

Separate neural pathways process different decision costs

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Behavioral ecologists and economists emphasize that potential costs, as well as rewards, influence decision making. Although neuroscientists assume that frontal areas are central to decision making, the evidence is contradictory and the critical region remains unclear. Here it is shown that frontal lobe contributions to cost-benefit decision making can be understood by positing the existence of two independent systems that make decisions about delay and effort costs. Anterior cingulate cortex lesions affected how much effort rats decided to invest for rewards. Orbitofrontal cortical lesions affected how long rats decided to wait for rewards. The pattern of disruption suggested the deficit could be related to impaired associative learning. Impairments of the two systems may underlie apathetic and impulsive choice patterns in neurological and psychiatric illnesses. Although the existence of two systems is not predicted by economic accounts of decision making, our results suggest that delay and effort may exert distinct influences on decision making.

In our everyday lives we make numerous decisions among different courses of action based on the costs and benefits associated with each. Often, when we are confronted with a choice, there is not a single option that is most advantageous in every respect. Each course of action can be perceived as having its advantages and disadvantages. For example, action A may lead to a larger reward than action B, but it may do so only after a longer time has elapsed or after more effort has been invested. These costs and benefits must be weighed before deciding which course of action to choose. Recently, neuroscientists have elucidated aspects of the mechanisms through which benefits or rewards influence decisions¹. Conversely, economists and behavioral ecologists are interested in the effect of different costs, including delay, effort and risk, on decision making in humans and animals^{2–6}. To date, however, few studies have addressed the neural mechanisms through which such costs influence decision making.

Studies of human patients suggest that an area in the frontal lobe is important for evaluating decision cost, but it has been difficult to ascertain which prefrontal area is critical^{7,8}. Although a series of studies investigating the effects of more selective frontal lesions in the rodent implicated two areas, the orbitofrontal cortex (OFC) and the anterior cingulate cortex (ACC), once again the evidence is contradictory^{9–14}. Some reports suggest that destruction of the OFC biases animals' decision making so that they are cost-averse or impulsive, choosing smaller immediate rewards over larger delayed alternatives¹⁰. This is not a consistent finding, however, and another study reports exactly the opposite effect⁹. It has also been claimed that ACC lesions bias animals' choices, making them cost averse^{11,13}, but another study did not find cost aversion after an ACC lesion¹⁴.

Here we propose that frontal decision-making processes may be more easily understood if the existence of two distinct decision-making mechanisms, concerned with different types of decision costs, is postulated. A recent comparative study of primate species demonstrates that a willingness to tolerate delay costs does not correlate with an inclination to exert more effort and to travel farther to obtain greater reward^{5,6}. The two types of decision cost, delay and effort, may be represented by different cortical regions. Although such a separation of decision costs is not emphasized by standard accounts of economic decision making, it may prove a useful concept for understanding frontal contributions to decision making. Impaired decision making in neurological and psychiatric populations is characterized at different times by seemingly opposite patterns of both impulsiveness (delay aversion) and apathy (effort aversion)¹⁵.

We report here the effect of either ACC or OFC lesions on both delay- and effort-based decision making using analogous T-maze protocols^{11,16–18}. In both tasks, rats chose between a high reward option with a large cost or a low reward option with minimal cost. In experiment 1, the cost was a delay to the reward; in experiment 2 the cost was effort to be invested to obtain the reward. OFC lesions caused rats initially to make more impulsive choices, but had no effect on effort-based decisions. By contrast, ACC lesions resulted in less willingness to exert effort to gain the high reward while not altering patterns of delay-based choices. Experiment 3 showed that the deficits were ones of decision making rather than the consequences of changes in baseline activity levels. Both deficits were ameliorated after the experience of choosing to overcome the cost, suggesting that the decision-making function of the areas can be understood in the context of their involvement in fundamental aspects of associative learning.

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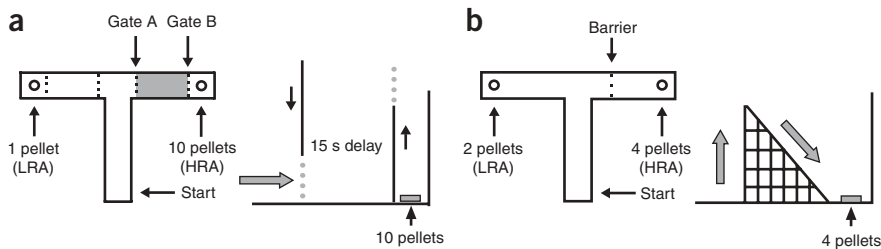


Figure 1 Experimental apparatus. **(a)** Experiment 1: delay-based decision-making test apparatus. Rats were placed in the start arm of the T-maze and chose between the two goal arms. When rats entered one of the goal arms, Gate A was immediately inserted, keeping the rat in the goal arm. Gate B was then retracted after the required delay. Selecting the HRA initially led to ten food pellets after 15 s, whereas the LRA led to only one food pellet immediately. **(b)** Experiment 2: effort-based decision-making apparatus. Rats were placed in the start arm and allowed to choose between the two goal arms. If rats chose the HRA containing the wire mesh barrier, they had to climb over it to receive four food pellets. Choosing the LRA meant they could obtain two food pellets without climbing a barrier.

RESULTS

Experiment 1: delay-based decision making

In experiment 1.1, we tested 32 hungry rats on a simple T-maze cost-benefit delay-based decision-making task. Rats chose between the two goal arms of the maze, which differed in the costs the rat incurred to gain different sized food rewards (**Fig. 1**). On each trial, the rat was placed in the maze and chose between the two arms: the low-reward arm (LRA) and the high-reward arm (HRA). Rats were initially trained for 36 trials over 6 d to discriminate between the reward sizes in the two arms by allowing them to choose between the LRA and HRA without there being a delay cost associated with either arm (**Supplementary Fig. 1** online). At the end of this training period, rats were choosing the HRA on at least 90% of trials. Next, a delay of 5 s was introduced into the HRA, meaning that when a rat chose the LRA it immediately received a single food pellet, whereas if it chose the HRA it had to wait 5 s, confined in the arm by the movable gates, before receiving ten food pellets. Each day rats received seven trials, two forced and five choice trials (see Methods and **Supplementary Note** online). Once rats chose the HRA on at least 80% of trials in a single day, the delay was increased to 10 s, and then to 15 s after the same criteria were met (**Supplementary Fig. 1**). Rats received a total of 84 trials with a delay cost in the HRA during training (24 forced, 60 choice). Immediately before surgery, rats were tested on two more blocks of 6 d each (blocks A and B, together consisting of another 84 trials; 24 forced, 60 choice). At the end of block B, all rats chose the HRA on the majority of trials (**Fig. 2**). On the basis of their preoperative performance and position of the HRA (left/right), rats were then assigned to one of three lesion groups in a counterbalanced fashion: OFC, ACC and sham (group [$F_{2,29} = 0.46; P = 0.955$]).

After surgery (**Fig. 3**, and **Supplementary Figs. 2** and **3** online) rats with OFC ($n = 11$) lesions chose impulsively, switching from selecting to wait for the HRA to choosing the LRA for an immediate small reward (**Fig. 2**). In contrast, both sham ($n = 11$) and ACC lesion ($n = 10$) rats continued to choose the HRA and to wait for a larger reward (presurgery block B versus postsurgery block C: group \times block interaction [$F_{2,29} = 12.341; P = 0.000$]). There was some decline in the performance in the sham-lesion control group. This was consistent with the rats not having formed habits but instead needing to weigh up the costs and benefits of each course of action and re-establish decision references after the break from testing. Similar effects were seen after each of the shorter preoperative breaks (**Fig. 2** and **Supplementary Fig. 1**). A further ANOVA focused just on postoperative performance (block C) and showed a significant effect of group ($F_{2,29} = 9.155$;

$P = 0.001$), caused by the OFC-lesioned rats making significantly more LRA choices than either ACC ($P = 0.03$) or sham ($P = 0.000$) groups. Various statistical approaches, either ANOVAs (group [$F_{1,19} = 2.62; P = 0.122$]) or posthoc tests ($P = 0.57$), all confirmed that ACC-lesioned rats, by contrast, were as willing as shams to wait for the HRA.

These findings concur with one previous study demonstrating impulsive choice following OFC lesions when selecting between a small immediate or large delayed reward¹⁰, but they are in direct contrast to another in which the OFC-lesioned rats tolerated longer delays for larger rewards than controls⁹. One proposed explanation for the discrepancy is that rats in the study reporting impulsivity had lesions before training, whereas in the

other study they learned the task prior to surgery^{9,19}. This explanation seems untenable in light of the present finding of increased choice of the immediate LRA even after prelesion training. The OFC is also implicated, however, in associative learning and the representation of reward expectancies¹⁹. Interestingly, an associative learning hypothesis has also been advanced by behavioral ecologists to explain the manner in which rats discount the value of outcomes as a function of the delay expected until their occurrence, with the strength of the attribution between the choice and its consequences being scaled as a function of the temporal delay between the two²⁰. One possibility, therefore, is that the increased impulsivity exhibited by the OFC-lesioned rats in the present study resulted from a degraded representation of the expected availability of reward in the two goal arms, thus causing them to choose the option with a lesser cost.

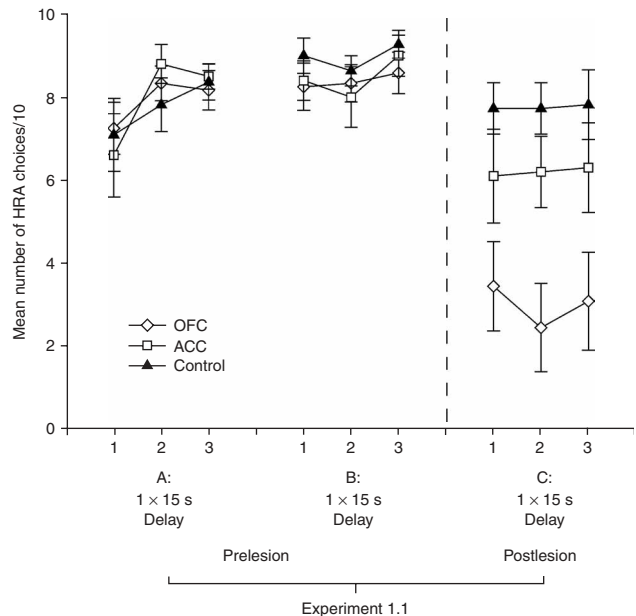


Figure 2 Delay-based decision making: experiment 1.1. Mean (\pm s.e.m.) number of trials in which rats in all lesion groups chose the HRA. In experiment 1.1, there was a 15-s delay in the HRA (blocks A, B and C). In order to be comparable with experiment 2 and previous work, each data point represents the combination of 2 d (*i.e.*, 10 choice trials). Each block consists of 6 d of five choice trials per day.

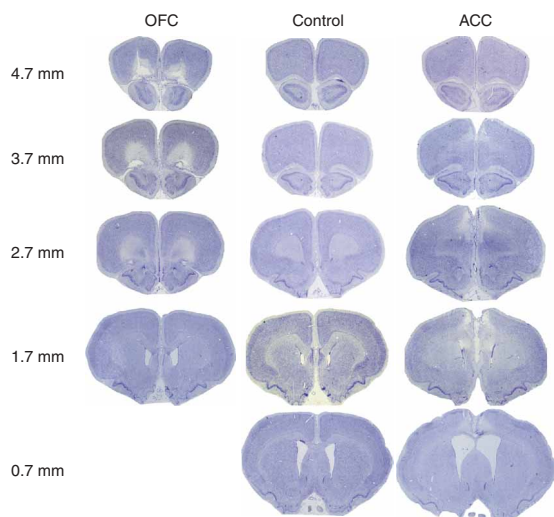


Figure 3 Representative pictomicrographs of OFC, ACC and sham lesions. Pictomicrographs of coronal sections (mm anterior to bregma) showing standard cell loss in representative OFC and ACC lesion rats compared to a sham lesion rat. OFC lesions reliably destroyed medial, ventral, lateral and dorsolateral orbital cortex. The olfactory bulb was partially damaged in only a very small number of rats. ACC lesions consistently destroyed both Cg1 and Cg2 regions bilaterally anterior of bregma.

A second experiment (experiment 1.2) was conducted in which both LRA and HRA were delivered after 15 s delays (block D). By equating the costs in the two goal arms, rats had the opportunity to experience both reward outcomes at the same cost. The choice can be made simply on the basis of the reward differential, thus removing the need to integrate both costs and benefits before deciding. All rats rapidly switched to selecting the HRA on the majority of trials (Fig. 4, block D; main effects of block, C vs. D [$F_{1,29} = 78.14$; $P = 0.000$]), so that by day 3 of testing, all rats were choosing the HRA option on almost every trial. That the OFC-lesioned rats chose the HRA when the costs were equated demonstrated that their change in choice behavior in experiment 1.1 can not be explained by alterations in spatial or reward memory.

The effect of providing further experience of both reward outcomes was examined by reinstating a delay cost with just the HRA option. The delay in the LRA was removed and the delay in the HRA was increased to 20 s. While this caused a slight drop in the number of trials on which all rats chose the HRA (blocks D and E), all the rats still preferred to wait for the HRA on the majority of trials (Fig. 4, block E). A comparison of block E with the earlier block C in which decisions had also been in the context of a single delay revealed a significant interaction of Group and Block ($F_{2,29} = 9.42$; $P = 0.001$) because the OFC performances were now similar to those of shams. The rats' repeated experience of the larger reward in the HRA arm of the T-maze on many trials in block D may have fostered the representation of the large expected reward associated with that response. A postoperative testing schedule may not reveal impulsive decision making if a rat is first provided with extensive experience of the association between the HRA and a given option in the absence of any delay⁹.

Two other explanations of the discrepancy between previous studies of OFC function in delay-based decision making have been proposed. One suggests that the previously reported increase in tolerance to delay displayed by OFC-lesioned rats⁹ is caused by a deficit in behavioral flexibility²¹. The other account suggests that the discrepancy is due to

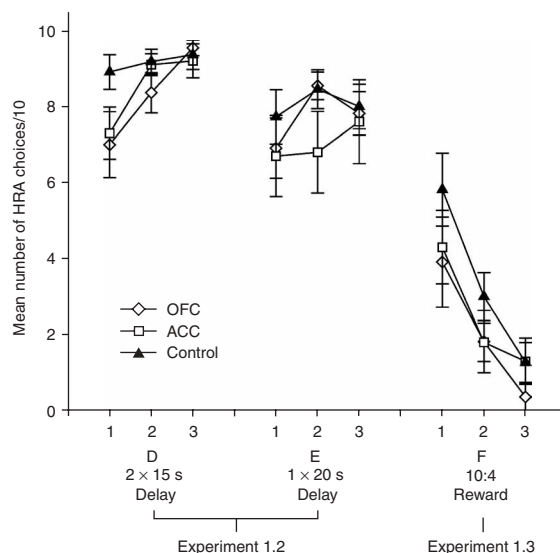
Figure 4 Delay-based decision making: experiment 1.2 and 1.3. Mean (\pm s.e.m.) number of trials in which rats in all lesion groups chose the HRA. In experiment 1.2 (block D), both the LRA and HRA were delayed by 15 s, whereas in experiment 1.3 there was a 20 s delay in the HRA (block E). In experiment 1.3, the HRA:LRA reward ratio changed to 10:4. There was a 15-s delay in the HRA (block F). Each data point represents the combination of two days (*i.e.*, 10 choice trials). Each block consists of 6 d of five choice trials per day.

differences in the reward ratios used in the two studies^{22,23}. A final test was therefore performed (experiment 1.3), in which the reward ratio between the HRA and the LRA was changed from 10:1 to 10:4 pellets (block F). This manipulation caused all the groups to switch to choosing the LRA option over the 3 days of testing (Fig. 4). There was no evidence for perseveration in the OFC group, with the speed of reversal from the HRA to the LRA being the same between the three groups (main effect of group and interactions, $P > 0.1$).

Experiment 2: effort-based decision making

In experiment 2.1, we tested 30 hungry rats on an effort cost/benefit T-maze decision-making task. As in experiment 1, rats chose between two rewarded goal arms, which differed in the magnitude of costs the rat incurred to gain different sized food rewards (Fig. 1). However, whereas in experiment 1 rats based their decisions on the cost of a delay to a reward, in experiment 2 they based their decisions on the cost of expending physical effort to obtain rewards. When rats chose the LRA, they received two food pellets whereas if they chose the HRA they had to climb a 30 cm high barrier to obtain four food pellets. After an initial training period, all rats chose the high-effort HRA on every trial (Fig. 5, blocks A and B). As in experiment 1, rats were assigned to one of three lesion groups, OFC, ACC or sham, based on their preoperative performance and position of the HRA (group [$F_{2,27} = 0.013$; $P = 0.987$]).

In contrast with experiment 1, rats with ACC lesions ($n = 11$) showed a significant change in the frequency of high effort HRA choices after surgery (Fig. 3, and Supplementary Figs. 4 and 5 online), preferring to select the LRA option that required minimal effort (Fig. 5). Both sham ($n = 12$) and OFC ($n = 7$) lesion rats continued to choose the HRA on the majority of trials. As in experiment 1, there was some decline in the performance of the sham-operated control group in the postoperative period, which may have been consistent with the re-establishment of decision references after the surgery



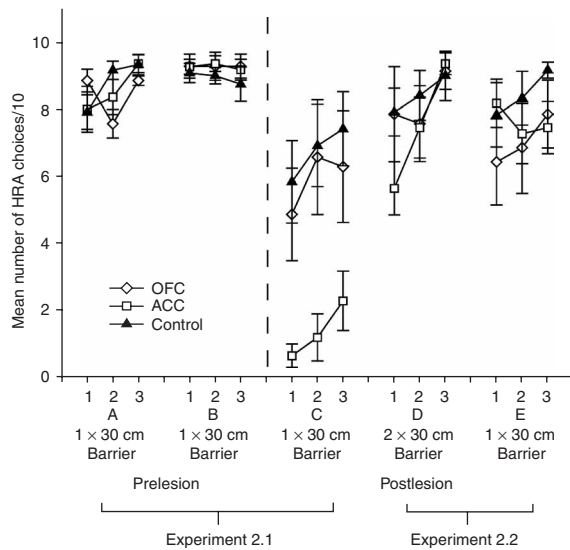


Figure 5 Effort-based decision making. Mean (\pm s.e.m.) number of trials in which rats in all lesion groups chose the high-effort HRA. In experiment 2.1 sham and lesion rats chose between climbing a 30-cm barrier in the HRA and no barrier in the LRA (blocks A, B and C). In experiment 2.2 there were 30-cm barriers in both arms (block D) or a single 30-cm barrier in the just HRA (block E). Each block consisted of 3 d of ten trials per day.

interval. The difference between lesion groups was confirmed by comparing the last prelesion block (B) with the postlesion testing block (C), which revealed a significant group \times block interaction ($F_{2,27} = 10.51$; $P = 0.000$). Further *post hoc* analysis of postsurgery performance showed that the ACC group was significantly different from both OFC ($P = 0.029$) and sham groups ($P = 0.002$), but that the OFC-lesioned rats and shams showed a similar pattern of effort-based decisions ($P = 1$). Additional analyses reported in the **Supplementary Note** support this interpretation.

Given the results of experiment 1, which showed that providing further postsurgical experience of both options could ameliorate a decision-making deficit, we ran a second experiment (experiment 2.2) in which an identical 30-cm barrier was placed in the LRA. This meant that both the HRA and LRA contained identical effort costs. This also tested whether any change in the ACC-lesioned rats' choices was the result of an inability to scale the barrier or a deficit in spatial or reward memory rather than an alteration in the way in which they assessed their decisions. The addition of a second 30-cm barrier in the LRA caused all rats to switch to choosing the HRA on nearly every trial (Fig. 5, block D; main effect of block [$F_{1,27} = 30.6$; $P = 0.000$]). Whereas there had been differences between the ACC-lesioned rats and the other groups when there was only a barrier in the HRA, there were none in block D (group [$F_{2,27} = 0.49$; $P = 0.618$]).

To test the effect of providing rats with experience of each outcome with the effort levels equated, the barrier in the LRA was subsequently removed (block E). All rats chose the HRA slightly less when only a single barrier was placed in just the HRA (Fig. 5, block E). A comparison of block E against the earlier block C in which decisions had also been in the context of a single barrier revealed a significant interaction of Group and Block ($F_{2,27} = 10.16$; $P = 0.001$) because the ACC performances were now similar to those of shams.

Experiment 3: spontaneous locomotor activity

One possible explanation for the effects of ACC and OFC lesions on different decision-making tasks might be that there are changes in activity levels rather than changes in the way that decisions are made. It could be argued that a general hyperactivity might have led OFC-lesioned rats to choose impulsively in experiment 1 or a general lethargy might have led ACC-lesioned rats to choose less effortful options in experiment 2. Experiment 3 was not, however, intended as an assessment of whether rats were still able to make the motor

response required to climb the barrier in experiment 2 as that had already been addressed by the equal cost manipulation in block D of experiment 2.

The spontaneous locomotor activity of all rats that took part in experiments 1 and 2 was assessed during 2 h spent in the dark after *ad libitum* access to food. As there were no differences in activity levels between the groups used in experiments 1 and 2, the data from both were combined. Contrary to the alternative account outlined above, it was found that ACC lesions made rats hyperactive relative to OFC and sham groups (Fig. 6). A repeated-measures ANOVA of the number of beam breaks revealed a main effect of group ($F_{2,59} = 7.16$; $P = 0.002$), the ACC-lesioned rats being significantly more active than both OFC ($P = 0.002$) and sham-lesion rats ($P = 0.025$).

DISCUSSION

The results demonstrate separable decision-making processes in rodent frontal cortical areas when rats make choices involving either effort or delay costs. Experiment 1 demonstrated that lesions of the rat OFC induced impulsive choices, whereas lesions of the ACC did not. Before surgery, rats nearly always chose to wait for a higher reward (delayed HRA). Excitotoxic lesions of OFC caused a dramatic change in delay-based decision making and the immediate LRA was chosen on the majority of trials. In accordance with previous studies¹⁴, both sham and ACC lesion rats continued to select the delayed HRA option. In experiment 2, by contrast, only lesions of the ACC, but not of the OFC, altered rats' effort-based decision making, biasing them to choose smaller rewards that were easily obtained over larger ones that could only be acquired by exerting more effort. Neither the increased impulsivity in OFC-lesioned rats nor the decrease in effortful investment exhibited by ACC-lesioned rats were caused by hyperactivity or apathy, respectively. Contrary to previous reports of the effects of OFC aspiration lesions²⁴, only the rats with ACC but not OFC lesions were more active than shams. The OFC and ACC deficits were impairments of decision making; control procedures 1D and 2D (Figs. 2 and 5) demonstrated that both deficits were reduced when the need to integrate

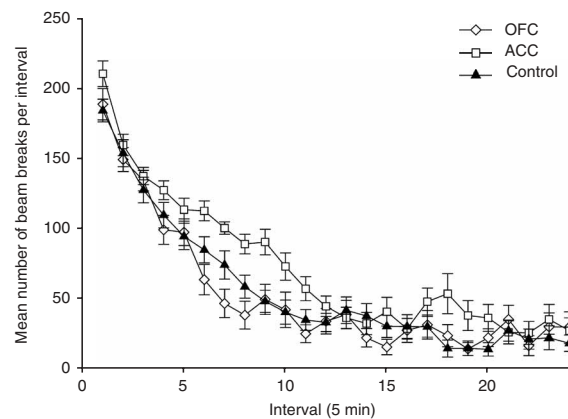


Figure 6 Spontaneous locomotor activity. Mean (\pm s.e.m.) total number of beam breaks rats in all lesion groups made per time interval (5 min). Rats' spontaneous locomotor activity was assessed over a total of 2 h in the dark.

both cost and benefit information prior to decision making disappeared by equating the costs associated with each decision option. The present data provide direct evidence that both delay- and effort-based decisions are subserved by independent neural systems in the brain.

The anatomical double dissociation in decision-making systems is notable and has not been emphasized by standard models of economic decision making⁴. Given the separation of their anatomical substrates, it is likely that delay and effort costs will impinge on decision making in different ways. It certainly seems the case that the two types of decision making are subject to separate evolutionary selection forces⁴⁻⁶. Cotton-top tamarins (*Saguinus oedipus*) are more inclined to tolerate high effort costs incurred in traveling farther to a larger food amount, whereas common marmosets (*Callithrix jacchus*) are more inclined to tolerate high delay costs in order to obtain larger food amounts. The natural feeding ecology of the two species also reflects different patterns of effort and delay-discounting in pursuit of larger rewards; whereas tamarins range over larger distances in pursuit of insects, marmosets must wait patiently for tree exudates in a circumscribed location. Other species also seem to take energetic expenditure into account when making foraging decisions³. Distinct cognitive processes shaped by evolution may underlie the way in which decisions involving effort and delay costs are taken. While deciding how much effort to expend may be related to considerations of the opportunity costs of not responding²⁵ and energy expenditure^{3,26}, deciding how long to wait for an outcome may be inextricably linked to associative learning mechanisms^{2,19,20,23}. Each mechanism is discussed in more detail below.

OFC and delay-based decision making

Studies of human patients with ventromedial prefrontal cortex damage, encompassing parts of the OFC and ACC, suggest that this region plays an important role in preventing impulsive decision making^{7,8}. Similarly, both regions are implicated in the pathology of attention-deficit/hyperactivity disorder (ADHD)²⁷. Our findings suggest the critical region mediating impulsive choice is the OFC, whereas the ACC is the locus of the hyperactivity effects. The distinction between impulsive decision making and hyperactivity might be compared with the distinction previously drawn between impulsive decision making and impulsive action^{28,29}. Other studies report premature motor responses after ACC lesions³⁰ and the same underlying deficit may account for the increase in responses in those studies and the increase in the locomotor activity in the present study.

While frontal lesions made rats cost-averse, such deficits were only present before rats had, postoperatively, chosen between the two reward outcomes in the context of equal costs. Once a rat had experience of high costs, it chose the larger reward and continued to make such choices even if an inequality in delay or effort was re-introduced. Additional analyses confirmed that the lack of any deficits was not simply the result of a recovery from the effect of the lesions (see **Supplementary Note**). Furthermore, subsequent tests of food preference and locomotion continued to demonstrate significant changes in behavior in both lesion groups (experiment 3 and data not shown).

Although the findings that OFC lesions induce impulsive choice and that the impairment can be ameliorated by experience of choosing between equal cost options may initially seem puzzling, this in fact helps resolve a recent controversy. Two previous studies report contrasting effects of OFC lesions on delay-based decision making^{9,10}. It has been suggested that the disparity might simply be caused by differences in reward ratios, by preoperative versus postoperative training protocols or by reversal learning deficits^{9,19,21}. The results of experiment 1 suggested that none of these explanations provide a complete account of the data.

First, it has been proposed that increasing the difference between reward ratios might ameliorate impulsivity observed following OFC lesions²³. This proposal is based on the finding that OFC lesion rats do not choose impulsively when faced with a reward ratio of 4:1 but they do when faced with a ratio of 2:1 (refs. 9,10). In summary, increases in impulsive choice have been observed when the reward ratio is 10:1 (present study) and 2:1 (ref. 10), and decreased impulsive choice with ratios of 4:1 (ref. 9). In conjunction, these studies suggest that the reward differential is not a critical determinant of whether or not impulsive choice will be seen after OFC lesions. Second, as in a previous study⁹, the rats in the present experiments were trained before surgery, yet OFC lesions still initially caused increased impulsive choice; therefore a simple pre- versus postoperative training explanation cannot account for the different findings reported in the literature. A question that remains for further research, however, is how the nature or amount of training on the cost-benefit contingencies preoperatively influences the choices of rats and the neural structures that encode such decisions^{23,31}. Finally, the continued choice of the larger reward after experiencing equal delay costs in both goal arms could not be ascribed to a perseverative deficit, as the OFC group adjusted their behavior as rapidly as shams when the reward or cost ratios were changed (blocks D and F).

Instead, the pattern of results across studies^{9,10} can be understood within the context of associative learning processes. Preferences for immediate over delayed rewards can be understood if the interposition of a delay between a stimulus and a reward makes the representation of the association difficult^{2,20,23}. The OFC, basolateral amygdala (BLA) and nucleus accumbens (NAc) are part of an interconnected circuit involved in associative learning and the representation of outcome expectancies¹⁹. Both BLA and NAc are essential for representing reward expectancies during delays; lesions of either BLA or NAc lead to decreased choice of larger reward options when the delivery of the large reward is delayed^{9,14}. Following lesions of the OFC, BLA neurons are less able to become cue selective and show reduced reward expectancy activity during delays³².

The initial increase in impulsive choice observed in the present study may therefore have occurred because, in the absence of explicit cues, OFC-lesioned rats had a degraded representation of the expected value of the outcome in the delayed reward arm. Without having full access to this information, when these rats reached the choice point in the T-maze, they were unable to utilize the normal outcome expectancies in the delayed HRA to resist the temptation of the immediately available outcome in the LRA. Training and experience of both outcomes at longer delays led the OFC-lesioned rats to return to choosing the larger but delayed reward. The recovery of decision preference was not simply due to additional time or training; instead, the rats' representations of the goal arms changed in ways that were dependent on specific behavioral manipulations. Extensive exposure to the larger reward during the equal cost manipulation allowed rats to re-evaluate their decision references and choose the larger reward even when the delay intervals associated with each response were subsequently made unequal once again. This is consistent with the finding that representations of expected outcomes in other parts of the brain, such as the BLA, are not abolished after OFC lesions, although they are degraded. Nevertheless, after more extensive training, cue-selective and reward expectancy responses are still evident in the BLA of OFC-lesioned rats even if they are not as numerous or prominent as in controls³².

It may be important to note that the study that reported decreased impulsive choice following OFC lesions began testing with equal delays associated with both large and small rewards⁹. The combination of both preoperative training, the presentation of equal costs at the beginning of the testing session and the presence of conditioned stimuli

during the delay period in this study⁹ may have allowed a representation to be generated in the intact BLA and NAc which was sufficient to bias choice toward the larger reward option, even as the associated delay began to increase.

ACC and effort-based decision making

As in previous studies^{11–13}, ACC lesions caused a bias away from the option requiring more effort to obtain greater reward. The involvement of the ACC in such decision making may be a consequence of its role in representing the relationship between actions and outcomes³³. It may also be linked to its importance in representing arousal states, which could provide a proximate indicator of energy expenditure and therefore be critical for making a decision about whether or not it is worth working hard for a given reward. ACC pyramidal neurons send projections to the hypothalamus and the periaqueductal gray, both of which are associated with autonomic control^{34,35}. Electrical stimulation of the ACC induces autonomic responses³⁶. A combined human imaging and lesion study identified ACC activations related to changes in autonomic arousal during both effortful cognitive and motor behavior³⁷.

When the cost of obtaining both high and low rewards was equated, ACC-lesioned rats shifted back to choosing the HRA response (Fig. 5, block, D)^{11–13}. This confirmed that the ACC lesion deficit was not an alteration in reward processing or spatial processing, nor was it the result of an inability to execute the more effortful response. Rather, the ACC lesion led to a biasing in the way the rats processed the effort costs associated with each response. As with the OFC delay-based deficit, however, the ACC effort-based change in choice behavior was not present following testing on the equal cost condition. Once again, such recovery can be understood within the context of the neural system governing effort-based decision making, of which the ACC is just a part. The BLA and dopamine in the NAc are necessary for effort decisions and related processes^{38,39} and neurons in these areas of the macaque brain represent information about how many more actions must be made, in other words, how much more work effort is needed, before reward can be expected^{40,41}. The special importance of the ACC is suggested by the fact that individual neurons encode a monkey's progression through the series of work steps toward reward⁴². Less is known about the ACC's interactions with the BLA or NAc than is known about the dependency of BLA activity on OFC activity³². Extrapolating from the work examining interactions between OFC and BLA, one possibility is that BLA/NAc representations of work costs may be degraded in the absence of an ACC representation of the rat's progress through a work sequence, particularly one that contains effortful actions such as barrier climbing, which could be linked to the importance of ACC in representing arousal states. This would mean that rats could not use the expected outcome to motivate a decision to avoid selecting the easily obtained LRA option, as is observed at the beginning of the postoperative period (experiment 2.1). BLA and NAc representations would, however, be sufficient to bias a rat toward the larger reward when effort costs are equal (experiment 2.2) and then to maintain responses toward the larger reward when effort costs for one option are increased after repeated experience of choosing the HRA (experiment 2.3). It should also be noted, however, that some previous studies report that rats with lesions that include the ACC return to pursuing the low effort action even after experience of equal effort costs, particularly if the damage is more extensive and includes adjacent prefrontal cortex^{12,13}.

Separate circuits for processing different types of decision

While the OFC or ACC may be selectively concerned with the processing of delay or effort costs, respectively, neither type of decision

depends on either frontal region in isolation³¹. The ACC is part of an extended circuit concerned with making decisions about how hard to work in a given context. Researchers have emphasized effort in descriptions of behavior and drawn attention to its central importance in accounts of dopamine function in the NAc^{39,43}. Similarly, excitotoxic lesions of the NAc produce deficits in delay-based decision making^{14,39}. Both ACC and OFC send afferent projections to the NAc, albeit to distinct subregions, suggesting there may be distinct fronto-striatal loops which process effort and delay costs^{44,45}. This notion is comparable to the hypothesis¹⁵, based on human behavioral disorders, that dysfunction in the ACC-subcortical circuit leads to apathy whereas damage to the OFC-subcortical circuit causes disinhibition and agitation. Human neuroimaging studies also report activation in fronto-striatal loops when people make decisions about future or immediate rewards⁴⁶. Other interconnected structures, such as the BLA, are also likely to have key roles in mediating both types of cost-benefit decisions^{9,38}. There is also evidence for a partial dissociation between dopaminergic and serotonergic neuromodulatory systems in relation to the two types of decision making^{18,47}.

The need to make decisions both about how much effort to invest and how much time to wait may be a general one even for animals other than mammals. Recently, structures in the avian brain that may be concerned with particular decision costs have been identified^{48,49}. The degree to which delayed or effortfully obtained rewards are devalued may depend on the ecological niche occupied by a particular species^{4–6}.

METHODS

Animals. Sixty-two male Lister hooded rats (Harlan Olac, Bicester, UK), aged approximately 2 months, were used in the experiment. Rats were housed in cage groups of three and maintained on a 12 h light/dark cycle. Training and testing always took place during the light phase. During the training and the testing phase, all rats were maintained at roughly 85% of their initial free feeding weight, but were allowed to gain 3–5 g per week. Rats had access to water at any time. All experiments were conducted in accordance with the United Kingdom Animals Scientific Procedures Act (1986).

Habituation. Before training, rats were handled and weighed every day for a week. A feeding schedule was then introduced to reduce their body weight to 85% of free feeding weight. Rats were habituated to the maze in groups of three. For two consecutive days, groups were placed in the start arm of the maze and were allowed to explore the T-maze for 5 min. Ten food pellets were placed in each goal arm food well (45 mg food reinforcement pellets, Formula A/I; P.J. Noyes). For the next 2 d, rats were individually placed in the start arm and allowed to investigate the T-maze. For this stage four food pellets were placed in each food well.

Experiment 1: delay-based decision making. Apparatus experiments were conducted in an elevated high-sided T-maze constructed from medium density fiber painted gray. The T-maze consisted of three arms, a start arm which was joined to two perpendicular goal arms (Fig. 1). Each arm was 60 cm in length, 10 cm wide and had walls 40 cm in height. A raised food well was placed 2 cm from the back wall of each goal arm. In addition, both goal arms contained two 40-cm high, 10-cm wide gray wooden gates, placed 5 cm from both the entrance and end walls, which could be opened or closed to control entry/exit of rats to arms and food wells.

Delayed reward training. For 14 rats, the left goal arm was the HRA, for the other 18 the HRA was the right arm. This was kept constant throughout all subsequent training and testing. Over a period of 2 d, rats received eight trials where they could sample the food rewards in both the HRA and LRA (all four vertical gates were retracted). Ten reward pellets were available in the HRA, but only one was available in the LRA. This reward ratio was used to address the hypothesis that the difference in results between two previous studies investigating the effects of OFC lesion in delay-based decision making^{9,10} was due to differences in reward ratios.

Over two further days, eight choice trials were run (four per day) where rats were permitted to eat the reward in only one of the goal arms. During this phase, once a rat entered a goal arm, gate A was inserted and gate B was retracted (Fig. 1), allowing immediate access to reward, but confining the rat to the selected arm. Rats were tested in groups of nine, producing an inter-trial interval (ITI) of approximately 10 min, which was kept constant throughout all training and testing.

Rats then moved on to the next phase of discrimination training, where one session of seven trials was run each day. To ensure rats sampled both the HRA and LRA options, the first two trials of each session were forced in opposite directions by closing gate A at the entrance to one of the goal arms. Rats then received five choice trials in which they could select either the HRA or LRA. This protocol was kept constant for the rest of training and testing. Training continued until all rats were selecting the HRA on at least 90% of trials. A delay of 5 s was then introduced in the HRA. Once rats chose the HRA on at least 80% of trials in a session, the delay was increased to 10 s, and then to 15 s after the same criteria were met. During delay training, rats received a forced trial to the HRA after each LRA choice. For further information concerning training, see **Supplementary Note** and **Supplementary Figure 1**.

Experiment 1.1. Pre- and postlesion testing employed the same experimental protocol used in training, except that forced trials were not given after rats selected the LRA on a choice trial. Rats received two forced and five choice trials per session for 6 d (this period was defined as a test block). For test blocks A, B and C, rats chose between an immediate reward in the LRA and a reward delayed by 15 s in the HRA. Two prelesion blocks were run (blocks A and B) with a 10-d interval between blocks. Following a 2-week recovery period postsurgery and once all rats had reached 85% of their postsurgery free feeding weight, test block C was run. The surgery/recovery period between the second prelesion test (block B) and the start of postlesion testing (block C) was 5 weeks.

Experiment 1.2. Experiment 1.2 investigated whether any deficit observed after surgery was the result of altered spatial memory or reward sensitivity rather than the consequence of a change in decision making. The rats were re-run with a 15-s delay in the LRA as well as the HRA (block D). This meant the cost of each reward was the same regardless of which arm they chose.

It was then important to establish whether experience of both rewards at similar delays had had any effects on the rats' choices. To examine this, rats were retested with a choice between reward delayed by 20 s in the HRA and an immediately available reward in the LRA (block E). To ensure rats were familiar with the new cost/reward contingency, rats received 12 forced trials (6 to the LRA and 6 to the HRA, pseudorandomly presented) over 2 d before block E.

Experiment 1.3. To test whether any change in decision making was the result of an alteration in reward sensitivity or response flexibility between blocks C and E, the reward ratio between the two arms was altered. The number of pellets available in the LRA was increased to four while the number in the HRA remained the same (block H). To aid comparison with the initial test blocks (A–C), the delay in the HRA was decreased to the original level of 15 s.

Experiment 2: Effort-based decision making. Apparatus experiments were conducted in the same elevated high-sided T-maze used in experiment 1. The only difference between experiments was that the vertical gates were removed. Instead, three-dimensional triangular barriers constructed from wire mesh were placed at the midpoint of the HRA. The placement of the barrier meant rats had to climb the vertical side of the barrier and descend the hypotenuse to obtain rewards (Fig. 1). As in experiment 1, on forced trials rats were blocked from entering one of the arms using a 40-cm tall and 10-cm wide gate made from medium density fiber.

Differential and barrier reward training. For 13 rats the HRA was on the left, and for 17 it was on the right. Rats received four trials in which they could access both rewards. They were removed from the maze once all pellets had been consumed. For the next 2 d, rats received ten random-order forced trials in which they could only select one of the goal arms (5 HRA and 5 LRA). From this point on in the study, the training and testing schedule was kept stable. Rats received 12 trials per day. The first two trials of each day were forced in each direction in a counterbalanced manner. Rats then received 10 trials where

they could choose between the arms. When rats selected the LRA during training they immediately received a forced trial to the HRA. Once all rats were selecting the HRA on at least 90% of trials, a 15-cm barrier was placed in the HRA. The barrier size was increased by 5 cm up to a maximum of 30 cm after all rats chose the HRA on at least 90% of trials. Rats were tested in groups of nine, resulting in an ITI of approximately 5 min.

Experiment 2.1. The same procedure used in training was used during the pre- and postlesion test phases, but no additional forced trials were conducted after LRA choices. Testing blocks consisted of three consecutive days of 12 trials (2 forced followed by 10 choice trials). During the two prelesion (blocks A and B) and first postlesion tests (block C), a single 30-cm barrier was placed in the HRA while no barrier was present in the LRA. There was a 10-d interval between blocks A and B. Postsurgery, rats were given a 2-week recovery period, and testing restarted after this period once they had all reached 85% of their postsurgery free feeding weights. The interval between the end of prelesion testing (block B) and the beginning of postlesion testing (block C) was 4 weeks.

Experiment 2.2. To test whether any change in rats' choices was a result of an impairment in spatial memory, motor ability or reward processing rather than caused by an alteration in the way they were assessing their decisions, a second identical barrier was placed in the LRA (block D). Therefore, the physical effort required to gain reward was the same in both goal arms, while the reward ratio between the HRA and LRA remained the same. Following the completion of block D, the barrier in the LRA was removed and another testing block was conducted to determine whether any deficit in block C was stable or whether it was sensitive to the double barrier/cost condition in block D.

Experiment 3: spontaneous locomotor activity. The spontaneous locomotor activity of rats in experiment 1 and 2 was assessed following completion of maze testing. The apparatus and procedure have been described in detail elsewhere²⁰. In brief, rats were individually placed in hanging wire cages each containing two horizontal photocell beams located along the long axis. Spontaneous locomotor activity for each rat was assessed in the dark after *ad libitum* access to food. Testing rats in the dark ensured reasonable activity levels. This, in turn, meant that the test provided a sensitive assessment of underlying differences in activity between groups that was uncontaminated by any differences in anxiety. The number of beam breaks in each test session was recorded.

Surgical procedure. In experiment 1 rats were anesthetized with 1 ml/100 g Avertin (Avertin consists of 100 g of 2,2,2-tribromoethanol dissolved in 62 ml tertiary amyl alcohol; 1.25 ml of which is then added to 5 ml of absolute alcohol and 62.5 ml of 0.9% saline). In experiment 2 rats were anesthetized with isoflurane (Animal Care), placed in a stereotaxic frame and the head secured with bregma and lambda level using ear bars. An incision was made along the midline and the area of bone above the target injection sites was removed. All injections were made using a 5- μ l syringe with a specially adapted 34-gauge needle mounted onto the stereotaxic frame.

Based on previous reports²¹ and pilot studies in our lab, rats in the OFC lesion group received three bilateral infusions of quinolinic acid (0.09M) at the following anterior-posterior, mediolateral and dorsoventral coordinates: anterior-posterior +4.0, mediolateral \pm 0.8, dorsoventral -3.4 (0.15 μ l); anterior-posterior +3.7, mediolateral \pm 2.0, dorsoventral -3.6 (0.2 μ l); and anterior-posterior +3.2, mediolateral \pm 2.6, dorsoventral -4.4 (0.15 μ l). Anterior-posterior and mediolateral coordinates were measured relative to bregma, whereas dorsoventral coordinates were measured from brain surface. ACC lesion group rats received four bilateral infusions of quinolinic acid: anterior-posterior +2.3, mediolateral \pm 0.5, dorsoventral -1.5 (0.2 μ l); anterior-posterior +1.6, mediolateral \pm 0.5, dorsoventral -2.0 (0.2 μ l); anterior-posterior +0.9, mediolateral \pm 0.5, dorsoventral -0.2 (0.2 μ l); anterior-posterior +0.2, mediolateral \pm 0.5, dorsoventral -2.0 (0.2 μ l). ACC lesion coordinates were the same as those used previously¹¹. For both lesions, infusions were made at a rate of 0.1 μ l every 30 s with a 30-s interval between injections. The needle remained in place for 3 min after infusion to ensure the quinolinic acid diffused away from the injection site. Sham lesion surgery was conducted in the same way, although the needle was not lowered into the cortex. After all injections had been completed, rats were sutured and injected with an analgesic (Rimadyl, Pfizer or Metcam, Boehringer Ingelheim).

Postmortem lesion analysis. At the conclusion of behavioral testing, rats were deeply anesthetized intraperitoneally with 200 mg per kg (body weight) of sodium pentobarbitone and perfused transcardially with physiological saline, followed by 10% formalin saline. The brains were removed and stored in formalin saline solution. Subsequently tissue was placed in sucrose-formalin solution for 24 h, frozen, sectioned coronally (25 μ m) and stained with Cresyl violet. An experimenter unaware of each rat's behavioral performance assessed the extent of the lesions.

Statistical analysis. The data from all experiments were analyzed using repeated measures ANOVAs with two within-subject factors, block and day, and a between-subject factor of group (ACC, OFC, sham) using SPSS software for windows (version 9.0). *Post hoc* Bonferroni tests were conducted if a main effect of group was found to determine which lesion had affected choice behavior. For experiment 2, the total number of high-reward choices per daily session (ten in total) was used to analyze choice behavior. In experiment 1, rats made five choices per day; therefore, data were collapsed across 2 d so that analysis was similarly based on ten trials.

Note: Supplementary information is available on the Nature Neuroscience website.

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COMPETING INTERESTS STATEMENT

The authors declare that they have no competing financial interests.

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