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Value, search, persistence and model updating in anterior cingulate cortex

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Dorsal anterior cingulate cortex (dACC) carries a wealth of value-related information necessary for regulating behavioral flexibility and persistence. It signals error and reward events informing decisions about switching or staying with current behavior. During decision-making, it encodes the average value of exploring alternative choices (search value), even after controlling for response selection difficulty, and during learning, it encodes the degree to which internal models of the environment and current task must be updated. dACC value signals are derived in part from the history of recent reward integrated simultaneously over multiple time scales, thereby enabling comparison of experience over the recent and extended past. Such ACC signals may instigate attentionally demanding and difficult processes such as behavioral change via interactions with prefrontal cortex. However, the signal in dACC that instigates behavioral change need not itself be a conflict or difficulty signal.

Despite many prominent reports relating dorsal anterior cingulate cortex activity (dACC), or rostral cingulate zone[1], to behavior and cognition both in health and disease[2], a general theory of its function remains elusive because no single factor links change in stimuli or behavior to neural activity. According to most current theories, dACC plays a key role in behavioral flexibility, but there are disputes about its specific contribution. Imagine you are exploring a complex environment when you encounter a valuable item (for example, an employment offer for a job-seeker or fruit for a foraging monkey). You may either engage with that item or ignore it if the environment is sufficiently rich to make trying elsewhere tempting or more valuable. In such situations, we argue that dACC signals information such as the average value of the environment (search value), influencing whether you continue your search, potentially entering a sequence of new actions, or remain with the item encountered[3]. dACC activity also reflects other information determining behavioral change, such as how well things have been going recently (average reward rate) over multiple time scales[4–6]. dACC activity also occurs when animals[7,8] or people[9] update models of the current task or environment so that new patterns of behavior can emerge. While evidence for encoding of such information in dACC activity is comparatively recent, there is already broad consensus that dACC activity in many species reflects outcomes of decisions—both successes and errors—and whether such feedback indicates a need for behavioral change[10–17].

By contrast, a prominent theory proposes that dACC "diversity can be understood in terms of a single underlying function: allocation of control"[18]. Arguably, it is nontrivial to identify exactly which process translates to control in many naturalistic settings. To return to our example, one could argue that continuing to explore and ignoring a tempting item encountered requires control, or one could equally argue that precisely the opposite behavior, engaging with the item encountered and ignoring distracting influences of potentially valuable alternatives, requires control. A third suggestion is that dACC signals the need for control when both options are almost identical in value[19]. Consequently, in one version of this account[18], foraging-related value signals are discussed as determining the value of exerting control[18]. However, a more recent version[19] questioned the existence of such signals in dACC and instead proposed that "dACC activity can be most parsimoniously and accurately interpreted as reflecting choice difficulty alone"[19].

Our argument is not that difficulty or conflict does not modulate dACC activity. Indeed such modulation is seen in most brain regions concerned with decision-making. Rather, we argue that difficulty or control allocation is insufficient to account for all dACC activity. Moreover, we argue below that the influence of difficulty or conflict on dACC signals may be a side effect of its role in evaluating behavioral change and model updating, not the other way around.

ACC and medial frontal anatomy in primates and rodents

Although human dACC has been suggested to be unique[20], its somatotopy[21,22] and activity coupling with other brain areas[1], which reflects anatomical connections[23], suggest important resemblances with monkey dACC (**Fig. 1**). A region's connectivity fingerprint is critical in constraining its function because connections determine the information regions receive and the influence they wield over other areas. Some of the areas dACC interacts with, such as frontal pole, have changed during evolution[24–26], but dACC's overall connectivity fingerprint remains similar in humans and other primates. Although there is no exact equivalent of primate dACC in rodents, there are similarities between the anatomy of primate area 24, of which dACC is a part, and area 24 in rodent ACC[27]. While rodent–primate ACC correspondences are not precise, they are stronger than for any granular prefrontal area[28].

In both humans and macaques, dACC is distinguished from adjacent medial frontal cortex such as the presupplementary motor area (pre-SMA). Although both pre-SMA and dACC share connections with, for example, dorsolateral prefrontal cortex (dlPFC)[29,30], dACC is

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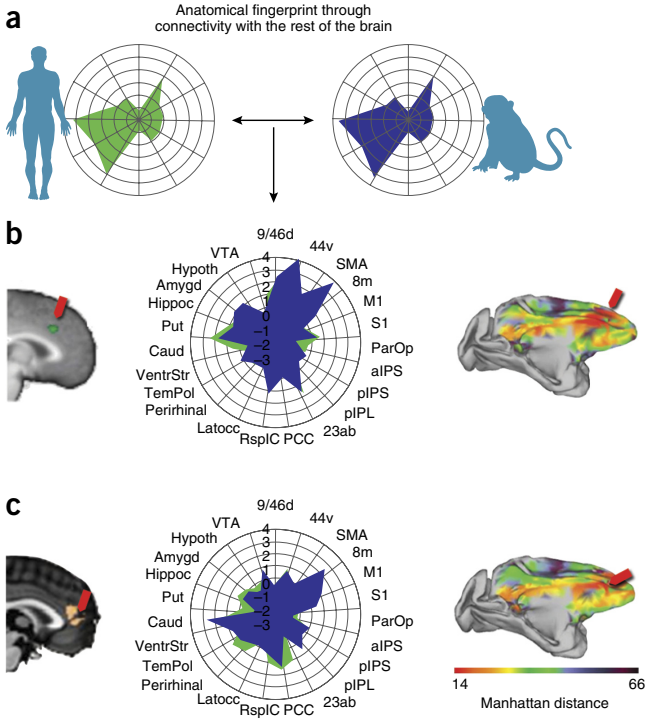

Figure 1 Comparing dACC and pgACC in humans and macaques. (**a**) To compare brain areas we first identify the unique connection fingerprint of the human area estimated from its fMRI-derived resting state activity correlations with other areas (left). There is strong positive coupling with an area when the green line is close to the circumference. The area with the best-matching fingerprint can then be identified in the macaque (right). Comparison of fingerprints suggests (**b**) dACC and (**c**) pgACC similarities in humans and macaques[1]. In each case, task-related human brain activity is shown on the left. dACC activity[11] is shown in **b**; **c** shows activity in pgACC covarying with participants' general willingness to forage amongst alternative choices despite costs[3]. The center shows connection fingerprints for the same areas based on a set of 23 key brain regions for the human (green) and best matching macaque area (blue). On the right, heat maps show fingerprint correspondence in the macaque frontal lobe. Color scale shows Manhattan distance, a metric of similarity, where red indicates strong correspondence and arrows indicate peak correspondence. dACC and pgACC have different patterns of connectivity, but areas corresponding to each are found in the macaque. Image adapted from ref. 1, National Academy of Sciences.

more strongly connected with subcortical regions coding reward and value. These regions include the amygdala[30], much of the striatum[31], dopaminergic and serotonergic transmitter systems[32] and adjacent ACC areas such as perigenual ACC (pgACC), the last of which in turn is notable for its ability to influence dopamine[30,33,34] via connections to the striosome. Also, unlike pre-SMA, dACC may exert direct influences over motor output; dACC projects to primary motor cortex and spinal cord[29]. Therefore, while we might expect dACC and pre-SMA to sometimes be coactive, perhaps with dlPFC, the different connections suggest this will not always be true. Furthermore, if we are interested in how value signals are translated into behavioral change and persistence, we should focus on dACC.

Value signals in frontal cortex and dACC

When monkeys make decisions, dACC neuron activity reflects choice value in terms of potential rewards and effort costs[35–41]. Sometimes value signals arise later than in other areas, such as orbitofrontal cortex, but other times they are more prevalent and arise earlier in dACC[35,41].

We are beginning to understand how value signals arise within dACC; they reflect the recency-weighted history of previously chosen rewards. dACC neurons have activity reflecting reward history with different time constants (**Fig. 2**)[4,6]. Such reward history signals reflecting different time constants are also detectable in human dACC, where they can be compared to predict future rewards and guide decisions to persist or change behavior[5]. Independent of difficulty effects, dACC can compute the value of persisting in the current environment, compared to the value of switching away from it[5]. Furthermore, dACC lesions impair the use of reward-history-dependent values to determine the balance between behavioral persistence and change[42].

Several additional lines of evidence demonstrate that value-related activity in dACC neurons is unrelated to response selection difficulty. For example, response selection becomes easier as monkeys progress through a sequence of actions toward a reward (i.e., accuracy increases and reaction times (RTs) decrease), but many dACC neurons increase their activity[43]. Moreover, despite repeated attempts, to our knowledge no efforts to identify dACC single-neuron activity encoding difficulty in monkeys have succeeded[10,44,45].

At least one study has claimed to find dACC neurons responsive to conflict or cognitive load in humans[46]. However, arguably the key contrast of behavioral conditions supporting the claim might reflect not just conflict but also the possibility of alternative courses of actions; increased neural activity is predicted by most theories if the contrast is between conditions varying in number of response associations, number of distracting alternative courses of action, and effort costs. However, after careful testing of a large sample of dACC neurons in monkeys in an experiment focusing directly on difficulty, not a single neuron actually encoding response difficulty *per se* was found[44]. Instead each neuron with activity related to a particular response became active whenever there was even partial evidence for that response. Therefore, neurons encoded actions or action values and may also have signaled alternative task goals, but never difficulty. However, as a result of such coding, many neurons became active in conflict situations, and their aggregate activity gave the impression of a difficulty signal that could not be dissociated from that expected from true difficulty neurons by a technique such as functional MRI (fMRI).

Similarly, Ebitz and Platt[45] pointed out that while dACC neurons reflected a potentially valuable goal that might become an alternative focus of monkey behavior (a function for which we argue dACC is critical), "action conflict signals were absent." As already noted, however, we are not really concerned with whether conflict or difficulty signals are present; instead we claim that any such effects are insufficient to explain away evidence of other signals in dACC. What is clear is that, in monkey dACC, value signals exist without clear relation to difficulty.

Of course value signals are also found beyond dACC: in parietal cortex, striatum, amygdala and the dopaminergic system. There has been a surprising tendency, however, to assert that value signals within frontal cortex exist only in ventromedial prefrontal cortex (vmPFC)[47]. However, at least three different 'vmPFC' regions show specific value and decision-related activity and have distinct roles in behavior: area 13 (ref. 48), area 14 (refs. 49,50) and pgACC (refs. 47,51,52) (**Fig. 3a**). It should therefore come as no surprise if value signals exist in other frontal areas, such as dACC. It is, however, likely that any value signals in dACC will, as elsewhere, have distinctive features.

Human dACC and the value of behavioral change

Neurophysiological experiments suggest individual dACC neurons carry value signals but that aggregate population activity also reflects

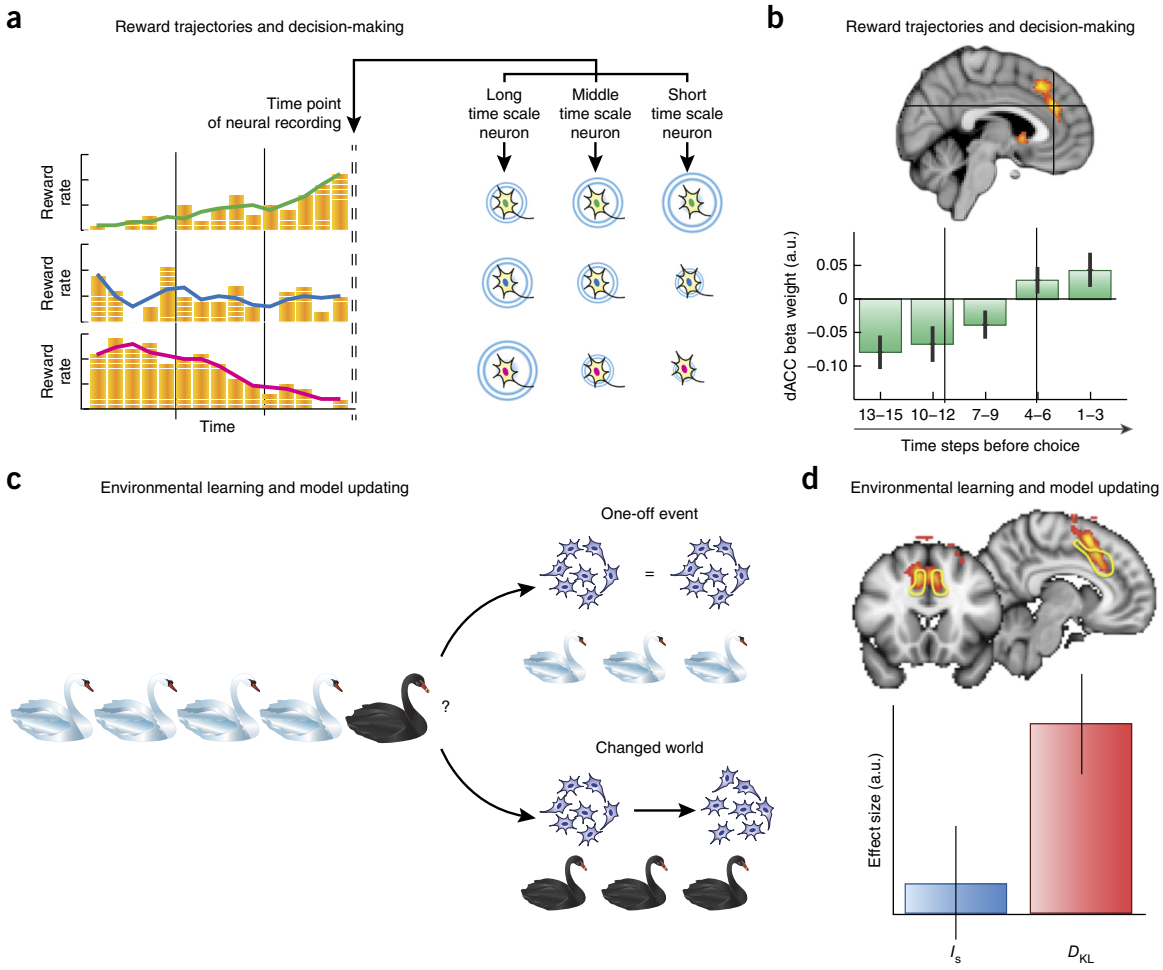

Figure 2 Derivation of value signals in dACC and presence of model-updating signals in dACC. (**a**) Deriving value signals from history of past rewards over multiple timescales. Left: choices' values are estimated from their reward history. Choices may initially be associated with low (few coins, green line), medium (blue) or high (magenta) values, but these values change over time. Right: neural activity in macaque dACC reflects reward history on different timescales, allowing simultaneous representation of value estimates over different time periods[4,6]. All other things being equal, neurons sensitive to reward over longer timescales will be more active when a choice is initially associated with high levels of reward (bottom) than low levels (top), and the opposite applies to neurons with short timescales. (**b**) Human dACC reflects reward history over different time scales simultaneously. The relative weighting of activity related to rewards received over different time scales suggests comparison of rewards over shorter and longer terms, allowing humans to project future expected reward trajectories[5]. (**c**) dACC is active when internal models are updated, not just when task difficulty increases because surprising events occur[9]. Imagine only observing white swans. The first time you see a black swan, should you ignore it as an outlier or update your model and expect black swans? Both scenarios are surprising and difficult to respond to, but only one leads to model updating. (**d**) Activity in dACC and adjacent pre-SMA reflects model updating (D_{KL}), not surprise (I_S). Mean effects (error bars show s.e.m.) shown for the dACC region of interest (yellow outline). Error bars indicate s.e.m. Images in **a** and **b** adapted from ref. 5, Nature Publishing Group. Images in **c** and **d** adapted from ref. 9, National Academy of Sciences.

difficulty. Two recent reports explain how an fMRI experiment should be conducted when there may be multiple influences on a brain area's activity[53,54]. Both focused on vmPFC rather than dACC. One factor was value and the other was decision confidence (approximately the inverse of difficulty[19,54]). Both factors influenced brain activity, and temporal evolution of their effect was visualized with a general linear model time-course analysis[54] (**Fig. 3b**).

An analogous approach has been used to identify activity related to the value of exploring an environment, a behavior called foraging[3]. Participants decided whether to engage with a default option or whether to explore alternative options. The decision to explore depends on the search value (average value of alternatives) and the engage value (value of the default options).

The experimental design and schedule ensured that search value and difficulty shared little variance (<2.5%). Therefore brain activity could be securely related to either difficulty or search value. Using whole-brain general linear model analysis, including control regressors of difficulty and log(RT), search value was linked with dACC (**Fig. 3e**). In addition, there was a smaller and later negative effect of engage value on dACC (**Fig. 3f**). Therefore, dACC has precisely the signals needed for determining the value of behavioral exploration. Marginally significant effects of difficulty and log(RT) occurred in dACC toward the end of the decision period (**Fig. 3g**). An equivalent analysis in which dACC activity was binned by search value or difficulty suggested similar conclusions (**Fig. 3f,g**). Difficulty effects may be stronger in or anterior to pre-SMA (**Fig. 3e**)[19]; many other experiments link pre-SMA and adjacent supplementary eye fields to difficult response selection[55].

Interpreting multiple signals in dACC

It can be difficult to know what conclusions to draw when different experiments provide conflicting evidence for presence or absence

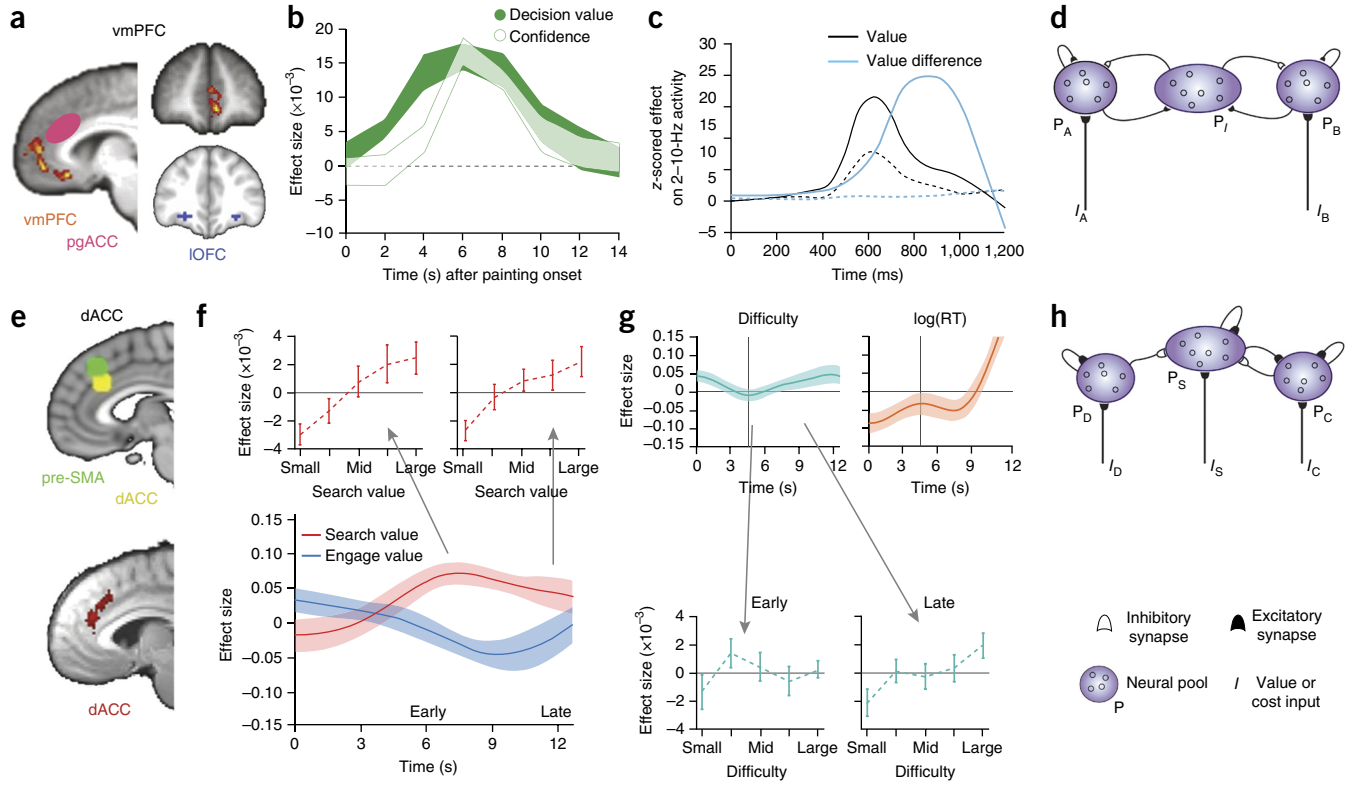

Figure 3 Comparing multiple value signals in vmPFC (top) and dACC (bottom) and decision-making processes. (**a**) Relative value difference (chosen – unchosen option value) signals in vmPFC[49] (orange) are distinct from reward activity in lateral orbitofrontal cortex (lOFC)[1,75] (blue) and pgACC[47] (magenta). (**b**) vmPFC reflects both value (green) and confidence (white)[54]. (**c**) vmPFC first reflects the sum (black) and then the difference between (blue) choice values (solid lines, correct trials; dashed lines, errors)[59]. (**d**) Diverse vmPFC signals are explained by a neural network model[58]. P_A and P_B are neuronal pools activated by option A or B value. Each pool has recurrent self-excitation and mutual inhibition, mediated by pool P_I, which instantiates the competitive value comparison process leading to a single attractor state for the chosen option. (**e**) Top: the dACC region of interest (yellow) is anatomically distinct from the region near pre-SMA, where difficulty effects are strong (green)[19]. Bottom: search value effects (red) are seen in dACC, even after controlling for difficulty and log(RT) (ref. 3). (**f**) fMRI time course of dACC shows search value (red) followed by engage value (blue) signals. (**g**) This occurs even after controlling for factors such as difficulty (blue) and log(RT) (red). Insets at top of **f** show activity binned by search value (clear effects at both beginning and end of trial). Insets at bottom of **g** show difficulty effects emerging only late in trial. Arrows show approximate times from which bins were drawn. (**h**) Network model of dACC. Distinct neural populations receive different value input and interact via mutual inhibition and excitation. Compared to the symmetric representation of different option values in **d**, this network model of dACC has a larger population representing environmental value (P_S) and is sensitive to environmental context. P_S interacts with a neural population, P_C, representing costs. Default value here is P_D. Error bars indicate s.e.m. in all panels. Image in **a** adapted from ref. 49, Elsevier. Image in **b** adapted from ref. 59, Nature Publishing Group. Images in **c** and **d** adapted from ref. 54, Nature Publishing Group.

of signals in dACC, but again we can find inspiration in the manner in which controversies regarding vmPFC activity have been resolved. Various experiments had suggested that during decision making vmPFC activity reflects the sum of values of possible choices, the choices' difference in value or simply the value of the choice ultimately taken[49,56,57]. A biophysical neural network model of the decision process[58] makes it possible to reconcile these claims and demonstrate that dACC activity may correspond to signals in a decision-making circuit generated at different time points during evolution of a decision[59] (**Fig. 3c**,**d**). Pools of neurons encode the value of each potential choice and become active in proportion to its value. Recurrent excitation between neurons in each pool and inhibition between pools ensures the network moves to an attractor state in which one pool, representing one option, remains active and a choice is made. Model activity reflects first the sum of choice values and then difference in choice values. High-temporal-resolution recordings show the same to be true of vmPFC (ref. 59).

Variants of this model are likely applicable in many cortical areas concerned with selection. Drawing on work linking comparator processes to dACC[57] and our own studies[3,24,25] we propose a neural network model of dACC (**Fig. 3h**) predicting presence of both value signals and difficulty effects. In such a hypothetical network, variance in activity is related first to search value and then, slightly later, to engage value. When these values are closer together the decision is difficult and the network takes longer to move into an attractor state. This means that, later during decision-making, variance in activity correlates with difficulty and RT even though there are no units explicitly signaling difficulty. Difficulty correlates arise because difficulty affects the temporal dynamics of the comparison process. Interestingly, this is the time-varying activity pattern observed in dACC (**Fig. 3f**,**g**). Note that, in the absence of high-temporal-resolution measurements, the properties and signs of predicted difficulty effects depend on assumptions made about the model and how it is reflected in the time-integrated fMRI signal. For example, if high-firing attractor states persist after the RT, one might see a negative effect of difficulty in fMRI, whereas if activity diminishes as soon as a threshold is crossed, one might expect a positive correlate. Either way, it is clear that merely measuring a correlate of difficulty does not mean an area's primary function is to signal difficulty.

Another prediction of such models is that if a decision is very easy, because options have very different values, then it may not be possible to detect value signals in the network's aggregate activity with a low-temporal-resolution technique such as fMRI. In some experiments examining very easy decisions[19], the brevity of the comparative process makes any detectable value effects in fMRI unlikely. Moreover, we know that faster and more efficient alternative selection mechanisms can be used if choices can be made with very simple heuristics[59]. In other words, no decision-related value signals are expected if there is no real decision to make.

Foraging, task switching and updating of internal models

Search value, the average value of an environment, is signaled in dACC. In many natural situations animals do not choose between simultaneously presented options but instead decide whether to engage with sequentially presented options as they are encountered[60]. Engaging incurs an opportunity cost because potential opportunities to pursue better options are lost. Therefore, search value signals (indexing potential opportunity costs) in dACC could guide foraging.

Importantly, our theory is not that dACC activity is simply synonymous with foraging value. Although, like others[61], we have drawn inspiration from consideration of foraging problems primates evolved to solve, many of the neuroeconomic decisions people make in modern environments involve similar factors. A job-seeker considering one position and forgoing alternatives is making a decision about opportunity costs. Similar signals could guide task switching. The opportunity cost of alternatives makes maintaining engagement in a particular task difficult, and so it should be possible to integrate search-value-related ideas into models of cognitive control that focus on dACC–dlPFC interactions[62,63].

By the same token, not every task with a link to naturalistic decision-making can be performed by dACC alone. pgACC activity is also related to participants' general willingness to forage amongst alternative choices despite costs[3] (**Fig. 1c**). In another recent experiment[47], without a requirement for search value to guide behavior (and therefore, perhaps not surprisingly, no dACC activity) the need to persevere or to continue engaging with the current environment again led to pgACC activity. Homologous regions are also involved in cost/benefit decision-making in monkeys and rodents[34,51,64].

dACC is also implicated in attention switching when it is driven by the updating of internal models of behavior[65]. In an fMRI experiment[9], two types of unexpected events occurred. On model-update trials, subjects responded to a target in an unexpected location and its color indicated that future targets would appear nearby. However, on surprise-only trials, differently colored targets in an unexpected location indicated one-off events and no need to update internal models of where future targets would appear. We quantified and carefully dissociated model updating and difficulty of responding in this experiment. Difficulty is equivalent to the surprise associated with a particular target location, as characterized by its Shannon information, I_S. Model updating is captured by the Kullback-Leibler divergence (D_{KL}) between the posterior and the prior probability estimates of target location. dACC activity occurred on update trials, as a function of D_{KL}, but not on surprise-only trials, even though both were associated with RT increases (**Fig. 2c**,**d**). Once again, behavioral change-related activity is found in dACC, but difficulty itself has little explanatory power. Detailed descriptions of rodent ACC neuron activity during discarding and updating of internal models have also been reported[7,8].

Lesions and inactivation of dACC

Stay or switch decisions might sometimes be difficult, but investigations of dACC disruption in humans and macaques have revealed complicated impairments that cannot be related to difficulty in a simple way[66–69]. Unlike lesions to other frontal areas, dACC lesions have little impact on cognitive control; instead impairments are most prominent when decisions concern assessment of the relative value of behavioral persistence versus change[42,70,71]. Perhaps the most striking deficits seen after bilateral lesions, even when limited to the ventral bank of the cingulate sulcus, are failures to act at all[72]; it is difficult to account for such dramatic effects with subtle arguments about detecting difficulty. Such profound failures are, however, expected if an average sense of the value of possibilities afforded by the environment is lost.

Summary and future directions

dACC is active during decisions and when outcomes are assessed. Value, model updating and outcome-related activity in dACC have in common that they all regulate behavioral adaptation and persistence. Although behavioral adaptation may, in turn, entail difficult response selection, it is now clear from the work of several laboratories, using both single neuron recording[73] and fMRI[74], that dACC activity reflects the value of behavioral change and not just its difficulty. Moreover, the actual process of behavioral adaptation may be implemented not just in dACC but through dACC's interactions with dlPFC[62,63].

Surprisingly, despite considerable debate about dACC, there have been few attempts to understand adjacent ACC regions. Understanding the precise anatomical arrangements of activity patterns is important because sometimes differing views of function can be reconciled by focusing on different subdivisions of medial frontal cortex. As we have noted (**Fig. 3**), value and difficulty effects are prominent in adjacent but different areas. Understanding dACC in the context of interactions with neighboring areas such as pgACC will be important. Ecological foraging theory suggests additional ways of thinking about the kind of decisions we evolved to solve, and this can be exploited to design new decision-making experiments that may clarify ACC activity. Interpreting neuroimaging studies of dACC, however, will only be possible in combination with computational models that make predictions about the temporal dynamics of activity and not just about its presence or absence (**Fig. 3**). Finally, detailed neurophysiological and lesion studies, as well as inactivation studies, will be needed to aid interpretation of human neuroimaging studies of dACC.

COMPETING FINANCIAL INTERESTS

The authors declare no competing financial interests.

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