and Ipl1 moves from kinetochores to spindle microtubules shortly after the initiation of anaphase (5, 27, 28). Microtubule attachment to kinetochores in anaphase may be stabilized by the loss of Ipl1, helping to keep the checkpoint inactive. However, Ipl1 mutants respond to treatment with nocodazole, whereas anaphase-arrested cells do not (Fig. 1A), which suggests that additional factors, such as Mps1 degradation, have turned off the checkpoint in anaphase (29). The organization of other “chromosomal passenger proteins” also changes as cells enter anaphase (30), so as spindle microtubule dynamics (31), and these factors may also influence checkpoint behavior in anaphase. Finally, the checkpoint destabilizes Cdc20, as well as inhibits its activity, which reinforces the mutual antagonism between the checkpoint and APC^Cdc20.

We have presented evidence for a mechanism that inactivates the spindle checkpoint as yeast cells enter anaphase. When mitosis starts, the APC is off, the checkpoint is on, and checkpoint proteins are stable. As long as one chromosome has not aligned, the checkpoint inhibits the APC. When this chromosome bioriented, a threshold is crossed, the APC becomes active, cells enter anaphase, and the destruction of Mps1 (and possibly other checkpoint proteins) permanently inactivates the checkpoint. The opposing activities of the checkpoint and the APC let cells switch rapidly between prometaphase, when they can sensitively monitor chromosome alignment, and anaphase, when they are irreversibly committed to entering the next cell cycle, despite the lack of tension at the kinetochores.

References and Notes


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Frames, Biases, and Rational Decision-Making in the Human Brain

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Human choices are remarkably susceptible to the manner in which options are presented. This so-called “framing effect” represents a striking violation of standard economic accounts of human rationality, although its underlying neurobiology is not understood. We found that the framing effect was specifically associated with amygdala activity, suggesting a key role for an emotional system (1), but its underlying neurobiology is not understood. We investigated the neurobiological basis of the framing effect by means of functional magnetic resonance imaging (fMRI) and a novel financial decision-making task. Participants (20 university students or graduates) received a message indicating the amount of money that they would initially receive in that trial (e.g., “You receive £50”), Subjects then had to choose between a “sure” option and a “gamble” option presented in the context of two different frames. The “sure” option was formulated as either the amount of money retained from the initial amount (e.g., keep £20 of the £50; “Gain” frame) or as the amount of money lost from the initial amount (e.g., lose £30 of the £50; “Loss” frame). The “gamble” option was identical in both frames and was represented as a pie chart depicting the probability of winning or losing (Fig. 1) (14).

The behavioral results indicated that subjects’ decisions were significantly affected by our framing manipulation, with a marked difference in choices between the two frames (Fig. 2A). Specifically, and in accordance with predictions arising from prospect theory, subjects were risk-averse in the Gain frame, tending to choose the sure option over the gamble option written by an emotional system (12, 13). However, despite the substantial role of the framing effect in influencing human decision-making, the underlying neurobiological basis is not understood.

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The financial decision-making task. At the beginning of each trial, participants were shown a message indicating the starting amount of money that they would receive (e.g., “You receive £50”) (duration 2 s). Subjects were instructed that they would not be able to retain the whole of this initial amount, but would next have to choose between a sure option and a gamble option (4 s). The sure option was presented in the Gain frame trials (A) as an amount of money retained from the starting amount (e.g., keep £20 of the £50) and in the Loss frame trials (B) as an amount of money lost from the starting amount (e.g., lose £30 of the £50). The gamble option was represented as a pie chart depicting the probability of winning (green) or losing (red) all of the starting money. The expected outcomes of the gamble and sure options were equivalent. Gain frame trials were intermixed pseudo-randomly with Loss frame trials. No feedback concerning trial outcomes was given during the experiment.

Fig. 2. Behavioral results. (A) Percentages of trials in which subjects chose the gamble option in the Gain frame and the Loss frame. Subjects showed a significant increase in the percentage of trials in which the gamble option was chosen in the Loss frame with respect to the Gain frame [61.6% > 42.9% (P < 0.005, t6 = 3.31)]. This effect of frame was consistently expressed across different probabilities and starting amounts (fig. S1).

Reaction times for decisions were not affected by frame [Gain frame, 1895 ms; Loss frame, 1884 ms (P > 0.1)]; this result provides evidence that difficulty was well matched between the two frames. Moreover, subjects performed highly accurately on “catch” trials (14) (fig. S2) where the expected outcomes of the sure and gamble options were unbalanced, indicating their continued engagement with the task throughout the experiment. Despite the marked though variable impact of the frame on subjects’ choice behavior (Fig. 2B), the majority (16/20) of subjects seemed unaware of any biasing effect when specifically questioned in a debriefing session that followed the experiment.

Subjects performed the behavioral task inside an fMRI scanner, allowing us to obtain continuous measures of regional brain activity. The subjects’ individual decisions during the entire fMRI experiment were recorded and used to construct four regressors of interest: sure decisions in the Gain frame (Gsure), gamble decisions in the Gain frame (Ggamble), sure decisions in the Loss frame (Lsure), and gamble decisions in the Loss frame (Lgamble). Given that the frame effect relates to subjects’ asymmetrical pattern of decisions across frames, the key experimental contrast of interest is the interaction between the decision to gamble (or not) and the valence of the frame: [(Gsure + Lgamble) - (Ggamble + Lsure)]. It is noteworthy that this interaction contrast is balanced with respect to both decision type and frame valence. Consequently, we could identify brain areas that were more active when subjects chose in accordance with the frame effect (i.e., Gsure + Lgamble), as opposed to when their decisions ran counter to their general behavioral tendency (Ggamble + Lsure). This contrast revealed significant activation in the bilateral amygdala (Fig. 3, A and B). To ensure that this activation in the amygdala was not being driven by a significant effect in one frame alone (e.g., Loss frame), we conducted an independent analysis for each frame. This confirmed that robust activation in the amygdala was equally observed for simple effects of decision type (sure or gamble) in each frame separately. Thus, amygdala activation was...
significantly greater when subjects decided to choose the sure option in the Gain frame \([G_{\text{sure}} - G_{\text{gambles}}]\) [Montreal Neurological Institute (MNI) space coordinates \((x, y, z)\) 18, –4, –24; \(Z\) score = 4.0], and the gamble option in the Loss frame \([L_{\text{gambles}} - L_{\text{sure}}]\) [MNI space coordinates –16, 0, –26; \(Z\) score = 3.80; 12, –2, –22; \(Z\) score = 4.67], in keeping with a central role in mediating the frame effect.

A different pattern of brain activation was identified when subjects made decisions that ran counter to their general behavioral tendency. In this reverse interaction contrast \([\{(G_{\text{gambles}} + L_{\text{sure}}) - (G_{\text{sure}} + L_{\text{gambles}})\}\] we observed enhanced activity in the anterior cingulate cortex (ACC) (Fig. 3, C and D) and to a lesser extent in the bilateral dorsolateral prefrontal cortex at an uncorrected threshold of \(P < 0.005\); \(\text{fig. S3}\) when subjects chose the gamble option in the Gain frame and the sure option in the Loss frame.

In light of the substantial intersubject variability in behavioral susceptibility to the frame, we next identified subject-specific differences in neural activity associated with their decision bias (that is, the decision × frame interaction) (Fig. 2A). Using the overall susceptibility of each subject to the frame manipulation as a between-subjects statistical regressor, operationalized as a “rationality index” \((14)\), we found a significant correlation between decreased susceptibility to the framing effect and enhanced activity in the orbital and medial prefrontal cortex (OMPFC), specifically in the right orbitofrontal cortex (R-OFC; \(r = 0.8, P < 0.001\)) and the ventromedial prefrontal cortex (VMPFC; \(r = 0.75, P < 0.001\)) (Fig. 4). In summary, those subjects who acted more rationally exhibited greater activation in OMPFC associated with the frame effect.

Our data provide a neurobiological account of the framing effect, both within and across individuals. Increased activation in the amygdala was associated with subjects’ tendency to be risk-averse in the Gain frame and risk-seeking in the Loss frame, supporting the hypothesis that the framing effect is driven by an affect heuristic underwritten by an emotional system. The amygdala plays a key role in value-related prediction and learning, both for negative (aversive) and positive (appetitive) outcomes (15–17). Furthermore, in simple instrumental decision-making tasks in animals, the amygdala appears to mediate decision biases that come from value-related predictions (18). In humans, the amygdala is also implicated in the detection of emotionally relevant information present in contextual and social emotional cues (19). It was previously shown that activation in the amygdala during the passive viewing of surprised faces is significantly modulated by the valence of preceding verbal contextual information (20). Our data extend the role of the amygdala to include processing the type of contextual positive or negative emotional information communicated by the frame in the context of a decision-making task.

In our study, activation of the amygdala was driven by the combination of a subject’s decision and the frame in which it took place, rather than by the valence of the frame per se. Consequently, our findings indicate that frame-related
valence information is incorporated into the relative assessment of options to exert control over the apparent risk sensitivity of individual decisions. The observation that the frame has such a pervasive impact on complex decision-making supports an emerging role for the amygdala in decision-making (21, 22).

When subjects’ choices ran counter to their general behavioral tendency, there was enhanced activity in the ACC. This suggests an opponency between two neural systems, with ACC activation consistent with the detection of conflict between predominantly “analytic” response tendencies and a more “emotional” amygdala-based system (23, 24).

Previous descriptions of the frame effect have been predominantly confined to between-subjects investigations. Our experimental design allowed us to distinguish the anatomical bases of the frame effect, both within and between subjects. Interestingly, amygdala activity did not predict the substantial intersubject difference in subjects. Interestingly, amygdala activity did not predict the substantial intersubject difference in knowledge that allows optimal decisions to be made in a variety of environments. However, in modern society, which contains many symbolic artifacts and where optimal decision-making often requires skills of abstraction and decontextualization, such mechanisms may render human choices irrational (31).

References and Notes
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Supporting Online Material
www.sciencemag.org/cgi/content/full/313/5787/684/DC1 Materials and Methods
Figs. S1 to S3
Tables S1 to S3
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