merical reference may play a role in the emergence of a fully formed conception of number. The challenge now is to delineate that role.

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REVIEW

The Role of the Medial Frontal Cortex in Cognitive Control

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Adaptive goal-directed behavior involves monitoring of ongoing actions and performance outcomes, and subsequent adjustments of behavior and learning. We evaluate new findings in cognitive neuroscience concerning cortical interactions that subserve the recruitment and implementation of such cognitive control. A review of primate and human studies, along with a meta-analysis of the human functional neuroimaging literature, suggest that the detection of unfavorable outcomes, response errors, response conflict, and decision uncertainty elicits largely overlapping clusters of activation foci in an extensive part of the posterior medial frontal cortex (pMFC). A direct link is delineated between activity in this area and subsequent adjustments in performance. Emerging evidence points to functional interactions between the pMFC and the lateral prefrontal cortex (LPFC), so that monitoring-related pMFC activity serves as a signal that engages regulatory processes in the LPFC to implement performance adjustments.

Flexible goal-directed behavior requires an adaptive cognitive control system for selecting contextually relevant information and for organizing and optimizing information processing. Such adaptive control is effortful, and therefore it may not be efficient to maintain high levels of control at all times. Here we review recent studies in cognitive neuroscience that have advanced our understanding of how the brain determines and communicates the need to recruit cognitive control. Convergent evidence suggests that the posterior medial frontal cortex (pMFC) and lateral prefrontal cortex (LPFC) are important contributors to cognitive control. Our focus is on the role of the pMFC in performance monitoring, especially in situations in which pMFC activity is followed by performance adjustments. Evaluating the adequacy and success of performance is instrumental in determining and implementing appropriate behavioral adjustments. For instance, detection of a performance error may be used to shift performance strategy to a more conservative speed/accuracy balance. Based on the evidence reviewed below, we develop the tentative hypothesis that one unified function of the pMFC is performance monitoring in relation to anticipated rewards. The monitored signals may index the failure (errors or negative feedback) or reduced probability (conflicts or decision uncertainty) of obtaining such rewards, and as such signal the need for increased control.

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Performance Monitoring

Flexible adjustments of behavior and reward-based association learning require the continuous assessment of ongoing actions and the outcomes of these actions. The ability to monitor and compare actual performance with internal goals and standards is critical for optimizing behavior. We first review evidence from primate, electrophysiological, and functional neuroimaging studies that points toward the importance of pMFC areas (Fig. 1A) in monitoring unfavorable performance outcomes, response errors, and response conflicts, respectively. These conditions have in common that they signal that goals may not be achieved or rewards may not be obtained unless the level of cognitive control is subsequently increased.

Although the pMFC can also be activated by positive events (such as rewards) (*1*, *2*), we focus here on negative events and their consequences. Because errors and conflicts are intrinsically negative, and because unfavorable outcomes are typically more consequential for the regulation of cognitive control than are favorable outcomes, our review focuses on the role of the pMFC in monitoring negative events.

Monitoring unfavorable outcomes. Electrophysiological recordings in nonhuman primates implicate the pMFC in monitoring performance outcomes. Distinct neuron populations in the pMFC, particularly in the supplementary eye fields and the rostral cingulate motor area (CMAr), are sensitive to reward expectancy and reward delivery (*1*, *3*, *4*). In addition, CMAr neurons exhibit sensitivity to unexpected reductions in reward (*5*). Likewise, specific groups of neurons in the depth of the cingulate sulcus (area 24c) react to response errors and to unexpected omissions of rewards (*5*). These findings are consistent with a role for these neuronal populations in comparing expected and actual outcomes.

Human neuroimaging studies implicate the pMFC, including the dorsal anterior cingulate cortex (ACC), along with other brain structures, in differential processing of unfavorable outcomes (Fig. 1B). These include studies using monetary rewards and punishments (*6*) and studies using abstract performance feedback (*7*). Similar parts of the pMFC are activated by primary reinforcers such as pain affect and pleasant tastes, suggesting that the pMFC plays a general role in coding the motivational value of external events.

Electrophysiological recordings in humans have identified the purported event-related brain potential correlate of the pMFC response to unfavorable outcomes: the feedback-related error-related negativity (or "feedback ERN"). This negative-polarity voltage deflection peaks approximately 250 to 300 ms after a stimulus indicating the outcome, and is greater in amplitude for negative performance feedback and outcomes indicating monetary losses than for positive feedback and monetary gains (*8*). The timing of this brain potential suggests that the pMFC computes or has access to a rapid evaluation of the outcome stimulus. Furthermore, initial studies report that the amplitude of the feedback ERN shows a graded sensitivity to the value of outcome stimuli that is normalized with respect to the subjectively expected outcome value (mean) and experienced range of outcome values (variance) (*9*).

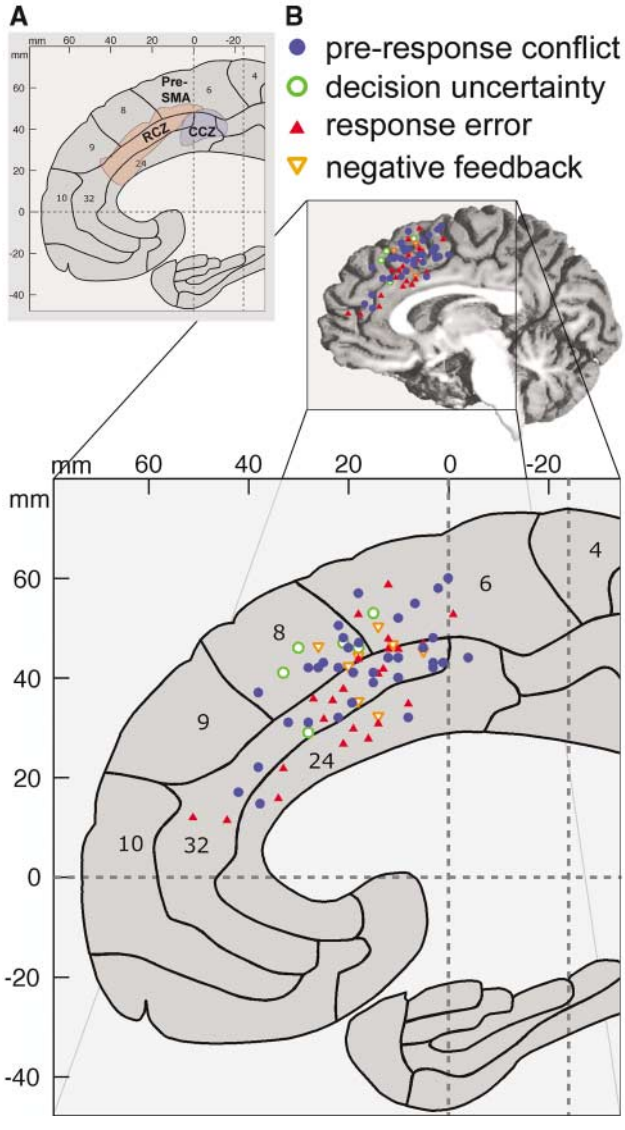

Fig. 1. Areas in the medial frontal cortex involved in performance monitoring. (**A**) Anatomical map of the medial frontal cortex. This is a schematic map of anatomical areas in the human pMFC, based on the atlas by Talairach and Tournoux (see supporting online material). The numbers indicate Brodmann areas. The area shaded in red encompasses the RCZ, and the area shaded in blue indicates the caudal cingulate zone (CCZ), as suggested by Picard and Strick (*11*). (**B**) Outcome of a meta-analysis of midline foci of activation reported in 38 fMRI studies published between 1997 and 2004 investigating brain activity associated with pre-response conflict, decision uncertainty, response errors, and negative feedback (*20*). In the upper part of the figure, the activation foci are superimposed on a saggital slice of an anatomical MRI scan at $x = 4$. In the lower part, the activation foci are superimposed on the enlarged schematic area map. The majority of activations cluster in the posterodorsal medial frontal cortex, in the region where areas 8, 6, 32, and 24 border each other.

Monitoring response errors. Primate studies show that, in addition to feedback-sensitive cells, the CMAr also contains error-sensitive cells (*4*, *10*). Corroborating these results, subsequent human functional neuroimaging studies have reported increased pMFC activation in response to errors as compared to correct responses in various two-alternative forced-choice tasks (*11*). The reported error-related activations cover a wide range along the anterior-posterior extent of the pMFC, with particular clustering in the rostral cingulate zone (RCZ) (*12*), the human homolog of the monkey's CMAr (Fig. 1B).

Consistent with these single-cell recordings and brain imaging studies, electrophysiological scalp recordings have found an error-sensitive event-related brain potential localized to the pMFC, which is attenuated in patients with damage to the dorsal ACC (*13*). This response-related ERN (or "response ERN") develops at the time of the first incorrect muscle activity and peaks about 100 ms later, indicating that the underlying generator has access to an efference copy of the initiated incorrect response (*14*). The response ERN is triggered by errors elicited under speeded response conditions, independent of the response effector (such as hands, feet, eyes, or voice), and increases in amplitude with the size or degree of error (*15*). Errors in these tasks result predominantly from premature responding, but continued stimulus processing after the response can provide sufficient information for outcome assessment. The morphology, polarity, and scalp distribution of the response ERN are similar to those of the feedback ERN, suggesting that the two ERN potentials may index a generic error-processing system in the pMFC.

A recent theory has extended the notion that the role of the dorsal ACC in coding outcome- and error-related information may be understood in terms of a common functional and neurobiological mechanism (*8*). The theory is predicated on prior research indicating that errors in reward prediction are coded by phasic changes in the activity of the midbrain dopamine system: a phasic increase when ongoing events are suddenly better than expected, and a phasic decrease when ongoing events are suddenly worse than expected (*16*). The theory builds on this research by proposing that these phasic dopamine signals are conveyed to the RCZ, where the signals are used to improve task performance in accordance with the principles of reinforcement learning. Furthermore, it proposes that the phasic dopamine signals modulate the activity of motor neurons in the RCZ, which is measurable at the scalp as changes in ERN amplitude. Phasic decreases in dopamine activity (indicating a negative reward prediction error) are associated with large ERNs and phasic increases (indicating a positive reward prediction error) with small ERNs.

A strong prediction of this theory is that the same region of the dorsal ACC should be activated by response errors and unexpected negative feedback. Also, during reward-based action learning, neural activity in this area should gradually propagate back from the feedback to the action that comes to predict the value of the feedback. These predictions have been confirmed using neuroimaging, ERN measurements, and computational modeling (*8*, *17*).

Monitoring response conflict. An alternative theory is that the pMFC, and in

particular the dorsal ACC, is involved in the monitoring of response conflict (*18*). Response conflict occurs when a task concurrently activates more than one response tendency; for example, when the stimulus primes a prepotent but incorrect response or when the correct response is underdetermined. Often, incorrect response tendencies are overridden in time by the overt correct response, resulting in high response conflict before the correct response (pre-response conflict). In contrast, occasional errors resulting from premature responding are characterized by response conflict after the response: The correct response tendency resulting from continued stimulus processing conflicts with the already executed incorrect response. In underdetermined responding (that is, under conditions requiring choosing from a set of responses, none of which is more compelling than the others), decision uncertainty occurs. Thus, decision uncertainty involves conflict similar to response conflict observed in tasks in which a prepotent response is overridden (*18*).

The conflict-monitoring theory is consistent with the neuroimaging evidence for pMFC activation in response to errors, reviewed above, and with the timing of the response ERN, indicating post-response conflict. In addition, the theory predicts that the pMFC should be active in correct trials characterized by high pre-response conflict, a prediction that has been confirmed by a large number of studies (Fig. 1B). Moreover, the predicted timing of such conflict-related activity is consistent with the occurrence of an ERN-like component, the N2, just before the response (*19*). Finally, the detection of high post-response conflict may be used as a reliable basis for internal error detection, thereby obviating the need for an explicit error detection mechanism (*19*).

The theory further holds that, upon the detection of response conflict, the pMFC signals other brain structures that the level of cognitive control needs to be increased.

Convergence and divergence in performance monitoring. The findings reviewed above suggest that the detection of unfavorable outcomes, response errors, response conflict, and decision uncertainty elicits largely overlapping clusters of activation foci in the pMFC. This assumption is consistent with a meta-analysis of the human neuroimaging literature (table S1), focusing on pMFC activations in response to these types of events (Fig. 1B) (*20*). The high degree of overlap should not be taken, however, as direct evidence for a generic role of neurons (or neuronal populations) in this brain area in monitoring various aspects of performance. First, although there is considerable overlap, there are some apparent differences as well, with foci associated with pre-response conflict clustering slightly more dorsally than foci activated during error and feedback monitoring (*21*, *22*). Second, single-cell recordings in monkeys suggest that different (neighboring) neurons within specific pMFC regions can be involved in different aspects of performance monitoring (*4*). Thus, the overlap between the activation foci identified in human neuroimaging studies does not necessarily imply identical functions for all neurons or neuronal ensembles within the pMFC.

A potential link between the outlined theories of pMFC functions is that pre-response conflict and decision uncertainty signal a reduced probability of obtaining reward, whereas errors and unexpected negative feedback signal the loss of anticipated reward. The pMFC, particularly the RCZ, is engaged when the need for adjustments to achieve action goals becomes evident. Interestingly, the monitoring processes examined here cluster primarily in the transition zone between the cingulate and paracingulate (areas 24 and 32), association (area 8), and premotor cortices (area 6), an area that has extensive connections with brain areas involved in the control of cognitive and motor processes and has been implicated in the regulation of autonomic arousal (*23*, *24*). This presumably places the pMFC in a strategically located position for signaling the need for performance adjustments and for interacting with brain areas involved in motor and cognitive, as well as autonomic and motivational, functions.

Performance Adjustments

Although the pMFC is consistently implicated in action monitoring, the mechanisms underlying the implementation of subsequent performance adjustments are less well understood. Two important questions are: (i) Is there a link between pMFC activation associated with performance monitoring and subsequent performance adjustments? (ii) What brain structures may be involved in the implementation of such control adjustments? In neuroimaging and neuropsychological studies, the LPFC has been broadly implicated in the coordination of adaptive goal-directed behavior (*25*–*29*). We review studies that address the first question, and we briefly evaluate the scant literature on functional interactions between the pMFC and LPFC in the service of adaptive control.

pMFC activity and immediate control adjustments. When stimuli elicit conflicting response tendencies or overt response errors, appropriate performance adjustments may be aimed not only at immediate correction of these tendencies but also at preventing errors on subsequent trials. A distinction can be made between two types of trial-to-trial performance adjustments: (i) shifts in the tradeoff between speed and accuracy of responding that place the cognitive system in a more cautious (as opposed to impulsive) response mode, and (ii) increases in control that improve the efficiency of information processing. Speed/accuracy tradeoffs may be expressed in ''post-error slowing,'' the observation that reaction times typically slow down after errors and correct, high-conflict trials (*18*). Changes in control, induced by such trials, can become evident in improved performance due to reduced interference from distracting information. For example, the increase in reaction times normally observed for incongruent stimuli (where target and distractor stimuli call for opposing responses) as compared to congruent stimuli (when distractors elicit the same action as the target stimulus) is typically reduced on trials after errors (*30*).

Several observations are consistent with a close link between modulations of pMFC activity and subsequent changes in performance. One study categorized trials in terms of their ERN amplitudes and found that the reaction time on the subsequent trial slowed progressively with increasing ERN amplitude on the current trial (*14*). In a similar vein, response errors on a two-alternative forced-choice task are foreshadowed by modulation of this pMFC activity during the immediately preceding (correct) response. Error-preceding trials were characterized by increased positivity in the time window typically associated with the ERN (*31*). This ''error-preceding positivity'' may reflect a transient disengagement of the monitoring system, resulting in occasional failures to implement appropriate control adjustments and hence in errors. Experimental factors that affect ERN amplitude may also affect subsequent performance adjustments. For example, alcohol consumption led to a reduction in the ERN amplitude and eliminated the post-error reduction of interference observed in a control condition (*30*). The relation between these findings and the associated neural circuitry was captured more directly in recent neuroimaging studies of Stroop task and response-inhibition performance (*32*, *33*): Post-hoc reaction time analyses revealed that greater ACC activity during error trials was associated with greater post-error slowing.

The latter studies also addressed the role of the LPFC in implementing control adjustments and its interaction with the pMFC. Trials exhibiting the greatest behavioral adjustments after errors and correct, high-conflict trials were associated with increased activity in the LPFC. Further, the degree of pMFC activity on conflict and error trials accurately predicted activity in the LPFC on the next trial. These and other findings are consistent with the idea that the pMFC, as a

monitor, and the LPFC, as a controller, interact in the regulation of goal-directed behavior (*18*).

pMFC activity and reward-based association learning. In addition to the link between pMFC activity and immediate adjustments in performance, there also seems to be a close relation between pMFC activity and reward-based association learning. A study of reward-based reversal learning in monkeys identified cells in the CMAr that fired only when two conditions were met: (i) reward was less than anticipated, and (ii) the reduction in reward was followed by changes in the monkeys' action selection (*5*). This finding has been corroborated by two recent functional magnetic resonance imaging (fMRI) studies of reversal learning, showing that ACC activity was observed under the same conjunctive condition (*34*, *35*). Reversal learning studies typically also show activation of the LPFC and other structures in association with changes in choice behavior (*36*). Whether these behavioral adjustments are implemented by or pMFC or whether the pMFC merely signals the LPFC or other structures to implement the adjustments remains to be explored.

Finally, there is evidence for an intimate relation between ERN amplitude and associative learning. In scalp electrophysiological activity, recorded from human participants who were required to learn stimulus-response contingencies on the basis of trial-to-trial positive or negative feedback, the feedback ERN to negative feedback decreased as participants were learning the contingencies, which is consistent with the theory discussed above that the ERN reflects a reward prediction error signal (*8*). Also, as participants learned the response associated with each stimulus, the response ERN associated with choice errors (provoked through the use of a stringent reaction time deadline) increased. In a temporal difference-learning model, not only did the ERN correlate with a reward prediction error but the brain activity underlying the ERN could also serve as a reinforcement learning signal for associative learning and hence optimizing task performance (*8*).

Conclusions and Future Directions

We have provided an overview of the evidence suggesting a critical role for the pMFC in performance monitoring and the implementation of associated adjustments in cognitive control. Our meta-analysis indicates that an extensive part of the pMFC—including areas 6, 8, 24, and 32, largely falling into a region referred to as the RCZ in humans—is consistently activated after the detection of response conflict, errors, and unfavorable outcomes. The similarities between two brain potentials generated by this area, the ERN and feedback ERN, are consistent with the view that the pMFC accommodates a unified functional and neurobiological performance-monitoring mechanism (*8*). This mechanism allows the pMFC to signal the likelihood of obtaining an anticipated reward (either definitive, as observed in studies of error detection and feedback processing, or probabilistic, as observed in studies of decision uncertainty and pre-response conflict).

Three conclusions from the meta-analysis should be emphasized. First, performance monitoring is associated with pMFC activations in a functionally integrated region (the RCZ) that cuts across various Brodmann areas beyond the "traditionally" reported ACC. Second, the most pronounced cluster of activations is in area 32 for all types of monitored events, suggesting the importance of this area for a unified performance monitoring function. Thus, the conclusion that error monitoring and conflict monitoring are performed by different areas, as derived from initial studies that were designed to identify differential involvement, is not ubiquitously confirmed by the meta-analysis. Third, activations related to pre-response conflict and uncertainty occur more often in area 8 and less often in area 24 than do activations associated with errors and negative feedback. Thus, although there is considerable overlap, there are some apparent differences as well, with activation foci associated with reduced probabilities of obtaining reward clustering slightly more dorsally than foci associated with errors and failures to obtain anticipated reward.

This generic monitoring function endows the pMFC with the capacity to signal the need for performance adjustment. Indeed, further evidence indicates a tight link between activity in this area and subsequent adjustments in performance, suggesting that the pMFC signals other brain regions that changes in cognitive control are needed. Although direct evidence is sparse, a likely candidate structure for effecting these control adjustments is the LPFC. Thus, monitoring-related pMFC activity may serve as a signal that engages control processes in the LPFC that are needed to regulate task performance in an adaptive fashion.

This conclusion notwithstanding, several questions remain. First, most studies of the pMFC and performance monitoring have tried to relate pMFC activity to control adjustments on the subsequent trial. An unresolved issue is whether the monitoring signal from the pMFC can also be used to resolve response conflicts on a within-trial basis (*34*). There is in principle no reason why such adjustments could not be implemented already within the same trial (to resolve conflict and correct the activation of inappropriate responses before they eventuate in an overt error). It is hard to tackle this question empirically using neuroimaging studies, because it requires disentangling the monitoring signal (indicating the need for control) and the answer to this signal (control implementation), which may be partly overlapping in time.

Another unresolved issue concerns the nature of the connection between the pMFC and LPFC. Anatomical studies in monkeys show dense reciprocal connections of the pMFC and LPFC (*37*, *38*). In humans, evidence for such connections is more indirect. Neuroimaging studies show concomitant activations in the LPFC and pMFC (*39*), suggesting close functional connectivity between these two areas. Little is known, however, about differential or selective reciprocal projections between various portions of the pMFC on the one hand and various subdivisions of the LPFC on the other. Possibly, this functional interplay is in part mediated by subcortical structures such as the basal ganglia and mesencephalic nuclei (*7*, *8*) or by the supplementary motor area (SMA) or pre-SMA (*29*, *40*).

Electrophysiological studies of patients with LPFC lesions have reported abnormal pMFC activity in response to errors (*41*). Such studies argue against the possibility of unidirectional information flow between the pMFC and LPFC, and instead suggest that performance monitoring and the regulation of cognitive control may be realized through intricate reciprocal projections between these two structures. It is a challenge for future research to further identify and characterize these interactions.

Although our review of the literature capitalizes on the role of the pMFC in performance monitoring, leading to performance adjustments on subsequent trials, other studies have suggested a more executive role for the pMFC in implementing control directly (*42*). Studies in nonhuman primates have shown that cells in the pMFC (especially in the monkey homolog of the RCZ) are well situated for this role, because this area has direct and indirect projections to primary and supplementary motor areas (*43*, *44*). It has been argued that some of these cells are involved in "goal-based action selection" (that is, selecting between competing actions in view of the anticipated reward associated with each of these actions) (*43*, *44*). The relation between these complementary functions remains to be further explored.

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22. The majority of activations fall into the border zone between areas 8, 6, and 32, with some extension into area 24. Recent research in nonhuman primates seems to suggest a functional-anatomical dissociation of regions subserving pre-response conflict monitoring from structures sensitive to errors and omission of reward (*1*, *4*). Although in humans this view is still under debate (*11*, *13*, *21*), the present meta-analysis does not provide unequivocal evidence for or against such a dissociation. Activations related to pre-response conflict and uncertainty occur more often in area 8 and less often in area 24 than do signal increases associated with errors and negative feedback (area 8, 32.5% versus 9.7%; area 24, 7.5% versus 25.8%), supporting the dissociation view. However, both groups of activations cluster primarily in area 32 (pre-response, 42.5%; error, 41.9%), suggesting that pre- as well as post-response monitoring processes share at least one underlying structure. It seems that the currently available spatial resolution in fMRI, in conjunction with anatomical variability and differences in scanning and preprocessing methods between studies, limit the ability to resolve this debate about a possible dissociation in the range of 10 mm or less.
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Supporting Online Material
www.sciencemag.org/cgi/content/full/306/5695/443/DC1
Materials and Methods
Table S1
References

REVIEW

Neuroeconomics: The Consilience of Brain and Decision

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Economics, psychology, and neuroscience are converging today into a single, unified discipline with the ultimate aim of providing a single, general theory of human behavior. This is the emerging field of neuroeconomics in which consilience, the accordance of two or more inductions drawn from different groups of phenomena, seems to be operating. Economists and psychologists are providing rich conceptual tools for understanding and modeling behavior, while neurobiologists provide tools for the study of mechanism. The goal of this discipline is thus to understand the processes that connect sensation and action by revealing the neurobiological mechanisms by which decisions are made. This review describes recent developments in neuroeconomics from both behavioral and biological perspectives.

The full understanding of utility will come from biology and psychology by reduction to the elements of human behavior followed by a bottom-up synthesis, not from the social sciences by top-down inference and guesswork based on intuitive knowledge. It is in biology and psychology that economists and social scientists will find the premises needed to fashion more predictive models, just as it was in physics and chemistry that researchers found the premises that upgraded biology. (p. 206) (*1*)

Consider the famous St. Petersburg paradox (*2*). Which of the following would you prefer, $40 or a lottery ticket that pays according to the outcomes of one or more fair coin tosses: heads you get $2 and the game ends, tails you get another toss and the game repeats, but now if the second toss lands heads up you get $4, and so on. If the nth toss is the first to land heads up, you get 2^n dollars. The game continues, however long it takes, until the coin lands heads up. We can assess the average objective, or expected, value of this lottery by multiplying the probability of a win on each flip by the amount of that win:

$$\text{Expected value} = (0.5 \times 2) + (0.25 \times 4) + (0.125 \times 8)\ldots$$
$$= 1 + 1 + 1 + \ldots$$

This simple calculation reveals that the expected value of the lottery is infinite even though the average person is willing to pay less than $40 to play it. How could this be?

For an economist, any useful explanation must begin with a set of assumptions that renders behavior formally tractable to coherent theoretical and mathematical analysis. Economists therefore explain this behavior by assuming that the desirability of money does not increase linearly, but rather grows more and more slowly as the total amount at stake increases. For example, the desirability of a given amount might be a power function

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