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2 **Debates on the dorsomedial prefrontal/dorsal anterior** 3 **cingulate cortex: insights for future research**

4 Nicolas Clairis¹ and Alizée Lopez-Persem²

5 **Abstract**

6 The dorsomedial prefrontal cortex/dorsal anterior cingulate cortex (dmPFC/dACC) is a brain area
7 subject to many theories and debates over its function(s). Even its precise anatomical borders are
8 subject to much controversy. In the past decades, the dmPFC/dACC has been associated with more
9 than fifteen different cognitive processes, which sometimes appear quite unrelated (e.g., body
10 perception, cognitive conflict). As a result, understanding what the dmPFC/dACC does has
11 become a real challenge for many neuroscientists. Several theories of this brain area's function(s)
12 have been developed, leading to successive and competitive publications bearing different models,
13 which sometimes contradict each other. During the last two decades, the lively scientific exchanges
14 around the dmPFC/dACC have promoted fruitful research in cognitive neuroscience. In this
15 review, we provide an overview of the anatomy of the dmPFC/dACC, summarize the state of the
16 art of functions that have been associated with this brain area, and present the main theories aiming
17 at explaining the dmPFC/dACC function(s). We explore the commonalities and the arguments
18 between the different theories. Finally, we explain what can be learned from these debates for
19 future investigations of the dmPFC/dACC and other brain regions' functions.

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11 **Running title:** Debates on dmPFC/dACC

12
13 **Keywords:** dACC; dmPFC; cognitive control; foraging value; hierarchical error representation

14 **Abbreviations:** dACC = dorsal anterior cingulate cortex; dmPFC = dorso-medial prefrontal
15 cortex; EVC = expected value of control theory; FVT = foraging-value theory; HER = hierarchical
16 error representation model; MSV = multiple signals view; PRO = predicted response-outcome
17 model

18 19 **Introduction**

20 In their impossible quests for the “philosophers’ stone” and the “*quinta essentia*”, alchemists made
21 many discoveries that are still widely in use. For instance, in the XIVth century, the French
22 Franciscan Jean de Roquetaillade, while searching for the “*quinta essentia*”, an “incorruptible”
23 substance that would not depend upon water, air, fire or earth, discovered the *aqua vitae*, a highly
24 concentrated solution of almost pure ethanol, that he sought would keep people in good health.
25 Unraveling the function(s) supported by some brain regions can sometimes appear a quest as
26 impossible as the alchemists’ quest. Still, the discoveries it may lead to can be just as fruitful. A
27 brain region located between the dorsomedial prefrontal cortex (dmPFC) and the dorsal anterior

1 cingulate cortex (dACC), has been the focus of many studies in the last two decades. This brain
2 area roughly corresponds to a cluster of activity commonly observed in functional neuroimaging
3 studies (Figure 1C). It reflects the average brain activity of a group of subjects and lacks precise
4 anatomical boundaries. Depending on studies, it has been labeled with at least ten different names,
5 which either refer to the cingulate cortex¹⁻¹⁶, to the prefrontal cortex^{4,16-23}, or to motor actions^{1,2,24-}
6 ²⁶. Because this brain area pertains to a functional cluster that overlaps both the cingulate gyrus
7 and frontal lobe, and lacks clear anatomical boundaries, we chose to designate it as the
8 dmPFC/dACC area. This label denotes its location in a general sense, encompassing both the
9 dmPFC and dACC regions. The dmPFC/dACC is involved in a wide range of cognitive functions,
10 such as time estimation²⁷⁻²⁹, body perception^{6,30}, computing foraging value^{2,31}, processing aversive
11 events³², or processing conflict³³, which partially overlap. Many scientists have attempted to unify
12 these functions into a single theory, resulting in numerous theories and models over the last three
13 decades. In the present review, the main unifying theories of the dmPFC/dACC will be explored
14 with particular emphasis on three major models (see ³⁴ for a more exhaustive list). These include
15 the error likelihood model³⁵, which has since developed into the predicted response-outcome
16 (PRO) model^{20,36,37} and the hierarchical error representation (HER) model^{3,38}, the conflict
17 monitoring theory^{33,39}, which was further developed into by the expected value of control (EVC)
18 theory⁹ and the foraging value theory⁴⁰. However, very early on, some researchers argued that it
19 would be impossible to identify one single theory that would be able to summarize all the functions
20 of the dmPFC^{4,7}. We will refer to this fourth view as the Multiple Signals View (MSV), which
21 differs from the others as it is not a unifying theory per se.

22 The various theories (HER/foraging value/EVC) and views (one vs. multiple signals) regarding
23 the role of the dmPFC/dACC have sparked a series of antagonist publications, which will be
24 reviewed here. First, we will provide an overview of the diverse signals observed in the
25 dmPFC/dACC and briefly introduce the theories that attempt to explain these findings. Next, we
26 will present the key points of agreement and of conflict between these different theories.

27

28

1 **Multiple signals for an anatomically ill-defined brain region**

2 **a) Anatomical discrepancies in what is the dmPFC/dACC**

3 One first difficulty in solving the different conflicts over the dmPFC/dACC function(s) is its
4 anatomical definition. Anatomical borders of clusters of activity in this brain area are ill-defined
5 and vary from one study to another. Furthermore, there is considerable inconsistency in how this
6 area is labeled, both between laboratories and sometimes even within the same laboratory across
7 different publications. Therefore, to develop a comprehensive theory of the dmPFC/dACC
8 function, it is essential to establish a consensus on the anatomical description of this cluster.
9 Otherwise, there is a possibility of referring to different brain areas using the same label or using
10 different labels for the same brain area. This becomes critical when researchers make reverse
11 inferences based on the assumption that the activation of a brain region associated with a particular
12 function implies the involvement of that cognitive process⁴¹.

13 For the sake of clarity in brain region labeling, in the current review, we first define four main
14 brain regions that surround the dmPFC/dACC (Figure 1): the pre-supplementary motor area (pre-
15 SMA) and the dorsomedial prefrontal cortex (dmPFC), which both belong to the frontal cortex
16 (Figure 1A) and the dorsal anterior cingulate cortex (dACC) and mid-cingulate cortex (MCC),
17 which belong to the cingulate cortex. These four brain regions can be defined anatomically (Figure
18 1B), or functionally (i.e., according to how activity peaks have been labelled by researchers in
19 functional neuroimaging studies, Figure 1C).

20 The functional dmPFC/dACC, as we observe it in the literature, seems to partially overlap those
21 four areas, along the cingulate sulcus (Figure 1C). It roughly corresponds to the junction between
22 Brodmann areas 4, 6, 24, and 32⁴². As with many other brain regions, its functional definition
23 implies that its name and location can vary between studies. This area has, for example, been called
24 the **anterior cingulate cortex (ACC)**¹⁻⁴, or **dorsal anterior cingulate cortex (dACC)**⁹⁻¹⁶,
25 referring to its location above the corpus callosum and close to the anterior part of the cingulate
26 cortex. Similarly, others have called it the **mid-cingulate cortex (MCC)**^{5,6,8,43} or **dorsal anterior**
27 **mid-cingulate cortex (daMCC)**⁷, referring to the fact that the neuronal morphology differs
28 between the anterior and the middle areas of the cingulate cortex (with a transition of laminar
29 thickness located dorsally to the genu of the corpus callosum)^{8,43,44}. Other studies also labeled it

1 **posterior fronto-medial cortex (pFMC)**^{22,23}, **medial prefrontal cortex (mPFC)**²⁰, or **dorso-**
2 **medial prefrontal cortex (dmPFC)**^{4,16–19}, referring broadly to its spatial location within the
3 prefrontal cortex. Finally, others labeled it with a functional name as **pre-supplementary motor**
4 **area (pre-SMA)** referring to its proximity (anatomically and functionally) with the supplementary
5 motor area (SMA)^{2,24}, or even as **supplementary motor area (SMA)**^{25,26}.

6 These labeling discrepancies are problematic because some of the aforementioned names refer to
7 areas with a specific profile regarding their anatomy^{8,43,45}, function^{1,2,5,46,47}, neurometabolism^{48–50},
8 and anatomical⁵¹ and functional connectivity^{52–56}. These discrepancies cause even more trouble
9 when attempting to investigate homologous brain regions in animal studies⁸. Furthermore,
10 inconsistencies in anatomical labeling can cause great confusion, especially when coordinates and
11 figures of the cluster location are not displayed, leading to uncertainty regarding whether one refers
12 to the same brain area or not. Therefore, for simplicity's sake, we adopted the term dmPFC/dACC.
13 Although, we acknowledge that this label is debatable, there is still no ideal label to mention this
14 brain area, when observed as a group-level activity cluster.

15 Moreover, note that the presence or absence of a paracingulate sulcus (pcgs) could greatly impact
16 the exact location of the functional clusters related to the dmPFC/dACC activity⁵. While all healthy
17 subjects possess a cingulate sulcus in both hemispheres, only 60% of people have a pcgs in the left
18 hemisphere and 40% in the right hemisphere⁵⁷ (**Figure 1B**). Although the impact of pcgs presence
19 on exact anatomical location of the dmPFC/dACC cluster has not been extensively studied, more
20 studies are now considering it⁵⁸. Better taking into account individual anatomy in functional
21 magnetic resonance imaging (fMRI) preprocessing software programs could help reconcile studies
22 with differences in the MNI coordinates of observed dmPFC/dACC clusters.

23 **b) A diversity of signals in the dmPFC/dACC**

24 Understanding what the dmPFC/dACC does is a challenge. Indeed, the dmPFC/dACC has been
25 linked to a tremendous number of functions^{59,60}. The dmPFC/dACC is one of the brain areas more
26 commonly activated across brain imaging studies⁶¹ which has even led some researchers to state
27 with humor that the cingulate cortex does everything⁶². Given the number of functions associated
28 with the dmPFC/dACC, one could hardly pretend not to have missed one in the literature. As stated
29 by other researchers, “*we all see something different in it, and what we see may tell us more about*

1 *ourselves-and our research priorities-than about the function of the region*"⁶³. Without pretending
2 to provide an exhaustive list, we provide here a list of some of the functions that have been related
3 to the activity of this cluster (Figure 2):

4 ***Time perception***: The dmPFC/dACC activity is associated with time perception^{27,29,64}. Its different
5 subparts are tuned to different durations in chronotopic maps²⁸.

6 ***Bodily representation***: Different parts of the dmPFC/dACC seem tuned to different parts of the
7 body in motor maps^{6,30}.

8 ***Uncertainty***: The dmPFC/dACC activity correlates with the volatility of the environment⁶⁵, with
9 choice uncertainty, reflected in choice difficulty^{23,66,67}, and also in encoding different learning rates
10 according to the volatility of the environment, with different subparts of the dmPFC/dACC tuned
11 to different learning rates⁶⁸.

12 ***Goal-directed behavior variables***: Many studies have tried to explain the role of the dmPFC/dACC
13 in goal-directed behavior. Some of these results contradict each other, while others suggest that
14 the dmPFC/dACC could encode several variables independently during value-based decision-
15 making. For example, the dmPFC/dACC activity has been associated with negative subjective
16 value^{69,70} and more generally in response to any type of aversive stimulus, including both **non-**
17 **painful and physically painful aversive stimuli**³², or even social rejection⁷¹. It is also associated
18 with the integrated net value^{14,18,72}, saliency⁷³, **physical effort anticipation and exertion**^{25,74-76},
19 **physical fatigue**⁷⁷, **cognitive control exertion**³³, the **expected value of exerting cognitive**
20 **control**⁹, the **difference between the value of exploring the environment and the value of**
21 **keeping with the ongoing behavior**³¹, **choice difficulty**^{23,66,67} and also **prediction-errors** and
22 **surprise**⁷⁸⁻⁸².

23 ***Model-updating***: To navigate our environments, we build internal models of the world. It has been
24 shown that the dmPFC/dACC gets more active when these internal models need to be updated
25 based on external events^{83,2}.

26 ***Autonomic sympathetic activity***: The dmPFC/dACC BOLD activity has been consistently
27 associated with heart-rate variability⁸⁴⁻⁸⁷ and pupil diameter size^{17,74,88-92} (see ⁹³ for a more
28 exhaustive review).

1 c) Anatomical overlap, convergences, and divergences of the previous 2 results

3 Interestingly, when looking at the common voxels activated by all these concepts through a meta-
4 analytic approach based on Neurosynth, we found clusters located in the dmPFC/dACC, the
5 bilateral anterior insula, and in the right dorsolateral prefrontal cortex (Figure 2). Note that the
6 identified cluster in this meta-analysis is somewhat posterior and does not cover the whole cluster
7 usually observed in fMRI studies, which is displayed in Figure 1C. Nevertheless, this result
8 confirms that all these different processes recruit the dmPFC/dACC. Some of these functions
9 sometimes overlap or even contradict each other.

10 *Overlaps:* It has been suggested that the mere correlation between the dmPFC/dACC activity and
11 uncertainty can be explained by the exertion of cognitive control by the dmPFC/dACC¹³.
12 Similarly, it has been suggested that the correlation between the dmPFC/dACC activity and time
13 reflects cognitive control processes⁹⁴. Another striking example is the case of pain. The dmPFC
14 and the ventral ACC are often activated in situations that trigger pain^{95–98}. Neurons in the cingulate
15 cortex respond to physical pain⁹⁹, making it part of the “pain matrix”¹⁰⁰. However, cingulotomy, a
16 treatment for chronic pain syndrome¹⁰¹, was abandoned, due to inconsistent results and personality
17 changes¹⁰¹. Neuroimaging studies are mostly correlational, and not causal. Because a given brain
18 area is recruited when a specific cognitive function is operating does not necessarily mean that the
19 brain area is performing that cognitive process. Stimulating neurons in the human dmPFC and the
20 adjacent ACC did not cause pain^{99,102}, suggesting that this area activity is triggered by painful
21 stimuli rather than causing the subjective sensation of pain. It was therefore proposed that the
22 dmPFC/ACC activity is elicited by any salient stimulus that requires a reaction¹⁰⁰.

23 *Contradictions:* The dmPFC/dACC has been related to **negative subjective value**^{69,70}, to the
24 **integrated net value**^{14,18,72} and to **saliency**⁷³. These three claims are not compatible with each
25 other. One states that the dmPFC/dACC activity should increase when anticipating more aversive
26 events, the second that it should increase with the anticipation of more positive events therefore
27 promoting the execution of a motor action when the net value is appetitive¹⁰³ and the last that it
28 should increase with the exposure to both positive and negative events.

29 In summary, given the number of findings related to the dmPFC/dACC, gathering all the literature

1 into one single theoretical framework of the dmPFC/dACC activity thus appears as an unsolvable
2 issue. However, this multiplicity of results has called for the development of theories, each aiming
3 at reducing the number of dimensions associated to the dmPFC/dACC, either by explaining all, or
4 at least part of the functions associated to it.

6 **A multiplicity of theories of the dmPFC/dACC**

7 Studying the brain at a finer scale could reveal specific anatomical areas that have different
8 connectivity and activity despite their proximity therefore explaining the wide range of functions
9 correlated with the dmPFC/dACC. Alternatively, one tempting approach is to unite them under a
10 single theory of the dmPFC/dACC's function (Figure 3). The functional overlaps between some of
11 the functions related to the dmPFC/dACC confirm the validity of this “one theory to rule them all”
12 approach, however, note also that, as proposed by the multiple signals view (MSV), some of these
13 functions are independent and could be encoded in parallel by the dmPFC/dACC. Some of the
14 more influential theories of the dmPFC/dACC will be briefly exposed below.

15 **Cognitive control theories**

16 *Conflict detection and Information theory:* Only a few years after the invention of functional
17 magnetic resonance imaging (fMRI) in the 1990s, Cohen's team started gathering evidence that
18 the dmPFC/dACC was involved in conflict detection and conflict monitoring by using fMRI. A
19 series of publications revealed that the BOLD activity of the dmPFC/dACC increased in situations
20 involving higher levels of difficulty and conflict^{11,12,104-108} leading them to build up the **conflict-**
21 **monitoring theory** of the dmPFC/dACC. They also showed that the dmPFC/dACC BOLD
22 activity increased when errors were detected^{105,109}. As Botvinick and colleagues mentioned, “*The*
23 *occurrence of pain and feedback indicating error commission fall into the same class of signals*
24 *as conflict, all of which indicate that the current distribution of attention is failing to prevent*
25 *negative outcomes.*”³⁹. In other terms, the dmPFC/dACC becomes more active in **situations**
26 **requiring behavioral adjustment**, due to an increase of cognitive conflict, or aversive outcomes.
27 This increase in dmPFC/dACC activity would then trigger increased activity in the dorsolateral
28 prefrontal cortex (dlPFC), which is assumed to implement cognitive control to adjust behavior¹⁰⁷.

1 Grounded on the conflict monitoring theory, Fan later built the **information theory** of the
2 dmPFC/dACC. In this theory, the main role of recruiting cognitive control is to deal with
3 uncertainty by trying to reduce it to a manageable level allowing to react appropriately¹¹⁰. The role
4 of the dmPFC/dACC is to detect situations where uncertainty is high and could be reduced by the
5 application of cognitive control by the dlPFC. Within this theory, conflict processing consists in a
6 subcase of an increase in uncertainty which drives the recruitment of the dmPFC/dACC¹¹¹. This
7 would explain why the dmPFC/dACC has been associated with both cognitive control and
8 uncertainty. Thus, it was suggested that the dmPFC/dACC was broadly recruited by situations
9 related to more uncertainty¹¹¹.

10 *Expected value of control (EVC)*: Later, Shenhav, Botvinick and Cohen developed a new theory
11 called the **expected value of control (EVC) theory**⁹. Applying more cognitive control is
12 subjectively costly as cognitive control goes along with a sensation of mental effort. While the
13 conflict theory does not take the cost of cognitive control into account, the EVC theory states that
14 one will spend cognitive control only when the EVC computation suggests that doing so is worth
15 the effort. The EVC theory posits that the dmPFC/dACC detects situations where the
16 implementation of more cognitive control would be beneficial, despite its cost. Based on the result
17 of the EVC computation, the dmPFC/dACC will then eventually recruit the dlPFC to implement
18 cognitive control. Situations involving conflict between multiple responses can induce a change in
19 EVC (due to potential changes in control demands), and therefore the potential allocation of
20 cognitive control.

21 **Error-likelihood theories**

22 A wide range of evidence shows that the dmPFC/dACC activity increases in response to unsigned
23 prediction errors (also referred to as surprise)^{58,79,81,112–114} and to error detection^{92,115–117}. This led
24 to the development of the error-likelihood theories of the dmPFC/dACC.

25 *Error likelihood model*: Brown and Braver developed the **error likelihood model** in 2005³⁵. This
26 model posits that the dmPFC/dACC is involved in computing the likelihood of committing an
27 error, even in cases with no error or response conflict. This theory states that the dmPFC/dACC
28 activity level would serve as an early-warning signal for other brain areas to detect when cognitive
29 control needs to be implemented based on the predicted level of errors associated with a given
30 context.

1 *Predicted response-outcome model and Hierarchical error representation model*: Later on, in
2 2010-2011, Alexander and Brown made this model evolve into the **predicted response-outcome**
3 **(PRO) model**^{36,37,118}. The central aspect of the PRO model is that the dmPFC/dACC computes the
4 various possible outcomes related to a given set of actions to allow for action selection. Then, at
5 the time of the feedback, the dmPFC/dACC would compute the difference between the prediction
6 and the actual outcome (prediction error) to update its internal models of the world.

7 A few years later, in 2015, Alexander and Brown updated their PRO model to the **hierarchical**
8 **error representation (HER) model**³⁸. The HER model shares the same principles as the PRO
9 model but it specifies its anatomo-functional organization by including hierarchic prediction errors
10 organized in a rostrocaudal gradient depending on the level of the prediction error. Sensory and
11 concrete prediction errors would be encoded rostrally, while more abstract and theoretical
12 prediction errors, for example, at the level of rules, would be encoded caudally⁸². The HER model
13 also assumes that the dmPFC/dACC and dlPFC interact bilaterally. The dmPFC/dACC prediction
14 error signals would drive learning by the dlPFC, while the dlPFC would modulate specific
15 predictions generated by the dmPFC/dACC. The role of the dlPFC would be mostly to maintain
16 in working memory a representation of stimuli that reliably co-occur with prediction errors, while
17 the dmPFC/dACC generates these prediction errors³⁸.

18 Brown and Alexander also developed another modified version of the PRO model named the PRO-
19 control model¹¹⁹. This variant incorporates both a proactive control signal and a reactive control
20 signal. The proactive control signal inhibits actions that lead to aversive outcomes because they
21 entail a high risk. While this proactive signal was originally present in the PRO model, the authors
22 extended its functionality by including the capacity to stimulate actions leading to desirable
23 outcomes through excitatory projections to the dorsolateral prefrontal cortex. On the other hand,
24 the reactive control signal is derived from the computation of negative prediction errors, allowing
25 it to rapidly and temporarily inhibit the future selection of actions that previously led to undesirable
26 outcomes.

27 **Foraging-value theory**

28 Rushworth, Kolling and colleagues, aiming to apply optimal foraging models of ecology to
29 humans, demonstrated that the dmPFC/dACC was involved in the value of foraging the
30 environment instead of exploiting the current patch^{31,40}. The foraging value theory (FVT) is

1 inspired from behavioural ecology¹²⁰ and considers that many naturalistic situations do not involve
2 two well-defined options as it is often the case with binary choice tasks conducted in laboratory
3 settings. In this vein, the FVT considers that individuals constantly weigh the option of exploiting
4 an ongoing option (such as a default option) against the possibility of switching to explore other
5 alternatives, when making decisions about which action to take. This theory has received some
6 support in non-human primates' electrophysiological recordings of the dmPFC/dACC^{121,122}, and
7 other similar accounts by neuroimaging studies in humans showing that the dmPFC/dACC activity
8 increases to signal the need to switch from exploitation to exploration of the environment^{19,123,124}.
9 In the framework of this theory, the dmPFC/dACC would monitor the value of alternative actions
10 and compare them to the current action to indicate when going back to foraging is more valuable
11 than keeping with the ongoing action. In addition, research has shown that the dmPFC/dACC is
12 also involved in processing physical fatigue⁷⁷. While traditional views of fatigue solely focused on
13 muscular exhaustion, recent studies propose that fatigue may also involve the computation of
14 opportunity cost^{125–128}. This account is compatible with the FVT, as it states that dmPFC/dACC
15 activity should increase with opportunity cost, *i.e.*, when switching from the current behaviors to
16 alternative ones is more rewarding. However, Rushworth and colleagues do not claim that this
17 theory can account for all dmPFC/dACC activity, they do propose that foraging-value encoding is
18 just one of the multiple functions performed by the dmPFC/dACC¹.

19 **Multiple signals view (MSV)**

20 As aforementioned, foraging-value encoding is but one of the functions attributed to the
21 dmPFC/dACC by the upholders of the FVT. They, as well as other researchers (see ^{7,129} for
22 instance), propose that not all the dmPFC/dACC-related activity can be summarized by a single
23 theory. This view states that the dmPFC/dACC neurons may have distinct roles depending on the
24 ongoing task and brain networks at work. The multiple signals view (MSV) could also be
25 understood as a multiple functions view. Indeed, it proposes that the dmPFC/dACC not only
26 represents multiple signals, but also that it implements different functions depending on the context
27 and task at hand. While a unifying theory implies that multiple signals can be conveyed to the
28 dmPFC/dACC area and integrated according to its main single function, the MSV proposes that
29 this brain region can compute several independent functions simultaneously (either in parallel or
30 based on the current task requirements). This view is supported by considerable evidence about a

1 vast range of distinct functions that are related to ACC and dmPFC activity in humans^{2,31,65,130}, in
2 non-human primates¹³¹ and rodents^{132–134}, which have been summarized in several reviews^{15,53,135–}
3 ¹³⁸. The MSV suggests that rather than searching for a single theory to explain all dmPFC/dACC
4 activity across all paradigms and situations, it is better to document the independent functions of
5 the dmPFC/dACC depending on the situation.

6 7 **Agreements and conflicts around the role(s) of the** 8 **dmPFC/dACC**

9 As seen in previous sections, the dmPFC/dACC is associated with multiple cognitive functions,
10 with some overlap, suggesting that different theories may explain some of these functions. Many
11 teams have tried to demonstrate how these theories explain the observed results in the literature
12 (Figure 3). Some researchers have even compared the different theories to determine which one is
13 better. The next section explores the commonalities and criticisms/conflicts between these
14 theories.

15 **a) Agreements**

16 **The dmPFC/dACC has a key role in goal-directed behavior**

17 *Selecting optimal actions to increase reward rate*

18 One striking aspect of all the theories outlined in the previous section is their agreement that the
19 dmPFC/dACC plays a key role in goal-directed behavior. Indeed, they concur that the
20 dmPFC/dACC activity is stimulated by behaviors involving pursuing or achieving goals. In the
21 case of the FVT, the dmPFC/dACC signals when it is more beneficial to return to foraging instead
22 of continuing with the current behaviour, to improve the utility of the current behavior. The conflict
23 theory posits that the dmPFC/dACC activity indicates when an ongoing task induces cognitive
24 conflict (such as determining the correct answer in a Stroop task) that must be dealt with to sustain
25 a good reward rate. The EVC theory proposes that the dmPFC/dACC calculates the value of
26 spending more cognitive control based on the integration of various signals, including the cost of
27 cognitive control and the expected reward from increasing cognitive control. The information
28 theory also contends that the dmPFC/dACC activity identifies situations with high uncertainty that

1 can be reduced by applying more cognitive control. Increasing cognitive control decreases
2 uncertainty and increases reward rate by providing a better understanding of the world, which is
3 corroborated by previous findings in which the dmPFC/dACC activity is triggered when internal
4 models of the world need updating². The error likelihood, the PRO and the HER models also all
5 assert that the dmPFC/dACC enables the updating of internal models of the world by computing
6 prediction errors at different levels, thereby increasing the likelihood of selecting optimal actions
7 over time.

8 ***Integration of multiple signals***

9 Furthermore, as would be expected by a brain region related to goal-directed behavior, all models
10 indicate that the dmPFC/dACC integrates multiple signals. The HER model proposes that the
11 dmPFC/dACC integrates prediction errors across a broad spectrum of tasks, as evidenced by
12 several paradigms involving pain, cognitive control or visual perception^{58,82}. This finding was also
13 supported by a meta-analysis on prediction error⁷⁹. The FVT and the EVC theories also propose
14 that the dmPFC/dACC integrates costs (i.e., the cost of foraging in the case of FVT, the cost of
15 performing cognitive control in the case of EVC) and benefits (i.e., the expected mean reward rate
16 if one starts foraging for the FVT, the expected reward from increasing cognitive control for the
17 EVC) allowing to increase one's utility by adapting behavior (i.e., either through switching from
18 exploitation to exploration in FVT, or by triggering cognitive control in EVC).

19 In addition to the consensus among the different theories regarding the link between the
20 dmPFC/dACC and goal-directed behavior, several other lines of research provide further evidence
21 supporting the predominant role of the dmPFC/dACC in goal-directed behavior.

22 ***Task variables correlated with dmPFC/dACC activity relate to goal-directed behavior***

23 It is remarkable that the majority of variables that have been related to the dmPFC/dACC activity,
24 as discussed in the section *Multiple signals for an anatomically ill-defined brain region*), are
25 directly or indirectly related to goal-directed behavior. While a few of these variables, such as
26 chronotopic maps, may not have an immediate and apparent connection to goal-directed behavior,
27 most other functions, including model updating (for efficient goal achievement), body maps
28 (enhancing locomotor activity towards goals), and triggering autonomic nervous system
29 (facilitating effort expenditure) can be easily linked to goal-directed behavior.

1 ***Other theoretical accounts of the dmPFC/dACC function(s) relate to goal-directed behavior***

2 Other models of the dmPFC/dACC that we didn't develop in this review also propose a direct link
3 between the dmPFC/dACC and goal-directed behavior. For example, the hierarchical
4 reinforcement learning (HRL) model posits that the dmPFC/dACC is an essential node for
5 initiating, maintaining and organizing a sequence of goal-directed actions based on a hierarchical
6 reinforcement learning¹³⁹; the volatility model proposes that the dmPFC/dACC adapts learning
7 rate based on the detected volatility of the environment⁶⁵; and the Reward Value and Prediction
8 Model (RVPM) suggests that the dmPFC/dACC predicts the value of future outcomes when
9 reward is at stake¹⁴⁰.

10 ***Lesions to dmPFC/dACC alter goal-directed behaviors***

11 Studies of human brain lesions have revealed that unilateral¹⁴¹ or bilateral^{142,143} anterior cerebral
12 artery occlusion, which typically affect the dmPFC/dACC and the ACC, can result in akinetic
13 mutism, a phenomenon characterized by a loss of motivation to speak or to move, despite the
14 patients retaining full consciousness¹⁴⁴. Although reflexes and physical capacity to exert actions
15 remain relatively intact in these patients, lesions affecting the dmPFC/dACC generally engender a
16 decrease in their desire to act (volition) and their sense of responsibility (agency)¹⁴⁵. Recently,
17 another study has also found that lesions in the dmPFC/dACC regions of frontotemporal dementia
18 patients can lead to an increased aversion to perform efforts compared to healthy participants¹⁴⁶.

19 ***Stimulations of the dmPFC/dACC induce an "urge" to act***

20 Electrical stimulation of dmPFC/dACC intracranial electrodes in implanted epileptic patients
21 provokes an "urge" to act in a goal-directed manner, either to protect oneself or to move towards
22 a goal^{46,147,148}, again confirming the involvement of the dmPFC/dACC in goal-directed behavior.
23 Nevertheless, quite surprisingly, many patients under stimulation were not necessarily capable of
24 explaining towards which goal they were acting or why they were acting the way they were
25 acting⁴⁶, suggesting that the dmPFC/dACC can trigger a chain of actions, based on goal values
26 defined in other parts of the brain.

27 In summary, all these theories attribute a role to the dmPFC/dACC in goal-directed behavior and
28 adaptive fitness, and this is supported by numerous findings in the literature, including studies of
29 lesions and electrical stimulation in humans. However, the means by which the dmPFC/dACC

1 achieves this function and the variables it computes to do so vary greatly among theories.

2 **The dmPFC/dACC activity reflects the need for a change**

3 Another clear agreement is that when the dmPFC/dACC is more active, adaptation seems
4 necessary^{2,93,149,150}. In the case of the FVT, adaptation corresponds to a switch from exploitative
5 to explorative behavior when the foraging value encoded by the dmPFC/dACC is high. In the case
6 of the conflict theory and of the EVC theory, adaptation consists in applying more cognitive control
7 when it allows to better deal with the current situation. In most of these theories, cognitive control
8 is applied by the dorsolateral prefrontal cortex (dlPFC)^{107,9}, which is known to be functionally
9 tightly connected to the dmPFC/dACC^{52,54,55}. Finally, the error likelihood models propose that the
10 dmPFC/dACC activity calls for updating internal models of the world. All theories highlight that
11 the dmPFC/dACC activity relates to adaptation in behavior (explore/exploit, cognitive
12 control/habitual behavior) or updating internal models.

13 **Additional convergences**

14 Besides that most of these theories converge on the role of the dmPFC/dACC in goal-directed
15 behavior, all the teams involved in the debate also agree on three additional key aspects at the
16 conceptual level: 1) the dmPFC/dACC is one of the most interesting areas of the brain, as it has
17 been suggested previously⁶¹; 2) computational modeling can be used as a tool to test and support
18 theories on the brain; 3) the activity of the dmPFC/dACC seems to drive the activity of the
19 dorsolateral prefrontal cortex (dlPFC)^{2,9,38,110}.

20 **Unresolved debates**

21 Several antagonistic publications have revealed disagreements between the different teams
22 involved in these debates. One major issue comes from the lack of convergence between data
23 coming from multiple experiments over which theory is best explaining dmPFC/dACC activity in
24 a foraging task in humans. In the following section, we highlight those disagreements, and propose
25 that there are also different scientific approaches behind the arguments around the dmPFC/dACC
26 function(s) that can explain, at least in part, the reasons of the debate.

27 **Which theory/theories better account for the dmPFC/dACC activity: a matter of debate**

28 Importantly, throughout the past two decades, the authors of the different theories presented in this
29 review have actively engaged with the other theories surrounding the dmPFC/dACC. Rather than

1 ignoring alternative perspectives, they have confronted their own theories to rigorous evaluation
2 through a wide series of experiments that incorporate empirical data and simulations. In the
3 subsequent section, we provide a brief summary of these exchanges. However, it is important to
4 note that this summary offers only an overview and does not delve into the specifics of the
5 experimental designs used in the referenced studies. Therefore, to gain a comprehensive
6 understanding, we encourage readers to refer to these studies in the order suggested in Tables 1-3.

7 ***Foraging value or difficulty?***

8 One of the main debates surrounding the dmPFC/dACC function concerns its role in foraging
9 choice. Six publications illustrate this debate (Table 1). Following the 2012 study³¹ that proposed
10 the FVT theory and showed that the dmPFC/dACC reflected search value in the context of foraging
11 rather than difficulty or conflict, a study in 2014¹⁵¹ challenged this view. The authors of the latter
12 study argued that a potential confound between foraging value and choice difficulty could exist,
13 depending on the value range used¹⁵¹. Next, the two research teams involved in these studies
14 engaged in a series of publications^{1,2,149,152,153} aiming (but not only) at disentangling which of the
15 two variables (difficulty or foraging value) better reflected the dmPFC/dACC activity by using
16 several variants of the initial task. Despite tremendous efforts to address criticisms raised by the
17 other team, a consensus over whether the dmPFC/dACC better reflects difficulty or foraging value
18 remains elusive until now (but see next sections and our discussion for potential leads out of this
19 conundrum). Moreover, it is important to note that this debate has been centered on one experiment
20 and its variants. Also, this discrepancy is not circumscribed to these two research teams, as a large
21 and growing body of evidence in humans, non-human primates, and rodents supports the idea that
22 the dmPFC/dACC encodes foraging value on one side^{121,154-157} and difficulty on the other
23 side^{12,104,107,158-162}. This suggests that both functions could actually be supported by the
24 dmPFC/dACC either in different anatomical subdivisions of the dmPFC/dACC^{1,119} or with
25 different timings^{1,119,153}. Overall and until now, it seems that the debate around whether the
26 dmPFC/dACC encodes difficulty or foraging value is one of the hardest to resolve.

27 ***Error-likelihood model or conflict?***

28 The supporters of the error-likelihood models also confronted their own dmPFC/dACC model to
29 the other ones. A series of six antagonistic publications (Table 2) centered around whether the
30 dmPFC/dACC predicts error likelihood in a given context, as predicted by the error-likelihood

1 model, or whether it encodes conflict, as predicted by the conflict monitoring theory. Initially, the
2 error likelihood model posited that the dmPFC/dACC predicts error likelihood in a given context,
3 and not conflict or error detection³⁵. However, subsequent criticisms emerged when other
4 researchers defending the conflict monitoring theory identified conflict, error detection and
5 negative feedback signals in the dmPFC/dACC, while finding no significant correlation between
6 dmPFC/dACC activity and error likelihood in both fMRI and EEG studies^{163,164}. In response to
7 those criticisms, the authors of the error-likelihood model updated their model to take into account
8 these criticisms by positing that the dmPFC/dACC does not only predict the error likelihood in a
9 given context, but also the “predicted error consequence magnitude” (the product of those two
10 variables can be understood as the expected risk of a given behavior). They showed that, in line
11 with this modified version of the error likelihood model, the dmPFC/dACC activity increases in
12 situations when the expected risk (classically defined as the subjective probability of not being
13 correct) is high¹⁶⁵, even in situations with no response conflict¹⁶⁶. Furthermore, they proposed that
14 interindividual variability in risk-attitude could potentially explain why previous research did not
15 replicate the error likelihood encoding in the dmPFC/dACC¹⁶⁵. Nevertheless, they also later
16 demonstrated that both signals (conflict and error likelihood) seemed to be encoded by the
17 dmPFC/dACC in a task-dependent manner¹²⁹.

18 ***PRO model(s) versus FVT, difficulty, conflict and EVC***

19 More recently, the PRO model and its variant known as the PRO-control model have been
20 subjected to comparisons with other theories (Table 3).

21 *PRO-control vs FVT, difficulty:* Simulations of the PRO-control model¹¹⁹ on the foraging task used
22 to develop the FVT³¹ yielded results similar to the behavioral and neural findings reported
23 previously^{31,151}. In particular, the model exhibited human-like behavior in terms of foraging
24 choices. Also, the proactive control signal predicted by the model showed similarity to the changes
25 of activity of the dmPFC/dACC in response to variations in relative foraging value, as expected
26 by the FVT. Additionally, the reactive control signal aligned with the changes of dmPFC/dACC
27 activity in response to choice difficulty (negative surprise), as predicted by conflict monitoring
28 theory. Interestingly, these two signals displayed distinct temporal dynamics, with the model
29 activation being correlated early in the trial with relative foraging value and later with difficulty.

30 *PRO vs EVC:* Subsequently, the predictions of the original PRO model were applied to fMRI data

1 and compared to the predictions of the EVC theory⁸¹. The study found that the neural responses
2 observed in the dmPFC/dACC were better explained by the PRO model than by the EVC.
3 Nevertheless, a commentary authored by proponents of the EVC theory criticized this result,
4 claiming that the EVC was misunderstood and misinterpreted as an “Expected Value of Vigor”
5 model, which failed to better explain the fMRI data compared to the PRO model¹⁶⁷. Furthermore,
6 a recent independent study comparing the EVC, the error-likelihood model, and the original PRO
7 model during an emotion regulation task favored the EVC theory in explaining the dmPFC/dACC
8 activity¹⁶⁸.

9 In summary, while many studies have attempted to disentangle which of the different theories
10 could better reflect the dmPFC/dACC activity across different situations, none has consistently
11 outperformed the others. It is worth mentioning that to date, there has not been a formal comparison
12 of the PRO model, the PRO-control model, the HER model, the EVC theory and the FVT
13 predictions. Moreover, as suggested in some of the studies discussed above, this debate raises
14 questions 1) about the anatomical location of the cluster related to cognitive control *versus*
15 foraging value *versus* prediction error^{1,2,58,169}; 2) about the number of functions assumed by the
16 dmPFC/dACC, since, as suggested by the MSV^{15,170}, the dmPFC/dACC could be involved in
17 computing several independent functions, including both difficulty, FVT, conflict and prediction
18 error^{129,170}; and 3) about the timing when each function is encoded in the dmPFC/dACC since
19 difficulty-related signals are often observed to appear later than foraging value^{119,153,170}.

20

21

22 On top of these direct conflicts between theories, most researchers have realized that the
23 dmPFC/dACC correlates with time-on-task and have tried to explain it in the frame of their own
24 theory, while also ruling out that the link between dmPFC/dACC activity and their own theory
25 could be just a by-product of this correlation (see Box 1). The debate over the function(s) of the
26 dmPFC/dACC is not solved yet, but there are many interesting points to be taken from the
27 scientific discussions that took place, and we will try to summarize them in the two following
28 sections.

29

1 **One vs. multiple brain regions**

2 Differences in cluster location have been suggested as a partial explanation for disparate findings
3 among teams studying the dmPFC/dACC^{1,2}. It has been proposed that the cluster associated with
4 foraging value would be located in the dACC (inside the cingulate cortex, at the level of the frontier
5 between the ACC and the MCC in Fig. 1), while the cluster associated with choice difficulty and
6 conflict monitoring appears to be more dorsal and closer to the pre-SMA^{185,186,2}. Similarly, it has
7 been argued that the antagonism between the FVT and the EVC theories may be related to the
8 distinct spatial gradients followed by the dmPFC/dACC and the dlPFC³. One rostral-caudal
9 gradient is associated with abstract prediction errors, computed in the rostral regions, and concrete
10 prediction errors located in the caudal regions. Additionally, a dorso-ventral gradient dissociates
11 pain, control and foraging value signals in the ventral parts of the dmPFC/dACC, from the
12 computation of prediction error in dorsal regions recruited by situations where the EVC would be
13 higher³. Similarly, while both cognitive control theories⁹⁶ and error likelihood models¹⁸⁷ of the
14 dmPFC/dACC are compatible with its correlation with pain and negative affect, a recent study⁵⁸
15 showed that pain and conflict are encoded in different locations, with pain being encoded more
16 ventrally (in the MCC) than conflict (in the dmPFC/dACC).

17 While inter-individual anatomical differences in the brain have often been disregarded in
18 neuroimaging studies, future studies may consider the precise location of functional clusters.
19 Indeed, several factors of non-interest (fMRI sequence used, the size of the smoothing kernel used
20 during the preprocessing, the software used for fMRI analysis, etc.) can alter the anatomical
21 location of clusters. Those factors could prevent the generalization of results over multiple studies
22 depending on the preprocessing techniques used¹⁸⁸, at least in terms of precise anatomical
23 coordinates. In the case of the dmPFC/dACC, considering the proportion of subjects with or
24 without a pcgs in each hemisphere could allow for better disentangling where precisely the
25 functional clusters are located, since functional activities related to the dmPFC/dACC depend on
26 its presence^{5,58}. Such consideration might affect conclusions related to the dmPFC/dACC theories,
27 by dissociating sub-regions implementing each theory for instance. Moreover, improvements in
28 the anatomical frontiers of the different brain areas and of the software programs used for
29 delimitating these borders at the individual and group level will prove of great assistance to make
30 the field progress. Knowing whether all the signals that have been related to this cluster in the

1 brain actually relate to one single brain area or to multiple sub-structures, as suggested
2 previously⁵⁸, will be essential to build better maps of how the brain works. Moreover, variations
3 in subject neuroanatomy or the specific anatomical localization of the cluster of activity may
4 contribute to the disparities observed among the different studies. A comparative analysis of the
5 neuroanatomy of individuals across the datasets could potentially help in resolving the conflicts
6 surrounding the role(s) attributed to the dmPFC/dACC. By investigating the subject-specific
7 neuroanatomical differences, a deeper understanding of the underlying mechanisms of
8 dmPFC/dACC function may be gained, potentially shedding light on the discrepancies in
9 theoretical perspectives.

10 **One vs. multiple functions**

11 While the idea of “one brain area = one cognitive function” seems relatively valid for sensory or
12 motor areas, many suggest that we should completely abandon the assumption that “*brain regions*
13 *are both unifunctional and domain dedicated*”^{189,190}.

14 The overall brain activity pattern must be considered when looking at the function of a single
15 brain region. Indeed, cortical networks can reconfigure their functional connectivity according to
16 the task at stake^{191,192}, and the role of a given brain area can thus differ depending on the cortical
17 network that is currently active¹⁸⁹. Strikingly, the dmPFC/dACC belongs to both the salience
18 network and the executive control network¹⁹³. Altogether, this suggests that the dmPFC/dACC
19 could bear different roles depending on its co-activated partners (anterior insula for salience and
20 dorsolateral prefrontal cortex for executive control, for instance).

21 Altogether, the controversy over whether brain regions have multiple or single functions raises
22 a fundamental question about brain functioning. It dissociates two views. The first view suggests
23 that each brain region is specialized for a specific transformation of input information (a *cognitive*
24 *working* as proposed by Bergeron¹⁹⁰), without being specialized into a single cognitive function (a
25 *cognitive role*¹⁹⁰). The MSV supports this first view, where each brain area can be recruited by
26 different networks and cognitive functions. The second view suggests that each brain area
27 implements a specific cognitive function (for example: visual cortex and vision, motor cortex and
28 locomotor action, etc.), which is more consistent with dmPFC/dACC unifying theories. This view
29 allows for reverse inferences, such as “brain area X₁ is active, therefore the cognitive process Y₁
30 is currently active”, but requires great caution in its use^{41,194,195}.

1 This conceptual difference has also reached its peak in the debates over the dmPFC/dACC
2 function(s), given its association with multiple cognitive functions. Some teams aim to identify
3 the primary function of the dmPFC/dACC to account for all the related data in a parsimonious
4 way^{34,151}, while others argue that it is impossible to isolate a single function that would summarize
5 all the others^{1,2,7}, as the MSV.

6 Further studies will allow to better understand whether we should consider each brain area as
7 a functional node involved in many different cognitive functions or whether each brain area is
8 associated with a particular cognitive state and process. Though, it is essential to bear these
9 concepts in mind when discussing the functional roles of different brain areas.

11 Discussion

12 Understanding what is/are the cognitive function(s) supported by the dmPFC/dACC is a real
13 challenge. Nevertheless, like the alchemists' quests, even if it never gives rise to one single and
14 unifying theory, the research it has promoted has greatly advanced our knowledge of the human
15 brain. The vast amount of theoretical and practical work performed in the last decades has already
16 allowed to narrow down the possibilities about what the dmPFC/dACC does. For instance, it has
17 become clear that some functions often associated with its activity can be explained because they
18 are indirectly related to other functions, such as pain or uncertainty which are both better explained
19 by a relationship with cognitive control^{13,96,111}, or with saliency encoding for pain¹⁰⁰. Moreover,
20 careful examinations, in the same participants, of the correlates of both pain and cognitive control
21 have revealed that pain was related to a more ventral cluster than cognitive control in the brain⁵⁸.
22 Thanks to the different theories surrounding the dmPFC/dACC, great advances have been achieved
23 in disentangling what is provoking a rise in the dmPFC/dACC activity and what is causally
24 provoked by a rise in the dmPFC/dACC activity in terms of behavioral output. Moreover, many
25 authors have consistently put the different theories into competition when trying to interpret their
26 data, which has also helped to significantly advance our knowledge on the dmPFC/dACC. While
27 all theories identify the dmPFC/dACC as a key component of goal-directed behavior, indicating
28 the need for an internal and/or external adaptation, the exact computation performed by the
29 dmPFC/dACC is still a matter of debate.

1 Nevertheless, further studies are needed to better understand what the dmPFC/dACC is doing. We
2 foresee several main lines of research that could be followed and address them in what follows.

3

4 **Electrophysiological recordings in the dmPFC/dACC**

5 Most of the theories reviewed here have been developed based on fMRI studies which lack precise
6 time resolution, and do not provide a quantification of the proportion of neurons in a given area
7 for which activity correlates with a specific variable. As previously suggested^{153,170}, it is possible
8 that the dmPFC/dACC encodes different signals at different timings of a task with foraging value
9 encoded first and difficulty encoded later, which is also compatible with the PRO-control model¹¹⁹.
10 However, fMRI is not the best tool to test this assumption. Although, several of the theories have
11 received support from electrophysiological recordings in animal models, research on which theory
12 best accounts for electrophysiological recordings of the dmPFC/dACC remains subject to
13 debate^{37,196,2,34,197}. Future studies could therefore explore multi-unit and local field potentials
14 recordings in rodents, non-human primates or humans using intra-electroencephalography (iEEG)
15 to gain a better insight into the proportion of neurons related to each of the theories within the
16 dmPFC/dACC with precise anatomical locations.

17 **Developing new artificial intelligence-inspired approaches to the** 18 **dmPFC/dACC**

19 Future studies could draw inspiration from recent advances in artificial intelligence (AI). Artificial
20 neural networks, which were initially inspired by biological neural networks¹⁹⁸ have paved the
21 way for the development of intelligent robots that are based on the latest research in
22 neuroscience¹⁹⁹. After around 80 years of research on artificial neural networks, the field of
23 neuroscience is now drawing inspiration back from AI research. For instance, a recent architecture
24 has been proposed²⁰⁰ to construct autonomous intelligent agents, based on deep neural networks.
25 In this architecture, there is a configurator module that resembles the dmPFC/dACC in the way it
26 integrates multiple inputs to facilitate goal-directed behavior by identifying a sequence of subgoals
27 required to reach a global goal. Future studies could compare the artificial neural activity of the
28 configurator to the neural activity in humans and maybe proposes a new AI-inspired theory about
29 the function of the dmPFC/dACC (see for example other research, in which the dmPFC/dACC has

1 been associated with a monitoring module in a computational approach^{199,201}). Another similar
2 approach has been performed with the development of a multi-task learning model²⁰². In order to
3 behave optimally across a wide range of tasks and contexts, this model relies on habits as much as
4 possible, but, when it has no other choice, it relies on a set of controlled behaviours that correspond
5 to task-specific policies that could be perceived as more costly because they are less generalizable.
6 They propose that such model would be compatible with the EVC model, therefore comforting the
7 potential role of the dmPFC/dACC in computing the EVC. However, to our knowledge, their
8 model remains to be tested at the neural level. Interestingly, the Goal-Oriented Learning and
9 Selection of Action (GOLSA) model, which is an algorithm that incorporates neurobiological
10 Hebbian constraints²⁰³, has allowed to identify other brain areas than the dmPFC/dACC in
11 relationship to goal-directed behavior, such as the hippocampus, basal ganglia and ventral
12 prefrontal cortex²⁰⁴. These AI-based approaches therefore suggest that research on goal-directed
13 behavior by AI could open unexpected new avenues for better understanding the exact role of the
14 dmPFC/dACC.

15

16 **Taking into account dmPFC/dACC inter-individual anatomical** 17 **differences**

18 Future studies could benefit from considering interindividual sulcal morphology variability in the
19 brain. As we explained earlier, the presence or absence of a paracingulate sulcus in the
20 dmPFC/dACC can impact the location of functional clusters. This approach has also shed light on
21 other brain areas, such as the ventromedial prefrontal cortex (vmPFC) where different
22 morphological patterns^{205–207} can affect the localization of functional clusters related to
23 experienced value²⁰⁸ and the default mode network²⁰⁹. By using large datasets and classifying
24 participants according to sulcal morphology, future studies could clarify the exact location of
25 activity in response to different tasks, and potentially dissociate as many distinct brain regions as
26 there are theories, as some authors have suggested previously^{1–3,47}.

27

28

1 **Considering dmPFC/dACC connectivity**

2 Instead of focusing on precise anatomical boundaries within the dmPFC/dACC, it may be useful
3 to consider anatomical and functional connectivity. The anatomical⁵¹ and functional
4 connectivity⁵²⁻⁵⁶ of the dmPFC/dACC and its neighbours can vary greatly. Recent advances in
5 mapping the connectivity of the human brain, such as with the Human Brain Connectome
6 project²¹⁰ have been essential in refining our understanding of the brain organization, at both
7 individual and group levels. Comparative neuroscience can also benefit from such investigations.
8 For instance, Sallet and colleagues demonstrated that functional and anatomical connectivity could
9 serve at finding similarities between frontal regions in human and non-human primates²¹¹. These
10 approaches challenge assumptions in brain region labeling and uncover correspondences that were
11 not previously known. Although neurons in different subparts of the dmPFC/dACC may be
12 physiologically and neuroanatomically equivalent, they may connect to different parts of the brain
13 and serve different functions. To illustrate this argument, we used data released as part of the
14 Human Connectome Project²¹² to compute the functional connectivity of the dmPFC/dACC and
15 its four neighboring regions (Figure 4). All connectivity maps are qualitatively different, despite
16 the anatomical closeness of the seeds. Current dmPFC/dACC theories can also benefit from
17 integrating functional connectivity. For instance, the EVC theory posits that the dmPFC/dACC is
18 functionally connected to other brain regions involved in decision-making and cognitive control
19 (such as the dlPFC and the vmPFC)⁹. This integration of connectivity provides a mechanistic
20 account of how the brain processes and integrates information to guide decision-making and
21 cognitive control. Overall, future studies assessing each theory could benefit from considering both
22 anatomical boundaries and functional connectivity within the dmPFC/dACC, for instance by
23 coupling functional connectivity analyses with individual-level anatomical boundaries, to better
24 specify the brain regions of interest.

26 **Considering brain networks rather than single brain areas**

27 The consideration and reporting of co-activated brain regions, as well as the use of multivariate
28 analyses methods might help to better understand the function(s) of the dmPFC/dACC. While most
29 of our approach in this review focused on a single brain area, it is overall admitted that observing

1 which brain networks are at work, instead of attributing a cognitive role to each brain area, is more
2 relevant to the investigation of the brain functioning. According to this view, understanding the
3 dmPFC/dACC does not make sense without looking at its co-activated partners. Providing the
4 tables of activation, which is quite common in the field, will therefore greatly help to know which
5 network is at work. Multivariate brain measures that integrate the information over multiple brain
6 areas have also proven to be more robust^{213,214}. More generally, the recent development and growth
7 of new techniques to analyze fMRI-related data, such as gradient analyses²¹⁵ may also prove key
8 to better characterize the dmPFC/dACC activity depending on the task and network at work. It is
9 also important to note here that the robustness of fMRI results based on the average response of a
10 single brain region has been questioned in the last years²¹⁶. fMRI results seem to depend heavily
11 on the preprocessing methods used, which vary between different teams, therefore impacting
12 reproducibility¹⁸⁸. This phenomenon could partially explain why different teams obtain different
13 results, despite testing the same hypothesis.

14

15 **Digging into the link between dmPFC/dACC and physiological** 16 **arousal**

17 Numerous findings indicate a direct link between dmPFC/dACC activity and physiological arousal
18 levels determined by the sympathetic nervous system⁹³. These results suggest that the
19 dmPFC/dACC can read and directly trigger sympathetic nervous system activity, resulting in
20 increased levels of arousal, reflected by pupil dilation, increased heartbeat, blood vessel
21 constriction, glucose release, intestine inhibition, bladder relaxation and sweat⁹³. Furthermore, the
22 dmPFC/dACC is associated with the willingness to exert higher physical^{25,74,145,146,217}, and mental
23 efforts²¹⁸. In other words, the dmPFC/dACC may play a role in activating the sympathetic nervous
24 system, thereby facilitating physical and mental effort exertion⁹³. However, the reason why
25 sympathetic arousal is triggered by the dmPFC/dACC activity is not straightforward and has not
26 been thoroughly addressed by the theories discussed in the current review. This phenomenon is
27 nevertheless compatible with most of the current accounts of the dmPFC/dACC. For example,
28 when foraging value is high, it might be adaptive to increase the level of the sympathetic arousal
29 to get ready to engage with further exploration of the environment by senses (vision, audition, etc.)

1 and locomotor activity, therefore getting ready for performing higher efforts. Concerning cognitive
2 control theories, it has been argued that “the contribution of [the dmPFC/dACC] to laboratory
3 measures of cognitive control might stem from its evolutionarily older role in regulating ‘hot’
4 behaviours [...] that are elicited by stimuli and situations with affective and nociceptive
5 importance”⁹⁶ which are not so adaptive anymore in the face of a mental challenge, such as an
6 exam or a deadline. Moreover, others have also proposed that any physical activity is a conflict in
7 the sense that not doing anything or relying on habitual behavior would be the default action, thus
8 cognitive control would be required to keep on exerting efforts that have not been reinforced^{219,220}.
9 For the HER theory, it is also quite intuitive that prediction errors, which are salient events by
10 definition, trigger more arousal. Future studies will need to determine whether the dmPFC/dACC
11 acts solely as a driver of physiological arousal or whether it triggers sympathetic activity through
12 one or more of the computations identified by the theories outlined in this review.

13

14 **Conclusion**

15 In summary, the dmPFC/dACC is an anatomically ill-defined brain region found active in many
16 different cognitive scenarios. Several dmPFC/dACC theories have been proposed and developed
17 in parallel, sometimes with contradictory results, generating a lively and fascinating debate. All
18 authors from those studies agree that the dmPFC/dACC plays a major role in goal-directed
19 behavior and that its activity reflects the need for adaptation. Still, there is great variation among
20 these theories regarding what the dmPFC/dACC computes internally and which behavioral output
21 its activity should trigger. Our claim is not to take sides with one or the other theory, but to
22 summarize each argument and to underline why such a debate can generate rapid advances in our
23 knowledge about the brain. We highlighted practical and theoretical issues raised by the series of
24 publications around the role of the dmPFC/dACC. Overall, such scientific divergences are helpful
25 to science, and other brain regions could benefit from similar debates and diversity of approaches.

26

27

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1 **Figure legends**

2

3 **Figure 1 Functional and anatomical labelling of the dmPFC/dACC surrounding brain**
4 **regions. A.** Brain segmentation from the USCLobes atlas²²¹ in which the frontal cortex, parietal
5 cortex, cingulate cortex and corpus callosum are highlighted. **B.** Anatomical delineations in a brain
6 hemisphere with (left) or without (right) paracingulate sulcus. Main sulci (in black: *cgs* and *pcgs*)
7 are used to delineate the pre-SMA and dmPFC from the MCC and dACC. Secondary sulci (dark
8 grey) are used to delineate the rostral and caudal boundaries of the pre-SMA and dmPFC. The pre-
9 SMA and the dmPFC lie within the frontal cortex and are ventrally bordered by the cingulate
10 sulcus. The pre-SMA is immediately anterior to the SMA. Its posterior boundary appears to lie
11 between the paracentral sulcus (*pacs*) or the pre-paracentral sulcus (*prepacs*), but this boundary is
12 somewhat uncertain^{222–224}. The posterior vertical paracingulate sulcus (*vpcgs-p*) seems to
13 constitute an anatomical landmark for the anterior frontier of the pre-SMA and the posterior
14 frontier of the dmPFC³⁰. We propose that the anterior boundary of the dmPFC can be delineated
15 by the dorsomedial polar sulcus (*dmps*), which appears to limit Brodmann area 10 dorsally²²⁵. The
16 dACC and MCC are subdivisions of the cingulate cortex which are ventrally bordered by the
17 corpus callosum, and dorsally by the paracingulate sulcus (*pcgs*), when present, or the cingulate
18 sulcus (*cgs*), when there is no *pcgs*. The frontier between the dACC and the MCC is mostly based
19 on neuroanatomical criteria such as cytoarchitectural differences across the different cortical
20 layers^{43,44}, but it is roughly located above the genu of the corpus callosum^{44,226} and below the
21 anterior vertical paracingulate sulcus (*vpcgs*). We acknowledge that the dACC label is
22 controversial among neuroanatomists⁸. Our use of this term in this review corresponds to the dorsal
23 part of the anterior cingulate cortex, which is anterior to the mid-cingulate cortex (MCC)^{8,226}.
24 Abbreviations²²⁵: *cgs*: cingulate sulcus, *pcgs*: paracingulate sulcus, *cs*: central sulcus, *pacs*:
25 paracentral sulcus, *prepacs*: pre-paracentral sulcus, *vpcgs-p*: posterior vertical paracingulate
26 sulcus, *vpcgs-a*: anterior vertical paracingulate sulcus, *dmps* (limits area 10 dorsally): dorsomedial
27 polar sulcus. Note that some discrepancies exist in the literature about the labels. **C.** Functional
28 labels of the Pre-SMA, dACC, dmPFC and MCC. **Left.** Brain activations associated with each
29 label extracted from Neurosynth (association tests). **Right.** Same as (Left) but with the functional
30 cluster corresponding to the dmPFC/dACC depicted on top, extracted from (Lopez-Persem et al,

1 2016) for negative decision value during value-based forced choice²²⁷. Note that this functional
2 associations are displayed on the MNI152 template, as it reflects an averaged brain, without clear
3 sulcal delineation in the prefrontal and cingulate areas.

4

5 **Figure 2 Non-exhaustive list of multiple signals related to the dmPFC/dACC.** All maps have
6 been extracted through a uniformity test in Neurosynth (see <https://www.neurosynth.org/faq/#q18>
7 for more details). All maps are displayed in Montreal Neurological Institute (MNI) coordinates
8 and centered at $x = -4$. Each meta-analysis is based on a number N (displayed below each key
9 word) of neuroimaging studies based on Neurosynth automatic word extraction. For the
10 conjunction, made with the SPM12 toolbox (Wellcome Trust Center for NeuroImaging) ImCalc
11 function running in MATLAB 2021b, all maps have been binarized to keep only clusters surviving
12 a significant threshold of $p < 0.01$ after false discovery rate (FDR) correction for multiple
13 comparisons and they have then been multiplied with each other to only keep the voxels that are
14 shared across all these maps. The anatomical image used for the background is the anatomical
15 template used by Neurosynth.

16

17 **Figure 3 Schematic summary of the main dmPFC/dACC theories (without the Multiple**
18 **Signal View).** EVC: Expected value of control (red colors); FV: foraging value (green colors); PE:
19 prediction error (yellow colors). Note that the dorso-ventral or rostro-caudal orientation depicted
20 in the figure is for illustration purposes only, and we do not intend to suggest that those theories
21 are distributed specifically along these axes in the dmPFC/dACC.

22

23 **Figure 4 Connectivity of the dmPFC/dACC area.** Functional connectivity maps in medial (top)
24 and lateral (bottom) view for seeds (grey dots) in the dmPFC/dACC (first column), pre-SMA
25 (second column), dmPFC (third column), MCC (fourth column), dACC (last column). Seeds were
26 defined according to the functional labelling provided in figure 1C. Data are from the Human
27 Connectome Project²¹⁰ (HCP; Washington University-University of Minnesota Consortium of the
28 Human Connectome Project; RRID: SCR_008749; <http://db.humanconnectome.org>; S900
29 subjects release with 7T structural and resting fMRI data, 57 subjects) and correspond to the

1 average functional connectivity of 57 subjects. Only the left hemisphere is displayed for visual
2 purposes. The same subjects methods as in in Lopez-Persem *et al*, 2020²²⁸ were used.
3

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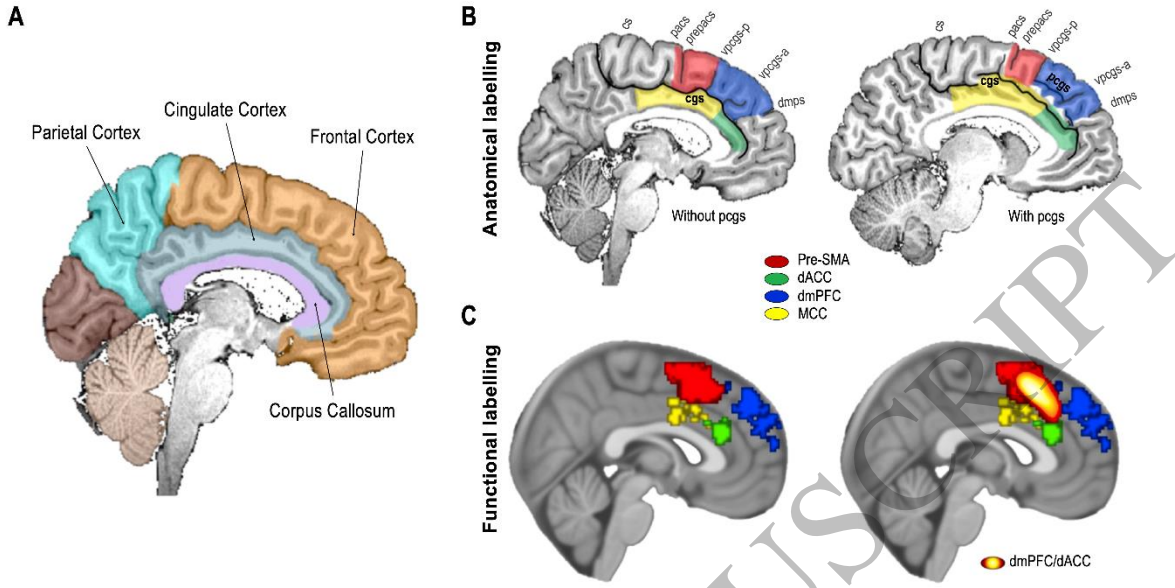


Figure 1
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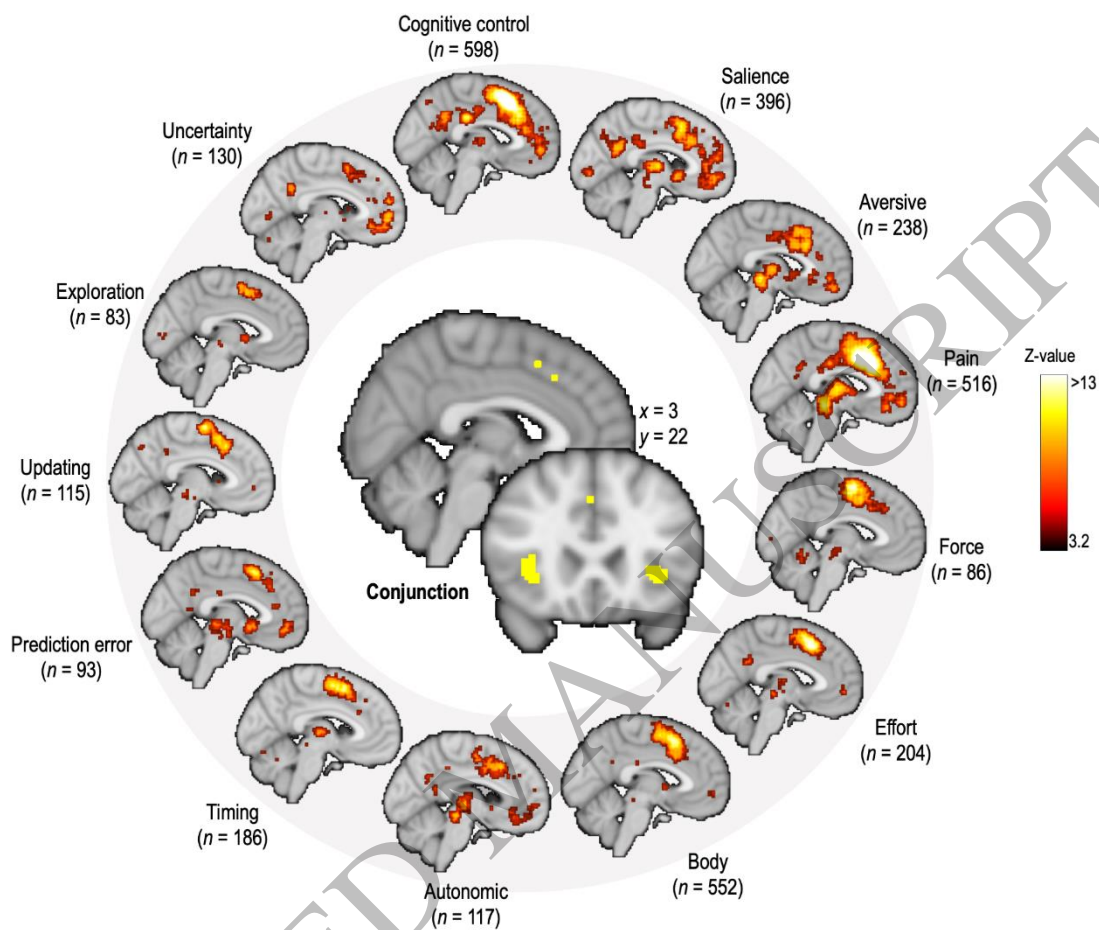


Figure 2
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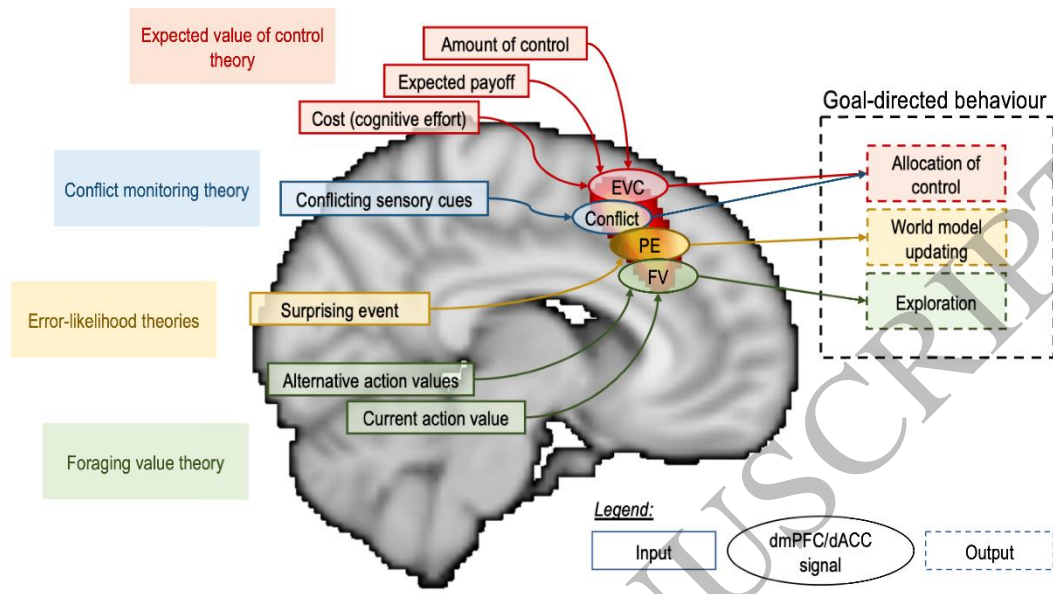


Figure 3
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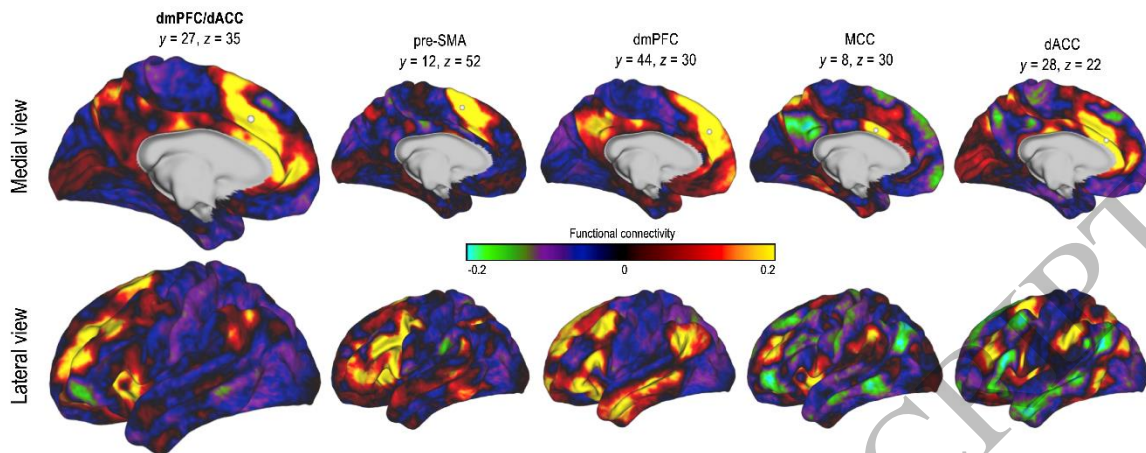


Figure 4
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1 **Box 1 dmPFC/dACC and time-on-task**

2 In addition to the main theories presented here, other researchers have argued that the
3 dmPFC/dACC activity reflects time-on-task rather than response conflict or error likelihood^{152,153}.
4 This is evidenced by its correlation with time perception^{27–29} and prolonged reaction times^{17,153–}
5 ¹⁵⁷.

6 According to **cognitive control theories**, this phenomenon has been interpreted as reflecting
7 higher levels of mental effort^{17,29,89}, because higher levels of conflict require more deliberation and
8 are thus related to slower reaction times¹⁵⁸. According to this view, the dmPFC/dACC activity
9 should not increase with reaction time in situations where it does not reflect mental effort or
10 conflict, but only when longer reaction time are necessary to increase confidence in a decision
11 where initial confidence is low^{159,160}. For instance, in tasks where the goal is to reach a target as
12 fast as possible, dmPFC/dACC activity should not be related to longer reaction times. Consistent
13 with this hypothesis, studies have shown that the dmPFC/dACC activity correlates with faster
14 reaction times in a task where the goal is to answer as quickly as possible when a target appears¹⁶¹.
15 Conversely, in a task where participants were asked to click on a button when a stimulus
16 disappears, the dmPFC/dACC activity was found to correlate with longer durations despite the
17 absence of any conflict¹⁵². The information theory also accounts for the correlation between
18 dmPFC/dACC activity and reaction times by explaining that it computes information uncertainty
19 and generates a behavioral response to it according to Hick-Hyman law. Hick-Hyman law posits
20 a linear link between information uncertainty and reaction times¹⁵⁷.

21 The **PRO model** also links the dmPFC/dACC activity to time-on-task, suggesting that the
22 dmPFC/dACC activity ramps up over time until an expected outcome occurs and then shuts off
23 once the predicted response occurs³⁶. If the outcome is unexpectedly delayed, either due to internal
24 factors such as slower reaction times¹⁸¹ or to external factors¹⁸², the dmPFC/dACC signal
25 continues to ramp up and, if the outcome does not occur at all when it was expected, the
26 dmPFC/dACC will increase its activity due to the prediction error. In agreement with the PRO
27 model, the increase in dmPFC/dACC activity during task performance and its immediate cessation
28 afterwards^{139,152,153} could partially explain why the dmPFC/dACC activity correlates with a wide
29 range of task variables in a rather unspecific manner⁵⁶. However, understanding why the
30 dmPFC/dACC activity correlates with time-on-task and whether this is related to one of the
31 dmPFC/dACC theories is still a matter to be solved. Furthermore, this would not explain why there

1 is a linear correlation between the dmPFC/dACC activity and the level of conflict in the
2 environment, foraging-value, or prediction-error, as this would only predict binary activation
3 during mental or physical effort (as opposed to rest).

4 Importantly, it is worth noting that the authors of the different theories have also demonstrated that
5 their variable of interest, namely foraging value for FVT, difficulty for cognitive control theories,
6 and prediction error for HER, was still significantly correlated with the dmPFC/dACC activity
7 after controlling for reaction time^{2,54,149,163}. These findings rule out the possibility that the
8 dmPFC/dACC only reflects time-on-task and does not correlate with the variables related to the
9 main theories presented here.

10 In summary, many of the theories described above can account for why the dmPFC/dACC
11 correlates with time-on-task. Conflict and information theories propose that longer reaction times
12 reflect the exertion of cognitive control in response to situation of uncertainty and/or conflict, while
13 error models suggest that the relation between dmPFC/dACC and longer reaction times is due to
14 prediction errors about internal or external events that are unexpectedly delayed. Other argue that
15 this correlation cannot be explained by these theories and that the dmPFC/dACC is merely
16 encoding time per se^{152,153,164,27,165}.

17

1 **Table 1 Foraging value and difficulty (conflict monitoring theory/EVC)**

Recommended order of reading	Reference	Type of experiment	Compared variables and associated theories (defended versus confronted)
1	Kolling <i>et al</i> , 2012 ³¹	1 fMRI experiment (N=20, 12 female)	Foraging value (FVT) versus conflict (conflict monitoring theory/EVC)
2	Shenhav <i>et al</i> , 2014 ¹⁴⁸	2 fMRI experiments (N=15 for experiment 1, 9 female; N=14 for experiment 2, 8 female)	Difficulty (conflict monitoring theory/EVC) versus foraging value (FVT)
3	Kolling <i>et al</i> , 2016 ¹⁶⁶	Re-analysis of the (Kolling <i>et al</i> , 2012) experiment ³¹ and of the (O'Reilly <i>et al</i> , 2013) experiment ⁸¹	Foraging value (FVT) versus difficulty (conflict monitoring theory/EVC)
4	Shenhav <i>et al</i> , 2016 ¹⁷⁹	1 fMRI experiment (N=34, 30 female)	Difficulty (conflict monitoring theory/EVC) versus Foraging value (FVT)
5	Zacharopoulos <i>et al</i> , 2018 ¹⁴⁶	1 fMRI experiment (N=30, 21 female)	Difficulty (conflict monitoring theory/EVC) versus Foraging value (FVT)
6	Kolling <i>et al</i> , 2018 ¹⁵⁹	1 fMRI experiment (N=25, 11 female)	Foraging value (FVT) versus difficulty (conflict monitoring theory/EVC)

2 This table lists the main research articles which have been at the core of the debate between difficulty encoding (compatible with conflict
3 monitoring theory, EVC and the reactive control signal in the PRO model) and foraging value (compatible with FVT and the proactive signal in
4 the PRO-control model) encoding in the dmPFC/dACC. The reader is kindly invited to delve into those papers to understand in more details the
5 arguments of the controversy. References are indicated in chronological order but the column on the left is providing a suggested order of reading
6 for the naive reader.
7
8

1 **Table 2 Error-likelihood model and conflict monitoring theory**

Recommended order of reading	Reference	Type of experiment	Compared theories (defended versus confronted)
1	Brown & Braver, 2005 ¹¹⁰	1 fMRI experiment (N=16, gender not reported)	Error-likelihood model versus Conflict monitoring theory
2	Nieuwenhuis <i>et al</i> , 2007 ¹¹¹	2 fMRI experiments (N=14, 10 female for experiment 1; N=14, 8 female for experiment 2) and 1 EEG experiment (N=8, 7 female for experiment 3)	Conflict monitoring theory versus Error-likelihood model
4	Brown & Braver, 2007 ¹⁶⁰	1 fMRI experiment (N=21, 9 female)	Updated Error-likelihood model versus Conflict monitoring theory
6	Brown, 2009 ¹²⁶	1 fMRI experiment (N=20, 11 female)	Updated Error-likelihood model versus Conflict monitoring theory
3	Yeung & Nieuwenhuis, 2009 ¹¹²	Simulations and 1 EEG experiment (N=16, 10 female)	Conflict monitoring theory versus Error-likelihood model
5	Jahn <i>et al</i> , 2011 ¹⁶¹	1 fMRI experiment (N=22, 11 female)	Updated Error-likelihood model versus Conflict monitoring theory

2 This table lists the main research articles which have been at the core of the debate between the error-likelihood model and the conflict
3 monitoring theory of the dmPFC/dACC. The reader is kindly invited to delve into those papers to understand in more details the arguments of
4 the controversy. References are indicated in chronological order but the column on the left is providing a suggested order of reading for the
5 naive reader.
6
7

1 **Table 3 PRO models, conflict monitoring theory, FVT, and EVC**

Recommended order of reading	Reference	Type of experiment	Compared theories (defended versus confronted)
1	Brown 2013	Perspective	PRO model versus conflict monitoring theory
2	Brown & Alexander, 2017 ¹⁵⁸	Simulations	PRO-control versus FVT and difficulty
3	Vassena <i>et al</i> , 2020 ⁷⁹	fMRI experiment (N=23, 13 female)	PRO versus difficulty and EVC
4	Shenhav <i>et al</i> , 2020 ¹⁶⁴	Commentary on Vassena <i>et al</i> , 2020	EVC versus PRO
5	Bush <i>et al</i> , 2022 ¹⁶⁵	fMRI experiment (N = 97, 61 female)	EVC versus PRO, error likelihood model, conflict monitoring theory, and error detection

2 This table lists the main research articles which have been at the core of the debate between PRO models (original PRO model and other variants)
 3 and the other theories of the dmPFC/dACC. The reader is kindly invited to delve into those papers to understand in more details the arguments
 4 of the controversy. References are indicated in chronological order but the column on the left is providing a suggested order of reading for the
 5 naive reader.
 6
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