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REVIEW

Structure–function relationships in the processing of regret in the orbitofrontal cortex

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Abstract The influence of counterfactual thinking and regret on choice behavior has been widely acknowledged in economic science (Bell in Oper Res 30:961–981, 1982; Kahneman and Tversky in Judgment under uncertainty: heuristics and biases. Cambridge University Press, Cambridge, pp 201–210, 1982; Loomes and Sugden in Econ J 92:805–824, 1982). Neuroimaging studies have only recently begun to explore the neural correlates of this psychological factor and orbitofrontal cortex (OFC) activity was observed in several of them depending of the exact characteristics of the employed paradigm. This selective OFC involvement and, moreover, a consistently found dissociation of medial and lateral OFC activity clusters allow inferences to the function of this structure in counterfactual thinking and regret. Vice versa, the differential contribution of OFC subregions to these processes also adds evidence to the current debate on the function of this cortical structure in decision-making that attracted increasing attention in recent years.

Keywords Orbitofrontal cortex (OFC) · Medial OFC · Lateral OFC · Regret · Decision-making · Counterfactual thinking

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Introduction

Until recently, economic theories on human decision-making viewed choices under risk as based entirely on rational cognitive processes (von Neumann and Morgenstern 1944). According to the dominant theory, humans choose between alternative options by computing the expected utility (EU) of each action, i.e., the desirability of the potential outcomes weighted by their probability, and then select the option with the greatest EU (Loewenstein et al. 2008). Human decision-making, however, often violates the assumptions of this axiomatic rational choice theory. A variety of these deviations were explained by prospect theory through purely cognitive biases, e.g., the overweighting of small and the underweighting of large probabilities (Kahneman and Tversky 1979). However, other anomalies in rational decision-making, i.e., loss and risk aversions, which were incorporated into prospect theory, are presumably based not only on cognitive biases but are also driven by negative emotions (Loewenstein et al. 2001; Camerer 2005). Therefore, the role of emotions and affect in decision-making has attracted an increasing interest in economic and cognitive decision-making research in recent years. Moreover, it has been shown that incorporating emotional factors in models of decision-making can enhance their explanatory power (Loewenstein and Lerner 2003).

One particularly powerful negative emotion that exerts an influence on decision-making is regret, which may even lead to irrational, suboptimal decisions (regret theory; Bell 1982; Loomes and Sugden 1982). Regret refers to the negative emotion associated with missing out on better outcomes that would have been obtained had a different choice been made. The theoretical and computational core of regret theory is a fictive prediction error, which compares a fictitious outcome to the outcome that has actually been obtained. Since the formulation of regret theory, numerous publications from different areas showed that incorporating regret into decision models enhances their explanatory power, thus reflecting the influence of this emotion on decision-making processes (Zeelenberg and Pieters 2007).

Functional neuroimaging studies of decision-making initially focused on the identification of the neural correlates of rational decision-making, e.g., prediction errors and expected values. Only recently, following the trail of behavioral economists, neuroscientists have begun to investigate anomalies in rational decision-making induced by cognitive biases and emotions, e.g., the endowment (Weber et al. 2007; Knutson et al. 2008; De Martino et al. 2009) and framing effects (Deppe et al. 2005, 2007; Gonzalez et al. 2005; De Martino et al. 2006), temporal discounting (McClure et al. 2004; Kable and Glimcher 2007), risk (Kuhnen and Knutson 2005; Brown and Braver 2007) and loss aversion (Tom et al. 2007).

In agreement with the widely acknowledged impact of regret on choice behavior, the neural correlates of this emotion during decision-making have also been explored in a range of recent studies (Camille et al. 2004; Coricelli et al. 2005; Shiv et al. 2005; Liu et al. 2007; Lohrenz et al. 2007; Chandrasekhar et al. 2008; Chiu et al. 2008; Chua et al. 2009). Although these studies consistently confirmed the substantial impact of regret on choice behavior, they partly disagree with respect to the underlying neural correlate, in particular the involvement of the orbitofrontal cortex (OFC).

The role of the OFC in decision-making has attracted increasing attention in recent years and is a matter of current debates (Schoenbaum et al. 2007). The aim of this review is therefore on the one hand to use the existing data and theories about OFC function to better understand its contribution to regret-related decisions and on the other hand to use the pattern of activity found in regret-related studies to better understand the function of the OFC. In other words, current knowledge about regret and its neural correlates can inform the debate about OFC function and vice versa. To achieve this goal, we will begin with a brief review of the behavioral regret literature to highlight the characteristics and impact of this emotion on decision processes.

Counterfactual thinking, regret, and fictive prediction errors

Regret theories

The cognitive process underlying regret is counterfactual thinking, which enables a person to process not only the actual, but also an alternative course of events, which could have occurred had different actions been taken. For instance, after many decisions, e.g. the question to invest in a particular equity stock or in less risky government bonds, individuals learn not only about the outcome of the chosen but also about the outcome of the unchosen option. Counterfactual thinking allows an individual to contrast the factual and the fictive outcome. This counterfactual comparison may lead to regret in cases where a better opportunity was missed, e.g., one decided to invest in safe bonds with lower return assumption and experienced a huge stock quotation increase, and to rejoice otherwise, e.g., the stock bubble bursts. The negative emotion of regret exerts a more substantial influence on decision-making than rejoice (Zeelenberg and Pieters 2007), somewhat paralleling loss aversion as stated by Tversky and Kahneman (1991): "The central assumption of the theory is that losses and disadvantages have greater impact on preferences than gains and advantages." Thereby the stronger behavioral influence of regret is explained by negative dominance, i.e., the general tendency to give more weight to negative than positive experiences (Baumeister et al. 2001; Rozin and Royman 2001).

This asymmetric, valence-dependent strength of the influence of counterfactual emotions on decision-making results in inconsistencies between the observed choice behavior and the predictions of EU theory (Coricelli et al. 2007). Accordingly, regret theory proposed that individuals are regret-aversive and therefore try to minimize potential regret during decision-making, which sometimes results in suboptimal and thus irrational choices (Bell 1982; Loomes and Sugden 1982). Empirical support for these early regret theories was mixed and appeared most strongly when the possibility of regret was made very salient to the decision maker. However, subsequently regret theory and, more generally, the influence of counterfactual thinking and emotions on decision-making was further developed, e.g., by incorporating disappointment as another negative emotion into the framework (Mellers et al. 1999; Zeelenberg and Pieters 2007).

Regret and its influence on decision-making have been characterized in recent years in detail with respect to several parameters. A first theoretically important distinction should be made between anticipated and experienced, or prospective and retrospective regret (Zeelenberg and Pieters 2007). Prospective regret, as incorporated in the original regret theories, is experienced when decisions are difficult and important, which leads to intense future-oriented counterfactual reasoning, and when decision makers anticipate to learn about the outcomes of both alternatives quickly.

A second important line of research concerns factors influencing the emotional salience of regret. The salience of regret depends not only on the characteristics of the decision, e.g., how important and difficult it is, and whether it can be reversed later, but also on personality traits. Subjects differ with respect to their regret sensitivity (Schwartz et al. 2002) and the salience of regret is crucially linked to the feeling of responsibility. To avoid regret people tend to avoid personal agency, i.e., they do not actively act, which leads to an "omission bias" (e.g., the 'never bust'-strategy in blackjack; Chau et al. 2000). In addition, the salience of the foregone alternative, i.e., how vivid it is experienced after the decision, influences the amount of regret. Factors that elevate the relative salience of a counterfactual anchor may thus alter evaluations of past decisions and hence influence the unfolding of future decisions (Baron and Hershey 1988). Finally, the emotional impact of regret is stronger not only than that of rejoice (negative dominance) but also of disappointment (Mellers et al. 1999; Chua et al. 2009), i.e., people tend to focus on the missed instead of the obtained outcome (Carmon and Ariely 2000).

Independent of this line of regret theory, the role of counterfactual thinking in evaluation and decision-making has been highlighted in many contexts (simulation heuristic, Kahneman and Tversky 1982; Roese 1999; Byrne 2002; Baird and Fugelsang 2004; Yechiam and Busemeyer 2006; Ert and Erev 2007; Epstude and Roese 2008). Experienced regret also plays an important role in adjusting choice behavior in social decision-making and interactive learning (Hart and Mas-Collel 2003; Marchiori and Warglien 2008). Its relevance is further emphasized by findings of its impaired action guidance in chronic smokers and schizophrenics (Chiu et al. 2008; Roese et al. 2008). And recently, it was shown that also non-human primates compute not only factual but also counterfactual outcomes (Hayden et al. 2009). Taken together, there is emerging evidence from various disciplines that counterfactual comparisons and regret are important factors in decision-making and the conditions influencing their behavioral impact are now well defined and, moreover, it is evident that this is a rather complex phenomenon.

Regret and fictive prediction errors

Economists aim to describe and predict human choice behavior using mathematical models that take into account factors such as the probability and value of potential outcomes. Bell (1982) and Loomes and Sugden (1982) incorporated regret into the utility function by adding a term corresponding to the counterfactual comparison. Regret theory as proposed by these authors describes the influence of anticipatory regret. Therefore, these approaches usually do not take into account that decision makers might adapt their choice behavior by experience; in other words, the utility function might change depending on the outcomes of previous decisions.

In contrast, psychologists and computational neuroscientists focus on serial decisions and have intensely studied the processes underlying decision-making using a variety of reinforcement learning models, e.g., temporal difference and Q-learning models (Sutton and Barto 1998). Many of these models share the assumption of a prediction error which is computed based on the difference between expected (predicted) and experienced reward. This error can then be used to form and adjust associations between actions or stimuli and their ensuing reinforcements. Therefore, this prediction error is thought to guide the behavioral adaptation of the organism to the environment by adjusting future behavior. Naturally, a prediction error can only be computed retrospectively, after the outcome of a decision was learned.

In analogy to the difference between the predicted and the factual outcome, i.e., the prediction error, computational neuroscientists also included the difference between the factual and counterfactual outcome as an additional learning signal in reinforcement learning models (Montague et al. 2006; Lohrenz et al. 2007; Chiu et al. 2008). This has led to the introduction of the term 'fictive prediction error', which is purely descriptive, but is related to the concept of regret. Also, computational models of reversal learning have recently incorporated counterfactual cognitions by updating not only the value of the chosen, but also the unchosen option (Hampton et al. 2006, 2007; Glascher et al. 2008; Boorman et al. 2009). The relevance of regret and fictive error signals for adjusting decision-behavior is highlighted by the increased explanatory power of such computational models in various experimental settings.

Neuroimaging studies on regret and the fictive prediction error

Neuroimaging studies on regret and fictive prediction errors employed various paradigms that can be roughly divided into two categories: either subjects have to choose between two gambles on each trial or they have to decide how much they want to risk on each trial. Only in the first, more traditional type of regret-paradigm, the OFC appears to be involved in outcome processing. The various experimental settings and the corresponding results will be described in detail to allow inferences about the relationship between the involved processes and the involvement of the OFC. Behavioral studies often investigate singular decision-scenarios, to study the influence of anticipatory regret on choice behavior, e.g., negotiating a signing bonus with or without the expectancy of feedback about the alternative missed offers (Larrick and Boyles 1996). Neuroimaging studies, on the other hand, adopted paradigms in which subjects repeatedly decided between alternative options (e.g., Mellers et al. 1999). In the latter studies, therefore, both anticipatory and experienced regret influenced learning processes, which were then reflected in choice behavior and brain activity.

Regret induced by a forced choice between two gambles

In the first type of paradigms, adapted from Mellers et al. (1999), participants choose between two gambles with different expected values or between a gamble and a safe alternative on each trial. Participants observe in complete feedback trials not only the outcome of the chosen, but also of the unchosen option which may lead to regret and rejoice (Camille et al. 2004; Coricelli et al. 2005; Liu et al. 2007; Chua et al. 2009). In partial feedback trials, which are contrasted with the former, only the outcome of the chosen gamble is shown to the subjects leading to disappointment or elation. In a variant of this task, subjects have to choose between alternative gambles, i.e., opening one of three doors, and the degree of regret was manipulated by varying the likelihood of choosing a door associated with an aversive outcome (Chandrasekhar et al. 2008).

Choice between two risky gambles

Coricelli and colleagues modified a paradigm of the first type where two spinners appeared on a computer screen (corresponding to gamble 1 and 2) and each spinner had two colored sectors associated with different values (−200, −50, 50, or 200) (Fig. 1a, Camille et al. 2004; Coricelli et al. 2005). The size of the colored sectors indicated their outcome probability (0.8, 0.5, and 0.2). The subject had to choose one of the two spinners after which a rotating arrow appeared in both wheels. After the arrow(s) stopped, the subject was able to observe outcomes of the selected or of both spinners dependent on the trial type. Partial and complete feedback trials were presented in blocks of 12 of the same trial type. Crucially, in complete feedback trials the two gambles were either maximizing expected utility (i.e., choosing the gamble with the highest expected value) or minimizing potential regret (i.e., choosing the gamble that minimizes the difference between the lowest possible factual outcome and the highest counterfactual outcome). Skin-conductance responses (SCR) were recorded in one study to assess the emotional value indirectly, and at the end of each trial, subjects rated their affective state. The affective ratings as well as the SCR analysis suggested that the negative valuation of a chosen outcome depended on counterfactual thinking about the missed opportunity because both parameters exhibited stronger effects than for disappointment (Camille et al. 2004; Coricelli et al. 2005). The effect of accumulated experienced regret led subjects to prefer the regret-minimizing gambles over the course of the experiment and immediate regret affected choices in the next trial (Coricelli et al. 2005). Among other areas, the OFC was correlated with the degree of experienced regret and OFC-lesioned patients did not exhibit any influence of regret on their choice behavior, acting somewhat more rationally than healthy controls.

Another recent study employed a slight modification of the same paradigm with more fine graded outcome probabilities and values. Moreover, complete and partial feedback trails were presented in intermixed order and subjects rated their desire to change the previous choice after each trial (Chua et al. 2009). After regret trials, participants indicated the strongest desire to change their decision and exhibited the strongest negative affective response. The mOFC exhibited stronger activity for positive valenced trails, i.e., rejoice and elation, whereas activity in the central and lateral OFC correlated positively with regret.

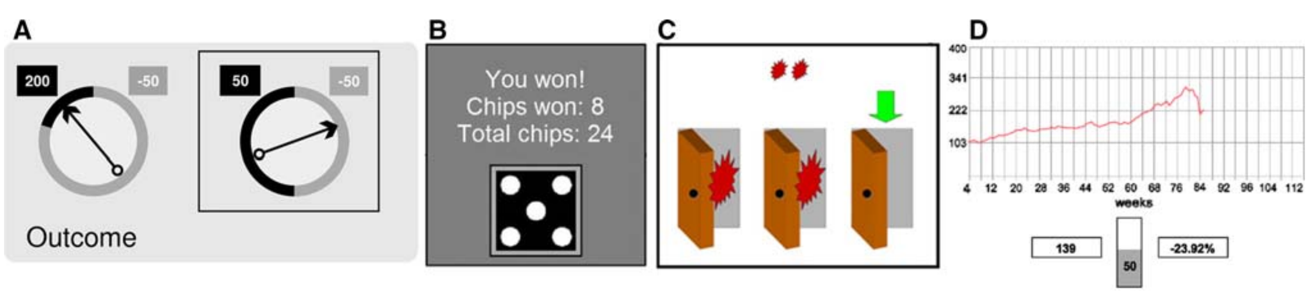

Fig. 1 Paradigms inducing regret and rejoice (outcome and counterfactual comparison phase). **a** Participant decided in the complete feedback condition for the right gamble and experiences regret because he/she lost 50 points whereas the other gamble won 200; Camille et al. (2004) and Coricelli et al. (2005); **b** participant decided for rolling the dice and experiences rejoice because the decision for the unsafe dice was in this trial advantageous over the safe bank; Liu et al. (2007); **c** participant decided for the right door and experiences strong rejoice because the likelihood of not getting shocked was low; Chandrasekhar et al. (2008); **d** participant invested only half of the money in stocks and experiences rejoice because the market decreases; Lohrenz et al. (2007) and Liu et al. (2007) (modified with permission)

Choice between risky and safe option

In a slightly different design, subjects could choose between putting their wager on a safe bank or betting on a dice with the chance to win (Fig. 1b, Liu et al. 2007). In trials in which subjects chose the safe option, the dice was nonetheless tossed and participants thus learned whether they could have won more money or avoided loosing money, thus inducing regret through counterfactual comparisons (Mellers et al. 1999). Regrettable decisions led to OFC activation. A study with orbitofrontal lesions patients adopted a similar design but provided feedback about the dice only when subjects chose this option (Shiv et al. 2005). Here, volunteers experienced regret only in trials in which they decided to gamble. While control subjects avoided gambling after a loss, choices of OFC-lesioned patients were unaffected by previous outcomes. Moreover, only the controls showed an increasing regret-minimizing choice behavior over the course of the experiment.

It should be noted for the sake of completeness that one study originally designed to investigate risk-taking induced regret in one condition (Kuhnen and Knutson 2005). In this design subjects had to decide between two stocks of different gain probability and a safe bond. In cases where the lower stock was chosen, the feedback activated the insula. However, due to the small number of trials in this specific condition, the lack of OFC activity may be related to a lack of power.

Different likelihoods of an aversive outcome

A different approach aimed to generalize the findings of the neural correlates of regret and rejoice to non-monetary reinforcers, in particular, the avoidance of an aversive outcome (i.e., a mild electric shock) (Fig. 1c, Chandrasekhar et al. 2008). Volunteers were asked to decide to open one of three doors presented on the screen on each trial. To experimentally manipulate the amount of regret and rejoice, it was indicated behind how many doors (0–3) an electric shock was hidden on each trial. Regret after selecting a door with an electric shock was assumed to be greatest when only one door was associated with the shock in the current trial and associated with no regret when all three doors were paired with a shock. After receiving a shock (or not), subjects rated their experience in terms of pleasantness. In addition, SCR was measured. The behavioral data showed that subjects took the decisions seriously and felt responsible for their decisions. Moreover, SCR data during outcome processing correlated with regret and rejoice. The authors not only identified areas in the OFC where activity correlated only with increasing regret, but also other areas where activity correlated with both increasing regret and rejoice.

Taken together, all three fMRI studies using regret-paradigms of the first type consistently revealed regret-related signal changes in the OFC (Coricelli et al. 2005; Liu et al. 2007; Chandrasekhar et al. 2008; Chua et al. 2009). In support of these findings, choice behavior of orbitofrontal-lesioned patients was not influenced by regret (Camille et al. 2004; Shiv et al. 2005).

Regret induced by the forced choice of the amount of risk

In a second type of paradigm, volunteers chose on each trial how much they were willing to risk in a single gamble. Subsequently, subjects were informed, for each trial, whether they could have won more by risking more or vice versa (Lohrenz et al. 2007; Chiu et al. 2008).

Montague and colleagues employed such a serial investment paradigm. Subjects had to decide on each trial how much they were willing to risk and were subsequently informed whether they could have won or lost more (Fig. 1d, Lohrenz et al. 2007; Fig. 1d, Chiu et al. 2008). More specifically, subjects decided on each trial how many units (0–100) they wanted to invest in a stock market. In cases where the market went up, larger investments would have been the better choice, thus generating a fictive prediction error (best outcome minus actual outcome). In cases where the market dropped, smaller investments would have been better. Behaviorally, the next decision (investment) was predicted by the previous trial and, additionally, by the fictive prediction error over gains (Lohrenz et al. 2007). Both factual and fictive prediction error correlated with activity in overlapping parts of the striatum, but the fictive prediction error was associated with additional activity in more dorsal striatal areas. Interestingly, a group of chronic smokers showed the same pattern of activity, but in contrast to the healthy controls, their behavior was not influenced by the fictive prediction error (Chiu et al. 2008). The OFC showed no regret-related activity.

Relationship between paradigms and regret-related activity

All neuroimaging studies designed to induce counterfactual thinking and regret observed a substantial effect on choice behavior, thus demonstrating the success of the experimental manipulations. However, the neural activity correlating with this behavioral effect differed systematically between studies, insofar as only the more traditional paradigms, where volunteers selected between various options, elicited OFC activity during outcome evaluation (Coricelli et al. 2005; Liu et al. 2007; Chandrasekhar et al. 2008). Moreover, the OFC activity was dissociated in medial and lateral clusters in all of these studies (Table 1; Fig. 2).

Relationship between paradigms and regret-related OFC activity

At first, one could argue that the failure to observe OFC activation in some of the studies is simply due to signal dropout, susceptibility artifacts and geometric distortions in this brain region, which is caused by the adjacent air-filled sinuses (Deichmann et al. 2003; Kringelbach and Rolls 2004; Weiskopf et al. 2007).

However, the observed pattern of OFC activity across studies can be understood in terms of a consequence of differences in the employed paradigms, making a purely technical cause of this differential OFC involvement unlikely. In particular, as in behavioral studies (see above), various characteristics of the first category of paradigms are well suited to increase both counterfactual thinking and the emotional salience of regret. Responsibility and control, which both lead to stronger feelings of regret, were enhanced by the requirement to actively decide between two gambles on each trial. Moreover, computing the optimal decision is more difficult or has greater aversive

Table 1 Regret and rejoice-related activity in the OFC and striatum with the sign of the correlation in parentheses and OFC lesion-based impairment

	Lateral OFC	Central OFC	Medial OFC	Striatum
Camille et al. (2004)			No regret (medial anterior lesion-overlap)	
Coricelli et al. (2005)	Regret (positive), rejoice (negative) [42 42 −18]		Regret (positive), rejoice (negative) [−8 32 −14]	Putamen Regret (positive), rejoice (negative) [−14 0 6]
	Immediate regret (positive) [42 26 −16]		Degree of regret (positive) [−10 30 −12] Cumulative regret [−10 40 −24]	
Chua et al. (2009)	Regret (positive) [−48 21 −12]	Regret (positive) [24 54 −12]	Regret and disappointment (negative), rejoice and elation (positive) [0 54 −6]	Regret and disappointment (negative), rejoice and elation (positive) Ventral striatum [−18 9 −12]
Liu et al. (2007)	Rejoice (positive) [42 56 −8] [−34 56 −12]	Rejoice (positive) [22 42 −14] [−18 44 −18] [24 56 −2]	Regret (positive) [0 56 −8]	Striatum Rejoice (positive) [14 18 −2] [−20 −4 22]
Shiv et al. (2005)			No regret [medial anterior lesion-overlap]	
Chandrasekhar et al. (2008)	Regret (positive), rejoice (positive) [48 21 −18] [51 39 −15] [−48 18 −12]		Regret (positive) [3 54 −24] [−9 60 −6] [0 60 −9]	Putamen Rejoice (positive) [−18 9 −9] [18 9 −9] Caudate Rejoice (positive) [12 15 0]
Lohrenz et al. (2007)				Caudate Fictive prediction error
Chiu et al. (2008)				Caudate Fictive prediction error

Coordinates in MNI space, for the fictive prediction error for space reasons only the structure name is listed, subregions of the striatum as they are labeled in the corresponding article

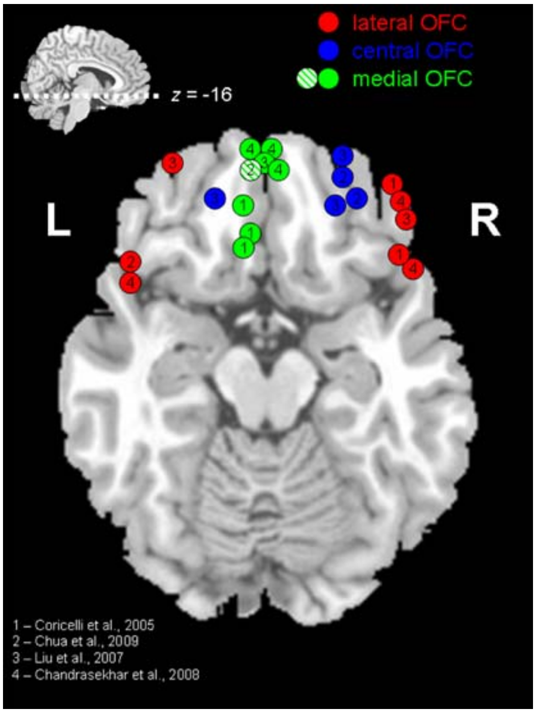

Fig. 2 Localization of activity clusters related to regret and rejoice in the OFC with respect to their laterality. All clusters are presented at a transversal slice at $z = -16$ (MNI space, see Table 1 for the exact coordinates). Due to the projection to this slice some of the clusters seem to be located outside of the OFC which is not the case at their original z-coordinates. Data points are slightly shifted for legibility purposes. ① Coricelli et al. (2005), ② Chua et al. (2009), ③ Liu et al. (2007), ④ Chandrasekhar et al. (2008)

impact, factors that also induce prospective and retrospective regret. The greater salience of the missed outcome, induced by the simultaneous presentation of factual and counterfactual outcomes, is also likely to enhance the feeling of regret. Finally, the affective outcome and desire to change the decision ratings further support the thorough evaluation of both outcomes in terms of counterfactual thinking and regret. Taken together, the characteristics of these tasks are known to augment counterfactual comparisons and the feelings of regret.

On the other hand, in the serial decision tasks one can "correct" a false decision quickly, a factor known to reduce the feeling of regret. That subjects aimed to atone for the disadvantageous decision is evident from the strong influence of regret on the decision in the very next trial. The illusion in the sequential tasks that something can be learned and that the fictive prediction error may indeed be a valid learning signal might explain the more consistent striatal activity (Hunt 2008).

The regret- and rejoice-related activities are distributed across the OFC along its whole x-axis, with prominent, well-defined clusters in its medial and extreme lateral parts which have been observed in all studies (Table 1; Fig. 2). Only two studies observed foci of activity also more centrally in-between these clusters (Liu et al. 2007; Chua et al. 2009). With respect to the y-dimension, the medial and central foci of activity are all located in the anterior OFC where the three most posterior foci ($y = 30$; 32; 40) have been observed in the same study (Coricelli et al. 2005). Only activity in the lateral OFC is distributed along its entire y-axis where most of the studies reported anterior as well as posterior foci of activity for the same counterfactual emotion, i.e., regret or rejoice. The described distribution of regret- and rejoice-related activities along the x- and y-axis of the OFC will be discussed in the following.

Medial–lateral dissociation in the regret-related OFC activity

The medial OFC signal consistently showed a positive correlation with the amount of experienced regret (Fig. 4a, b, Coricelli et al. 2005; Liu et al. 2007; Chandrasekhar et al. 2008). There is only one exception, showing a correlation with rejoice and elation, which is located in the center of the medial activation cluster and will be discussed later (Chua et al. 2009). The pattern of central and lateral OFC activity, on the other hand, was less consistent across studies. Both areas will be summarized as lateral OFC in the following discussion because the two studies observing central OFC activation also found the same effect in the lateral OFC (Liu et al. 2007; Chua et al. 2009). In addition, anatomical data further suggest such a broader functional dissociation along the x-axis of the OFC (Cavada et al. 2000). While lateral OFC was positively correlated with regret in two studies (Coricelli et al. 2005; Chua et al. 2009), it showed the opposite pattern in another study (Liu et al. 2007) and was correlated with both regret and rejoice in a third data set (Chandrasekhar et al. 2008).

However, this heterogeneous structure–function relationship of the lateral OFC across these four studies can be explained by the fact that the three tasks (the first two studies employed nearly identical paradigms) differ with respect to the consequences of the counterfactual comparison on subsequent choice behavior. We will argue therefore in the following that it might be the impact on choice behavior rather than the valence of the counterfactual comparison which correlates with lateral OFC activity. In agreement with this proposal, immediately experienced regret, which activates the lateral OFC, clearly drives subjects in the first study to avoid choosing the selected gamble again (Coricelli et al. 2005). In the other study using a similar paradigm, participants explicitly expressed a stronger desire to change their choice after experiencing regret than after disappointment (Chua et al. 2009). However, the relationship between outcome evaluation and choice behavior on the subsequent trial is more complex in the other two tasks. In the study by Liu and colleagues, subjects experienced rejoice after choosing the safe bank when the bet led to a loss or after choosing the bet that led to a gain (Liu et al. 2007). We conducted a reanalysis of the behavioral data with respect to the influence of rejoice and regret on the choice behavior in the next trial (Fig. 3). A regret/rejoice × stay/switch ANOVA with proportion of all responses as dependent variable showed that subjects switched their strategy significantly more often after rejoice [$F(1,14) = 19.4$, MSE = 0.007, $P < 0.001$, post hoc Tukey HSD showing a significant higher switch rate after rejoice than after regret, $P < 0.001$]. This choice behavior can be explained by the Gambler's fallacy, i.e., the phenomenon that humans expect a negative autocorrelation in random sequences. That is, an odd number is expected to be followed by an even number (Tversky and Kahneman 1974; Ayton and Fischer 2004; Burns and Corpus 2004; Sundali and Croson 2006). Therefore, a won bet, which is accompanied by rejoice, drives subjects to switch to the safe option on the next trial, because they expect that the next bet is more likely to lead to a loss. And vice versa, when subjects had chosen the safe bank and the bet was lost, subjects expect that the next bet will win, and are thus more likely to switch to the bet on the next trial.

In the last study (Chandrasekhar et al. 2008), the relationship between the result of the counterfactual comparison and choice behavior is even more complex, because it might be the result of a combination of both aforementioned behavioral effects, regret avoidance and gambler's fallacy. Higher rejoice due to selecting the only door not

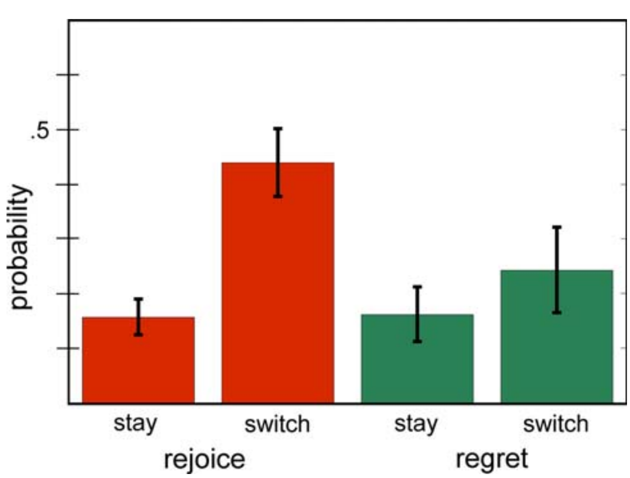

Fig. 3 Behavioral results of (Liu et al. 2007) reanalyzed according to the factors regret/rejoice and stay/switch (mean ± standard error or the mean). Significantly more, i.e., nearly twice as many, switches after rejoice than after regret

associated with a shock prompts volunteers to select another door in the next trial due to the Gambler's fallacy ("This cannot be the lucky door again."). At the same time, regret prompts volunteers to (irrationally) avoid this door on the next trial. Therefore, both stronger rejoice and regret putatively lead to consequences for choice behavior.

Although this interpretation of the processes triggered by regret and rejoice in the last study is speculative, it nonetheless provides a hypothesis to account for the differential response profile of the lateral OFC in these tasks. According to this hypothesis, the lateral OFC activation is not dependent on the valence of the counterfactual comparison but related to its consequences for the subsequent choice. In agreement with this interpretation, the paradigm not leading to lateral OFC activation (Lohrenz et al. 2007; Chiu et al. 2008), did not provide alternative options to switch to, but rather entailed more subtle changes in the degree of risk-taking.

Anterior–posterior dissociation in the regret-related OFC activity

As stated above, the medial and central foci of regret- and rejoice-related activities are located in their majority clearly in the anterior OFC (Fig. 2; Table 1). The most posterior foci ($y = 30; 32; 40$), which have been observed in a study using a traditional regret-paradigm, also exhibit activity correlated with regret (Coricelli et al. 2005). The only study which found a different effect, i.e., a correlation of activity with rejoice and elation, observed this effect in the center of the anterior medial OFC cluster. Taken together, there seems to be no anterior–posterior dissociation in the central and medial OFC activity.

On the other hand, the lateral OFC activity is located in anterior and posterior clusters. However, most studies reported anterior and posterior OFC activity in the same contrast,.i.e., correlated with the same counterfactual emotion. Thus, the activation pattern in the lateral OFC also does not suggest an anterior–posterior dissociation.

Implications for the processes of counterfactual thinking

Counterfactual comparisons influence subsequent choice behavior, but this effect is only associated with OFC activation in paradigms of the first type, i.e., in which choices are between two risky gambles. This suggests that distinct neural mechanisms may contribute to this behavioral effect. Striatal activity is consistently found to correlate with counterfactual comparisons, even in different striatal subregions, i.e., the ventral striatum, putamen, and caudate, and this effect can take the form of both an activation and deactivation. The striatal signal can thus be understood as a fictive prediction error corresponding to the real prediction error, by which behavior is adjusted according to experienced (counterfactual) outcomes. Such a fictive prediction error may thus be sufficient to account for the observed behavioral effects. Also, in the behavioral literature and in neuroimaging studies on (reversal) learning, some theorists treated experienced counterfactuals as a simple learning signal that improved their computational models (Hart and Mas-Collel 2003; Hampton et al. 2006; Ert and Erev 2007; Hampton et al. 2007; Glascher et al. 2008; Marchiori and Warglien 2008; Boorman et al. 2009). At the same time, the paradigms of the first type that enhance counterfactual thinking and emotions and, moreover, make anticipatory regret more likely, are characterized by additional medial and lateral OFC activity. In agreement with the additional activation of this important "second-level" reward processing area (Coricelli et al. 2007), other regret-theorists emphasized the relevance of the feeling of regret for the behavioral impact of counterfactual comparisons (Mellers et al. 1999; Zeelenberg and Pieters 2007). Taken together, it seems that a behavioral impact of counterfactual comparisons is possible without experiencing or anticipating a strong affective impact of that counterfactual comparison. On the other hand, specific experimental settings are likely to enhance the affective component of counterfactual thinking as known from the behavioral regret literature. Whether such an affective component enhances the behavioral effect of counterfactuals, all other factors being equal, is an open question.

The orbitofrontal cortex and regret

So far, based on the observed activation patterns related to fictive prediction errors across studies, inferences have been drawn regarding the computations potentially carried out in the OFC and the striatum. In particular, the contribution of the OFC in some paradigms may reflect increased processing of counterfactual comparisons, while the striatal signal may reflect an interpretation of counterfactual comparisons as learning signals. Moreover, the medial–lateral distribution of activation clusters in the OFC is likely to be of functional relevance and also the anterior focus of regret-related activity might be functionally meaningful. Whereas medial OFC activity typically correlates positively with regret, the functional properties of the lateral OFC response profile are more complex. In the following, we will relate these findings to the literature on OFC function not only with the intention to shed new light on the regret-related OFC activation patterns, but also to add new evidence to the ongoing debate about the role of the OFC in decision-making.

Subdivision of the OFC

Anatomical subdivision of the OFC

Regret studies point towards a functional medial–lateral dissociation of the OFC, which is in agreement with anatomical as well as functional data. The OFC is a large area, encompassing multiple gyri, and is classically divided into five Brodman areas, i.e., BA 10, 11, 47/12, 13, and 14 with a highly heterogeneous cytoarchitecture (Carmichael and Price 1994; Ongur et al. 2003). However, the dissociations observed in neurophysiological studies do not seem to follow these cytoarchitectonical borders. A broader subdivision may therefore better account for its functional specialization and several alternative but not exclusive anatomical parcellations of the OFC have been proposed, e.g., anterior–posterior as well as medial–lateral subdivision (Hof et al. 1995; Ongur and Price 2000; Barbas 2007a, b).

Of particular relevance for understanding the regret-related medial–lateral dissociation might be the finding that OFC connectivity also follows a medial–lateral division (Cavada et al. 2000). Probabilistic diffusion tractography revealed that the amygdala and the ventral striatum are more strongly connected to the medial OFC, whereas the dorsal striatum is linked to the entire OFC in humans and monkeys (Croxson et al. 2005). It should be noted that the stronger amygdala–medial OFC connectivity is contradictory to the findings using more traditional tracer methods in non-human primates (Carmichael and Price 1995). The differential connections of the striatal subregions to medial and lateral OFC was confirmed in another diffusion tensor imaging study (Cohen et al. 2009). Taken together, the anatomy of the OFC makes a functional parcellation, in particular, a medial–lateral dissociation of this area quite likely. However, the alternatively proposed anatomical anterior–posterior subdivision (Barbas 2007a, b) might also inform the interpretation of regret-related activity in the OFC even if this activity seems not to be functionally dissociated along the y-axis.

Functional subdivision of the OFC

The functional medial–lateral OFC subdivision was proposed based on the observation that positive evaluation of stimuli often leads to a medial OFC activity increase, whereas the processing of negative-evaluated stimuli are correlated with lateral OFC activity (O'Doherty 2007). Several studies found such a positive correlation between the pleasantness or acquired value of a stimulus and medial OFC activity (yielding deactivations for unpleasant stimuli), while the reverse pattern was observed in lateral OFC areas (O'Doherty et al. 2001; Anderson et al. 2003;

Kringelbach and Rolls 2003; O'Doherty et al. 2003b; Rolls et al. 2003; Elliott et al. 2008; Hare et al. 2008). In one elegant study, the valuation of a primary reinforcer (chocolate) changed due to feeding to satiety which was accompanied by decreasing activity in medial and increasing activity in lateral OFC (Small et al. 2001). More evidence for this functional medial–lateral dissociation comes from the observation that punishment avoidance activates medial OFC, while punishment activates the lateral OFC (Kim et al. 2006). However, there are also exceptions to this straightforward pattern (O'Doherty 2007) sometimes using relatively similar stimuli, e.g., chocolate consumption after feeding to satiety (Smeets et al. 2006).

A recent extensive meta-analysis investigated the regional specialization within the OFC in a systematic fashion (Kringelbach and Rolls 2004) and revealed three clusters: an anterior medial OFC cluster related to the pleasantness or hedonic value of a stimulus, a posterior central OFC cluster related to motivation-independent reinforcer representations, and an anterior lateral OFC cluster related to the representation of punishers. Thus this meta-analysis supports not only the above summarized functional medial–lateral dissociation but also a posterior–anterior gradient. According to this analysis higher level processing of reinforcers might be computed more anterior in the OFC (center of the anterior cluster $y = 41$). For example, subjective pleasantness ratings or the valuation of money as a secondary reinforcer are represented more anterior, whereas activity associated with the valuation of simple reinforcers, e.g., odors or taste, is located more posterior in the OFC. Such a hierarchical processing would be also supported by the anatomical data (Barbas 2007a, b).

An alternative but not necessarily exclusive perspective on the division within the OFC suggested that medial areas are involved in decoding and monitoring of reward values of reinforcers, whereas the lateral OFC evaluates punishers, which, when detected, may lead to a change in current behavior (Kringelbach and Rolls 2004). Support for this proposal comes also from studies on reversal learning, in which OFC-lesioned animals and humans are impaired. The studies of O'Doherty and colleagues consistently found activity related to the valuation of stimuli in medial OFC, whereas lateral OFC activity was correlated with stimulus value only in cases where this led to a behavioral adaptation, e.g., during reversal (O'Doherty et al. 2003a; Hampton et al. 2006, 2007; Glascher et al. 2008). Another recent study aimed explicitly to test the hypothesis that the medial–lateral subdivision of the OFC is not based on the valence but on the steadiness of the outcome by comparing the original and the inverted version of the Iowa Gambling Task (Windmann et al. 2006). While activity in the medial OFC correlated with reward evaluation in both versions of the task, activity in the lateral OFC depended on the context and signaled preparation for response shifts. Finally, a similar medial–lateral division of labor within the OFC and the adjacent ventral medial prefrontal cortex (vmPFC) have been observed in a recent study where subjects had to choose between two gambles but were informed only about the outcome of the chosen gamble (Boorman et al. 2009). The value of the chosen option was represented again by medial OFC/vmPFC activity. Crucially, subjects generated also hypotheses how likely the unchosen action would have been rewarded. Not only did the reward probability of the unchosen option correlate with lateral OFC activity, but also the likelihood to switch to the alternative action in the next trial.

Taken together, there is anatomical and functional evidence for a division of labor within the OFC. In particular, a medial–lateral as well as an anterior–posterior functional dissociation is supported by various studies. This converging evidence suggests that the observed segregation of regret-related activity into a medial and a lateral cluster is of functional significance. In addition, the fact that the majority of counterfactual-related activity was found in the anterior OFC might be of interest in the light of these findings. Next, we will therefore discuss the medial and lateral clusters of regret-related activity separately and will comment also on its focus in the anterior OFC.

Lateral OFC activity in decision-making and regret

As summarized in the previous paragraph, the lateral OFC has been associated with evaluating punishment, but recently more specifically with evaluating punishing stimuli that lead to behavioral consequences. Also, several other studies, apart from those investigating reversal learning, point towards the possibility that lateral OFC activity is associated with evaluating stimuli that lead to behavioral consequences, for example, lateral OFC activation was correlated with the purchase decision after the striatum coded the value of a product (Knutson and Bossaerts 2007). Specifically difficult choices (e.g., from a large restaurant menu) also activated the lateral OFC (Arana et al. 2003).

Thus, the regret-related lateral OFC activity may be associated with an adaptation of behavior. In the study by Coricelli et al., immediate regret was associated with increased lateral OFC activity and also with subsequent avoidance of the regrettable gamble (Coricelli et al. 2005). In the study using a very similar design, participants explicitly expressed their desire to change their decision after experiencing regret (Chua et al. 2009). Liu et al. reported increased lateral OFC activity associated with rejoice (Liu et al. 2007). However, our reanalysis of their behavioral data also revealed that, in this study, rejoice led to a switch to the other gamble significantly more often than regret. Lateral OFC activity is therefore also associated with avoidance of the previous gamble. Finally, Chandrasekhar et al. observed increased lateral OFC activity correlated with both higher regret and higher rejoice (Chandrasekhar et al. 2008). As argued above, both outcomes might be associated with avoiding the door opened in the particular trial in the next decision. Taken together, activity in the lateral OFC is associated with behavioral consequences in regret studies in terms of switching to a different decision option in the subsequent trials.

In this line of reasoning, the activity in the lateral OFC is not rigidly associated with reward or punishment per se, but depends on the context and its behavioral relevance. In agreement with this notion, such a context-dependent OFC activation during outcome evaluation has previously been reported. Both the subjectively more unlikely win after a series of wins and a loss after a series of losses in a guessing task activated the lateral OFC which can be interpreted as a prediction error due to the Gambler's fallacy (Elliott et al. 2000). In analogy to studies on regret, unlikely series of the same outcome are emotionally more salient and imply a higher significance of the next choice, either to finally interrupt the series of losses or to avoid the expected end of serial wins. In agreement with these findings and the findings in studies on regret, the lateral OFC also computes the contextual relevance of emotional information during decision-making, which leads to advantageous and disadvantageous decisions (Beer et al. 2006). Finally, studies using pleasant and unpleasant visual, olfactory, auditory, and verbal stimuli all observed lateral OFC activation, contrary to the aforementioned lateral OFC cluster for unpleasant stimuli (Royet et al. 2000; Lewis et al. 2007).

Thus, in contrast to the earlier proposal (Kringelbach and Rolls 2004), lateral OFC activity has been observed not only in response to stimuli with negative, but also with positive value. Moreover, this activity has been linked to the salience of the emotion, independent of its valence, and also to its relevance for choice behavior, as, for example, during reversal learning (Hampton et al. 2006, 2007; Glascher et al. 2008; Boorman et al. 2009). This pattern of findings fits well with the activity observed in regret studies, where lateral OFC activity is associated not with the value of the outcome, i.e., regret or rejoice, but with a behavioral switch to the alternative gamble. However, with respect to the anterior–posterior distribution of regret-related activity there appears to be no obvious functional significance because foci of activity in both parts of the OFC were often elicited by the same contrast.

Medial OFC in decision-making and regret

The role of the medial OFC in decision-making was most frequently explored with respect to coding and representing the subjective values of reinforcers. Such studies consistently report a positive correlation between pleasantness or subjective value and OFC activity, which contrasts with the negative correlation, observed with rejoice in nearly all of the studies (Fig. 4). Therefore, a straightforward valuation of the outcome cannot account for the observed medial OFC activity in most of the regret-related studies. The only exception is the study by Chua et al., who found indeed a positive correlation of medial OFC (and striatal) activity with rejoice and elation (Chua et al. 2009). However, the authors did not report the activity for the four conditions (elation, rejoice, disappointment, regret) separately. Therefore, it is unclear how the two negative and the two positive conditions might contribute differently to the reported mean difference. The effect of elation versus disappointment is in agreement with the often described positive correlation with the value of an outcome. Moreover, it is located as predicted by the posterior–anterior gradient of the processing hierarchy in the anterior OFC (Kringelbach and Rolls 2004).

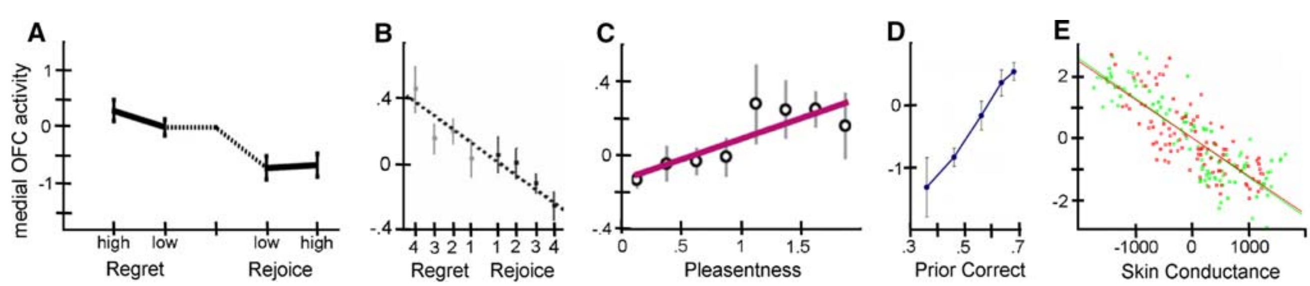

Fig. 4 Activity (*y*-axis, parameter estimates in arbitrary units) in the medial OFC: **a** and **b** regret-related activity increase, *x*-axis: objective amount of regret as indexed by the difference between factual and counterfactual outcome (Coricelli et al. 2005; Chandrasekhar et al. 2008), **c** pleasantness-related activity increase, *x*-axis: pleasantness ratings (Rolls et al. 2008), **d** successful reversal learning-related activity increase, *x*-axis: prior correct signal from the reversal learning state-based model (Hampton et al. 2006). **e** Correlation of OFC activity with SCR, *x*-axis: skin-conductance level in mV (Nagai et al. 2004) (modified with permission)

However, the simple notion that the medial OFC merely represents stimulus values in a linear fashion has been challenged by some studies, which demonstrate activation of this area (Breiter et al. 2001; Elliott et al. 2003), and even single neurons therein (Hosokawa et al. 2007), to both the highest and the lowest outcomes. Moreover, recent evidence indicates that the medial OFC computes complex valuation processes, i.e., is involved in integrative, complex, multi-attribute valuation processes (Wallis 2007). For instance, the medial OFC responds more to immediate than delayed rewards, integrates the trade-offs between amount and preference of a reward, represents the economic value of a reward independently of presented alternatives, and is needed for multi-attribute decisions (Kheramin et al. 2002; Mobini et al. 2002; McClure et al. 2004, 2007; Roesch and Olson 2005; Fellows 2006; Padoa-Schioppa and Assad 2006, 2008; Roesch et al. 2006; Rudebeck et al. 2006). Due to their counterfactual nature, regret and rejoice are complex evaluation processes and the regret-related activity in the anterior medial OFC would be in agreement with the proposed processing hierarchy (Kringelbach and Rolls 2004). Yet during complex integrative decision-making, medial OFC is positively correlated with the abstract value of a stimulus, which contrasts with the findings of medial OFC activity during outcome evaluation in most regret studies.

However, regret as elicited by the paradigms associated with OFC activation is not only an integrative multi-attribute evaluation, but it is more specifically based on enhanced counterfactual comparisons and emotions. The medial OFC has been linked to both types of processes. In the following, we will review the role of the medial OFC in these processes that are crucial for the emotion *regret* and relate these findings to regret-related activity in the medial OFC. When evaluating the relevance of the various studies it should be kept in mind that lesion and electrophysiological studies do not strictly dissociate subareas of the OFC, e.g., electrodes in the cited studies were often placed rather posterior centro-medially (substantially more posterior than the rare regret-related central activity). Finally, we will refer to the recently highlighted role of the medial OFC in instrumental conditioning and show some at first sight surprising parallels between the processes of instrumental conditioning and outcome evaluation via counterfactual comparisons.

The OFC in counterfactual thinking

An important perspective on the role of the OFC in regret focuses on its involvement in counterfactual thinking, comparison and evaluation. Since counterfactual thinking relies crucially on executive control, it was hypothesized that prefrontal areas are involved (Baird and Fugelsang 2004; Epstude and Roese 2008). Indeed, a reduction in spontaneous counterfactual thinking was observed in dorsolateral prefrontal as well as OFC-lesioned patients (Gomez Beldarrain et al. 2005).

Counterfactual outcome evaluation: disappointment and relief Counterfactual comparisons of outcomes are not only part of regret and rejoice but also play a role in disappointment and elation, i.e., upward and downward counterfactuals (Mellers et al. 1999; Roese 1999). In both cases, the subjective value of an outcome is influenced by counterfactual comparisons with alternative outcomes, the outcome of the unchosen gamble (regret/rejoice) or of the alternative state of the world (disappointment/elation). Studies involving the latter type of counterfactuals aimed to verify the OFC role in subjective valuation of stimuli by holding the objective value of a stimulus constant and varying its relative value by changing the context (i.e., the alternative outcome).

The first study on this context dependency was conducted in monkeys by Tremblay and Schultz (1999) who found that the firing rate of centro-medial OFC neurons correlated with the relative value of a food reward, depending on the value of alternative possible rewards. A recent fMRI study applied this experimental design to humans and found greater medial OFC activity for relative gains, i.e., elation, but lateral OFC for relative losses, i.e., disappointment (Elliott et al. 2008). Other studies reported medial OFC activity to be correlated with elation, downward counterfactuals, when subjects got to know that they chose the relatively better option or paid less for a product compared to its official price (Sailer et al. 2007; Weber et al. 2007).

Counterfactual option evaluation Counterfactual comparisons can be crucial not only in outcome, but also in option evaluation. For instance, the framing effect was investigated in a paradigm also involving the counterfactual comparison between choosing a safe bank and a risky gamble under a gain and a loss frame without learning about the outcome of the decision (De Martino et al. 2006). Subjects less susceptible to the framing effect showed increased medial OFC activity, possibly because they focused more on the counterfactual comparison between the two choices than on the frame. Also, loss aversion was assessed using counterfactual comparisons between two gambles (again with no outcome presentation). Subjects had to indicate whether or not to accept mixed gambles varying in the potential gains and losses (Tom et al. 2007). The more money could have been lost, i.e., the smaller the counterfactual value of the option, the stronger the deactivation of the OFC and vice versa. Another imaging study involving counterfactual thinking showed that when subjects consider items on a menu, the medial OFC is activated (Arana et al. 2003). OFC-lesioned monkeys failed in a decision task only when they relied on an internal representation of the potential outcomes, whereas trial and error learning was almost normal (Izquierdo et al. 2004). Anticipatory activity in the medial OFC was greater in trials with the relatively better outcome structure, whereas the lateral OFC showed the opposite pattern (Ursu and Carter 2005). However, a study on risk assessment observed activity for a relative loss in the insula rather than the OFC, in cases were the alternative option would have been the better choice (Kuhnen and Knutson 2005).

Finally, the acquisition of a reversal learning set involves counterfactual thinking (Murray and Izquierdo 2007). The relevance of counterfactual comparisons for reversal learning is highlighted by the implementation of the fictive prediction error in computational models. Higher medial OFC activity corresponds to higher correctness of the prior activity which is based also on successful counterfactual comparisons (Hampton et al. 2006, 2007; Glascher et al. 2008).

Regret and counterfactual thinking These studies report an involvement of the medial OFC in counterfactual thinking and more specifically a positive correlation between medial OFC activity and positive counterfactuals. This resembles somehow the positive correlation of medial OFC activity with (complex) evaluation but, again, shows the opposite sign as the reported negative correlations with rejoice. However, to experience regret, both the factual as well as the counterfactual outcome has to be evaluated. As a possible explanation, Wallis (2007) speculated that the OFC encodes a value representation of the outcome and keeps it in working memory for the counterfactual comparison. Following this reasoning, one could speculate that the increased activity in the medial OFC associated with regret is caused by the value of the better but missed opportunity. However, this interpretation seems rather unlikely because the factual outcome also has to be evaluated in parallel and in the majority of cases is a negative one leading to OFC deactivation.

The medial OFC in emotional processing and arousal

Many studies suggest a role of the OFC, together with the amygdala, in emotional processing (Murray and Izquierdo 2007; Rempel-Clower 2007). OFC lesions result in the absence of the typical SCR to negative valenced pictures (Damasio et al. 1990). In agreement with these findings, negative pictures (without choice requirements) activate the medial OFC (Northoff et al. 2000; Glascher et al. 2007). The medial OFC is also activated in emotional compared to cognitive perspective taking (Hynes et al. 2006). Rolls explained emotions as states elicited by instrumental reinforcers, i.e., reward and punishment, which are made explicit in terms of neuronal firing rates in the OFC (Rolls 2005). Based on this hypothesis, it was recently stated that the OFC might be specialized for simple emotions such as fear or anger, due to its role in representing the value of reinforcers (Rudebeck et al. 2008). In addition, its was proposed that the medial OFC is involved in top–down influences on object perception by providing a early 'affective prediction' about the subjective relevance of the perceived object (Barrett and Bar 2009).

Another perspective on the role of the OFC in emotional processing was developed based on the somatic marker hypothesis by Damasio (1996). According to this theory, the OFC is involved in the mapping of the autonomic state of the body (Critchley 2005). Of particular interest in the context of regret is that several studies reported a correlation of medial as well as lateral OFC activity with simultaneously recorded SCR responses (Fig. 4e, Critchley et al. 2000, 2001; Patterson et al. 2002; Nagai et al. 2004). However, the lateral OFC activity foci reported in some of these studies might be attributable to the employed task (i.e., gambling).

The involvement of the medial OFC in processing negative stimuli as well as its relationship to arousal is consistent with the observed positive correlation with regret. Regret is known to represent a strong negative emotion (Zeelenberg and Pieters 2007) which is also reflected in the emotional ratings of regret studies (Camille et al. 2004; Coricelli et al. 2005; Chandrasekhar et al. 2008; Chua et al. 2009). Moreover, these studies also measured correlations between SCR and regret, similar to the reports on a role of the medial OFC in mapping of the autonomic state. Therefore, the medial OFC activity in regret studies possibly reflects the counterfactual negative emotions and an associated increase in arousal.

The medial OFC in instrumental conditioning

The medial OFC is involved especially in the early phase of acquisition and extinction of an association in classical conditioning (Gottfried and Dolan 2004; Milad et al. 2005). Furthermore, devaluation experiments have shown that the amygdala is involved in associating a cue with the value of a paired outcome (REF). However, the OFC is crucial for keeping this association in working memory and to update it when the value changes due to devaluation (Pickens et al. 2003). These findings are in line with the proposal of Wallis (2007) regarding the role of the medial OFC in keeping values in working memory for counterfactual comparisons.

Lesions of the OFC but not of the amygdala impair extinction in instrumental conditioning (Izquierdo and Murray 2005). Instrumental conditioning is based on two different processes computed in distinct brain areas, i.e., goal-directed learning of associations between responses and outcomes and habit learning of associations between stimuli and responses. Devaluation of outcomes in instrumental conditioning showed that the medial OFC is critical involved in the first process, associating a response with its incentive value of the outcome (Valentin et al. 2007; Finger et al. 2008).

The sequential structure of regret-paradigms used in fMRI studies, where subjects have to choose between two gambles, share characteristics with instrumental conditioning. Subjects have to choose (sequentially) one of two responses and afterwards experience the value of the associated outcome. Crucially, the value of the outcome depends on the counterfactual comparison and over the course of the experiment subjects learn to avoid responses associated with counterfactually “devalued” outcomes (Coricelli et al. 2005; Shiv et al. 2005). Following this interpretation, the medial OFC activity in regret-paradigms would be signaling changes in the value of gambles due to counterfactual comparisons somewhat paralleling its role in coding the changes in the incentive value of a response during the early phases of instrumental conditioning and devaluation.

Conclusions

Relating the differences in the two types of regret-paradigms to the selective involvement of the OFC suggests that the consistently observed striatal activity reflects a fictive prediction error which is sufficient for eliciting the behavioral effect of counterfactual thinking. The OFC, on the other hand, is involved in paradigms which increase counterfactual comparisons and emotions and, moreover, may represent learning the associations between choosing a particular gamble and the corresponding outcome.

The pattern of OFC activity associated with regret and rejoice across these studies adds further evidence to the hypothesis that the OFC is not only anatomically but also functionally subdivided (Kringelbach and Rolls 2004; O’Doherty 2007). The medial OFC is consistently negatively correlated with rejoice which makes a role in (counterfactual) outcome evaluation and other kinds of more complex valuation processes unlikely as these have been shown to result in a positive relationship between subjective value and medial OFC activity. The pattern of regret-related activity would be more consistent with the role of the medial OFC in emotional processing and arousal. In addition, some parallels exist between choosing one of two responses in regret-paradigms and instrumental operant conditioning where especially goal-directed learning of associations between a response and its incentive activates the medial OFC.

The activity in the lateral OFC, on the other hand, can be best conceptualized in terms of signaling behavioral consequences for the subsequent decisions in response to counterfactual outcome evaluation as it has been suggested by studies on reversal learning. In addition, regret studies show that lateral OFC activity is not necessarily bound to the valence of the outcome, i.e., reward or punishment, but rather to its behavioral significance. Taken together, as intended by the current review, what is known about medial and lateral OFC function supports a better understanding of regret-related activity patterns and also vice versa the regret-related activity OFC patterns adds evidence to existing theories about OFC functioning.

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