mismatch between expected and actual outcomes, differences in subjective emotional ratings between the two groups should have been observed in both conditions. Also, normal subjects did not generally react more negatively than patients to losing, as a frustration hypothesis might predict.

Our core argument is that knowing the result of the alternative gamble, as compared with knowing only the result of the chosen gamble, generates a specific emotion that we called regret. Following our hypothesis, regret biased subjects' choice throughout the experiment. The effect of anticipated regret was confirmed by our model of choice (*4*), where we found an interaction between maximization of expected value (e) and minimization of future regret (r). Is this result confounded by the possibility that the parameters we used created frustration rather than regret? As part of another recent study (*6*), we had 17 normal subjects and 2 OFC patients perform exactly the same task, but this time using outcomes that matched the depicted probabilities. The results on emotional rating (Fig. 1 and fig. S2) confirm our original findings. The same model also showed that anticipated regret significantly contributes to the gambling choices of normal subjects' but not those of OFC patients (Table 1). Patients performed in a manner consistent with rational theory and earned more than normal subjects, who chose trying to avoid future regret.

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Supporting Online Material
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Figs. S1 and S2
Tables S1 and S2
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