

# Potential roles of the rodent medial prefrontal cortex in conflict resolution between multiple decision-making systems

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## Abstract

Mammalian decision-making is mediated by the interaction of multiple, neurally and computationally separable decision systems. Having multiple systems requires a mechanism to manage conflict and converge onto the selection of singular actions. A long history of evidence has pointed to the prefrontal cortex as a central component in processing the interactions between distinct decision systems and resolving conflicts among them. In this chapter we review four theories of how that interaction might occur and identify how the medial prefrontal cortex in the rodent may be involved in each theory. We then present experimental predictions implied by the neurobiological data in the context of each theory as a starting point for future investigation of medial prefrontal cortex and decision-making.

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## 1. Multiple decision-making systems interact to inform action-selection

Current theories suggest multiple decision systems underlie action-selection in mammalian brains (Daw, Niv, & Dayan, 2005; Kahneman, 2011; O’Keefe & Nadel, 1978; Redish, 1999, 2013), identifying three action-selection systems: *Pavlovian*, *Deliberative*, and *Procedural* (see van der Meer, Kurth-Nelson, & Redish, 2012, for review). These different decision-making systems entail different computational algorithms that are instantiated through distinct neural circuits. Yet common among them is evidence that the medial prefrontal cortex (mPFC) plays an important role. Interestingly, newer work has pointed to subregional specificity of mPFC’s involvement in these action-selection processes and their interactions (Balaguer-Ballester, Lapish, Seamans, & Durstewitz, 2011; Chudasama & Robbins, 2003; Durstewitz, Vittoz, Floresco, & Seamans, 2010; Euston, Gruber, & McNaughton, 2012; Horst & Laubach, 2012; Kesner & Churchwell, 2011; Milad & Quirk, 2002; Narayanan, Horst, & Laubach, 2006; Padilla-Coreano et al., 2016; Powell & Redish, 2016; Schmidt, Duin, & Redish, 2019; Sharpe & Killcross, 2015; Smith & Graybiel, 2013).

A multiple decision-system model necessitates a mechanism of interaction, particularly when systems suggest conflicting actions. However, while the identity of this mechanism remains unknown, there is reason to believe mPFC is fundamentally involved. Building from computational definitions of each system and points of interaction between them, we derive experimental predictions that will shed light on the underlying neurobiological mechanisms. This approach reveals potential explanations of how the multiple decision systems interact and the role of mPFC in decision-making.



## 2. Computation and neurobiology of decision systems

A predominant taxonomy categorizes action-selection algorithms based on their fundamentally different computations—*Pavlovian* responses, goal-directed *Deliberation*, and *Procedural* action-selection. The Pavlovian system builds associations between environmental stimuli allowing the release of species-important responses to those learned stimuli (Bouton, 2007; Dayan, Niv, Seymour, & Daw, 2006; Pavlov, 1927). Deliberative

decisions depend on a constructed representation, evaluation, and selection of potential outcomes. As outcome prediction depends on a model of the transition structure of the world, Deliberative processes are often referred to as “model-based” (Gilbert & Wilson, 2007; Johnson, van der Meer, & Redish, 2007; Niv, Joel, & Dayan, 2006; Redish, 2016). Procedural decision-making relies on recognizing and categorizing situations based on experience and responding with appropriate, well-learned action-chains (Barnes, Kubota, Hu, Jin, & Graybiel, 2005; Dezfouli & Balleine, 2012; Graybiel, 1998; Mishkin & Appenzeller, 1987) (see Redish, 2013, for review). As these processes do not require modeling explicit transition structures, Procedural responding is often referred to as “model-free” (Daw et al., 2005; Niv et al., 2006), but this is a misnomer as the situation-categorization process does contain a model of what aspects in the world are relevant (Cochran & Cisler, 2019; Gershman & Niv, 2010; Redish, Jensen, Johnson, & Kurth-Nelson, 2007).

Of the three action-selection systems, *Pavlovian responding* is the simplest computationally and provides fast responses. Pavlovian learning describes the association of a conditioned stimulus with a naturalistic behavior (Breland & Breland, 1961; Dayan et al., 2006; Pavlov, 1927). Experiments identify amygdala and periaqueductal gray as key players in Pavlovian responding, with nucleus accumbens shell involved in avoidance behaviors (Bravo-Rivera, Roman-Ortiz, Montesinos-Cartagena, & Quirk, 2015; Diehl et al., 2018; Diehl, Bravo-Rivera, & Quirk, 2019; Kim, Rison, & Fanselow, 1993; LeDoux, 2015; LeDoux & Daw, 2018; McNally, Johansen, & Blair, 2011). While the Pavlovian system provides the advantage of a rapid, potentially life-saving response, it does so at the expense of flexibility (Breland & Breland, 1961). Actions resulting from this system are instinctual in nature, yet, by translating simple stimuli across contexts, the Pavlovian system can act even in truly novel situations.

In situations where the structure of the environment is known, agents can use that known structure to plan novel actions within the world (O’Keefe & Nadel, 1978; Redish, 1999; Tolman, 1948). *Deliberation*, or “goal-directed action selection,” involves several complex processing steps, resulting in a computationally expensive process dependent on multiple brain structures. First, it requires an understanding of the external world, including knowledge of relevant features and how to effectively transition between situations. This model of the world is known as a *cognitive map* from which actions and their consequences can be identified through a search process.

The forward sweeping activity of hippocampal place cells along prospective paths has been identified as a potential mechanism for this search process (Amemiya & Redish, 2016; Johnson & Redish, 2007; Kay et al., 2020; Papale, Zielinski, Frank, Jadhav, & Redish, 2016; Pfeiffer & Foster, 2013; Redish, 2016). After identifying candidate options, the Deliberative system must evaluate and compare their values, a process that involves the nucleus accumbens core and orbitofrontal cortex (Steiner & Redish, 2012; van der Meer & Redish, 2009). Finally, Deliberation must use this value information to converge to a single action, though how this occurs remains an open question. The modularity and wide applicability of these four steps (cognitive map, search, evaluate, and action-selection) demonstrate the flexibility and versatility of the Deliberative decision system, yet they also reveal its computational complexity highlighting it as slow and energetically costly.

Like Deliberation, *Procedural* decision-making (also known as *Habit-based* learning) has the ability to learn arbitrary responses. Like Pavlovian systems, Procedural decision-making can respond quickly. Computationally, Procedural action-selection is achieved by developing situation-action associations and chunking discrete actions into fluid motions and complex behaviors (Barnes et al., 2005; Dezfouli & Balleine, 2012; Friedman, Homma, et al., 2015; Friedman, Jomma, et al., 2015; Graybiel, 1998; Hull, 1943; Rand, Hikosaka, Miyachi, Lu, & Miyashita, 1998). Procedural decision-making is thus faster to execute than Deliberation, but more flexible than the Pavlovian system where action repertoire is limited. However, Procedural action-selection develops slowly with experience and is generally difficult to adapt to new situations. Given that it lacks a comprehensive search process, the Procedural system can respond faster with more efficient action-chains than Deliberation. But the inflexibility of habits means that they are optimized for situations where the set of relevant actions is highly reliable. Studies have found this system to depend upon dorsolateral striatum (dlStr), motor cortex, and cerebellum (Berke & Eichenbaum, 2009; Graybiel, 1998; Molinari et al., 1997; Schmitzer-Torbert & Redish, 2004; Smith & Graybiel, 2016; van der Meer, Johnson, Schmitzer-Torbert, & Redish, 2010; van der Meer, van der Meer, Johnson, Schmitzer-Torbert, & David Redish, 2010). Most notably, dlStr cells have been found to exhibit rapid bouts of activity at the initiation of an action sequence, a process termed “task bracketing” and thought to reflect the release of the complete motor sequence (Barnes et al., 2005; Regier, Amemiya, & Redish, 2015; Smith & Graybiel, 2013, 2016; Thorn, Atallah, Howe, & Graybiel, 2010).



### 3. Prefrontal cortex and decision systems

While relatively straightforward relationships have emerged between the three decision systems and their respective neurobiology, the situation is less clear when considering the medial prefrontal cortex (mPFC). One immediate consideration is that the medial wall of the rodent prefrontal cortex is not a homogenous structure (de Bruin, Corner, Feenstra, Van Eden, & Uylings, 1991; Groenewegen & Uylings, 2000; Kolb, 1990; Laubach, Amarante, Swanson, & White, 2018; Uylings, Groenewegen, & Kolb, 2003). Instead, anatomical findings have revealed gradations and subdivisions along the dorso-ventral axis. As such, the rodent mPFC is often segregated into the anterior cingulate cortex (ACC) dorsally, transitioning into the prelimbic cortex (PL) in the mid-region, followed by the infralimbic cortex (IL) more ventral (Heidbreder & Groenewegen, 2003; Hoover & Vertes, 2007). Collectively, these subregions have long been thought to serve a central role in higher cognitive functioning, executive control, and decision-making (Kesner & Churchwell, 2011; Laubach, 2011; Laubach et al., 2018; Miller & Cohen, 2001). However, the exact role of each subregion, how their functioning relates to different decision systems, and the degree to which they interact all remain areas of ongoing research.

Early theories of mPFC posited that a division of labor may exist between ACC, PL, and IL with each subregion dedicated to one specific role. For decision-making, PL was thought to be involved in cognitive flexibility and planning, making it a good candidate for supporting Deliberative processes (Dalley, Cardinal, & Robbins, 2004; Fuster, 1997; Killcross & Coutureau, 2003; Kolb, 1990; Ragozzino, Wilcox, Raso, & Kesner, 1999; Rich & Shapiro, 2007; Tran-Tu-Yen, Marchand, Pape, Di Scala, & Coutureau, 2009). Infralimbic cortex on the other hand seemed to be involved in cases of repeated actions characteristic of Procedural responding (Barker, Taylor, & Chandler, 2014; Coutureau & Killcross, 2003; Graybiel, 2008; Killcross & Coutureau, 2003; Ostlund & Balleine, 2009; Smith & Graybiel, 2013). Finally, ACC has been linked to processing naturalistic stimuli such as rewards or punishments, giving preliminary reason to associate it with Pavlovian action-selection (Bussey, Everitt, & Robbins, 1997; Cardinal et al., 2003; Parkinson, Willoughby, Robbins, & Everitt, 2000), but other work has associated ACC with conflict resolution (de Wit, Kosaki, Balleine, & Dickinson, 2006; Fisher, Saksida, Robbins, & Bussey, 2020) or overcoming effort (Walton, Bannerman, Alterescu, & Rushworth, 2003).

While direct association between mPFC subregions and decision systems seems attractive, subsequent evidence suggests considerably more interaction both between the anatomical areas, and between the cognitive processes themselves.

Perhaps pointing directly to its role in decision-making, a considerable portion of our understanding of mPFC subregions comes from exploring the different decision systems (Deliberative, Procedural, and Pavlovian) that drive behavior.

Deliberative decision-making has received the most attention regarding potential mPFC involvement but has primarily concentrated on the PL region, particularly the dorsal aspects of PL, along with ventral aspects of ACC (Hasz & Redish, 2020b; Hyman, Whitman, Emberly, Woodward, & Seamans, 2013; Powell & Redish, 2016; Zielinski, Shin, & Jadhav, 2019). While a wide variety of tasks have been employed, they share the common feature that optimal performance is goal-directed and necessitates future planning (Hyman, Zilli, Paley, & Hasselmo, 2010; Powell & Redish, 2016; Rich & Shapiro, 2009; Schmidt et al., 2019; Zielinski et al., 2019). Furthermore, prominent goal-directed, task-relevant activity is observed in hippocampus during these behaviors (Cei, Girardeau, Drieu, El Knabi, & Zugaro, 2014; Gupta, van der Meer, Touretzky, & Redish, 2012; Ito, Zhang, Witter, Moser, & Moser, 2015; Johnson & Redish, 2007; Kay et al., 2020; O'Keefe & Nadel, 1978; O'Keefe & Speakman, 1987; Pfeiffer & Foster, 2013; Redish, 1999; Rosenzweig, Redish, McNaughton, & Barnes, 2003; Wikenheiser & Redish, 2015) highlighting their utilization of Deliberation. In regard to mPFC, these studies have provided compelling evidence that PL is important to Deliberative processing. Manipulations of PL disrupt the development of goal-directed strategies during learning and inhibit the expression of these strategies in fully trained rats (Dalton, Wang, Phillips, & Floresco, 2016; Killcross & Coutureau, 2003; Ragozzino et al., 1999; Riaz et al., 2019; Tran-Tu-Yen et al., 2009). Physiologically, PL activity coincides with events during which Deliberation would be expected: at decision points and instances when a change in strategy becomes necessary (Balaguer-Ballester et al., 2011; Durstewitz et al., 2010; Hasz & Redish, 2020a, 2020b; Hyman et al., 2010; Powell & Redish, 2016; Rich & Shapiro, 2009; Zielinski et al., 2019). Additionally, a series of studies have directly linked activity in PL/ACC with dorsal hippocampus. Coordinated activity has been found in both unit and LFP recordings (Adhikari, Topiwala, & Gordon, 2010; Adhikari, Topwala, & Gordon, 2011; Benchenane et al., 2010; Hyman et al., 2010; Ito et al., 2015;

Ito, Moser, & Moser, 2018; Jadhav, Rothschild, Roumis, & Frank, 2016; Jones & Wilson, 2005; Wirt & Hyman, 2019; Zielinski et al., 2019), and manipulation of PL activity has led to functional changes within hippocampal representations (Guise & Shapiro, 2017; Hok, Chah, Save, & Poucet, 2013; Ito et al., 2015; Schmidt et al., 2019).

Behavioral studies have also approached mPFC functioning through Procedural decisions; here concentrating on IL. Under extended training regimens, repetitive trials lead to the development of goal-independent Procedural responding, or habits (Coutureau & Killcross, 2003; Killcross & Coutureau, 2003; Smith & Graybiel, 2013). In rats with IL lesions prior to training, Procedural responding never develops, even with extended training well past what is normally required (Killcross & Coutureau, 2003). Instead, behavior appears to remain in a goal-directed mode. In the case of fully trained rats with well-established habits, IL manipulations lead animals to abandon Procedural responding and fall back on Deliberation, or in some cases revert to older habits that had been seemingly overridden (Barker, Glen, Linsenhardt, Lapish, & Chandler, 2017; Coutureau & Killcross, 2003; Smith & Graybiel, 2013). In line with these behavioral results, recordings from IL cells in overtrained rats found activity that coincides with Procedural responding (Smith & Graybiel, 2013). Bursts of IL firing occur at movement initiation, concurrent with the task bracketing activity of dlStr (Barnes et al., 2005; Jog, Kubota, Connolly, Hillegaart, & Graybiel, 1999; Regier et al., 2015; Thorn et al., 2010). Furthermore, these bouts of IL activity develop over training, mirroring the time course of both behavioral habits and dlStr activity (Smith & Graybiel, 2013).

A third body of literature has examined the role of mPFC during Pavlovian associations, most notably using fear conditioning and extinction paradigms. At a macro level, lesion studies indicate that mPFC is central to Pavlovian fear learning (Lebron, Milad, & Quirk, 2004; LeDoux, 2000; Milad & Quirk, 2002; Morgan & LeDoux, 1995) with newer findings suggesting opposing roles of PL and IL. Prelimbic inactivation leads to impairment in freezing, and neural firing in PL is correlated with the expression of fear learning (Corcoran & Quirk, 2007; Do-Monte, Quiñones-Laracuate, & Quirk, 2015; Sierra-Mercado, Padilla-Coreano, & Quirk, 2011) highlighting its role in initial fear leaning. In contrast, infralimbic manipulations do not impact these early stage Pavlovian processes, but instead influence fear extinction or the reinstatement of freezing at remote time points (Do-Monte et al., 2015; Milad & Quirk, 2002; Quirk, Russo, Barron, & Lebron, 2000; Sierra-Mercado et al., 2011).

Despite evidence that the Pavlovian system operates beyond simple fear memory, research into mPFC in these other regimes has lagged. Newer work has begun to study PL during Pavlovian mediated approach-avoidance situations, presenting rodents with an inherent conflict between approaching food and avoiding attack by an artificial predator (Amir, Lee, Headley, Herzallah, & Pare, 2015; Choi & Kim, 2010; Kim & Jung, 2018; Mobbs & Kim, 2015; Walters, Jubran, Sheehan, Erickson, & Redish, 2019). Recordings from PL during this task found responses to the food option, the potential predator, as well as interactions between the two stimuli (Kim et al., 2018). Furthermore, correlated firing was observed between cells in PL and the lateral amygdala, highlighting strong links between PL activity and structures involved in the Pavlovian decision system.

Complementing the decision-making focused approach to mPFC, a second body of literature has sought to query the neural activity of specific mPFC subregions during behavior. While generally not testing a proposed role in decision-making directly, these findings provide valuable information from which we can infer how activity within mPFC could be utilized in decision processing.

Within ACC, a body of work has found firing rate changes associated with the resultant outcome of behavioral choices. Following correct responding, ACC cells exhibit firing increases thought to be associated with the delivery of reward and a reinforcement of the decision that produced it (Hart, Blair, O'Dell, Blair, & Izquierdo, 2020; Hillman & Bilkey, 2010; Hyman et al., 2013). In other cases, incorrect decisions lead to increases in ACC activity which is thought to reflect a lack of reward delivery or perhaps mental exploration of alternative choices (Caracheo, Grewal, & Seamans, 2018; Hyman, Holroyd, & Seamans, 2017; Mashhoori, Hashemnia, McNaughton, Euston, & Gruber, 2018). Similar results have been found in PL (Horst & Laubach, 2012, 2013; Powell & Redish, 2014), suggesting this is either a general property of mPFC or that the boundaries of these structures may not be so clearly identified (Laubach, Amarante, Swanson, & White, 2018). Collectively, this work seems to point to a role for ACC (and possibly PL) in evaluating choice outcomes to update an understanding of the world.

A second set of studies on ACC have found robust evidence for coherent representations of task states at the population level (Balaguer-Ballester et al., 2011; Hyman, Ma, Balaguer-Ballester, Durstewitz, & Seamans, 2012; Lapish, Durstewitz, Chandler, & Seamans, 2008; Ma, Hyman, Durstewitz, Phillips, & Seamans, 2016). Furthermore, these neural state representations are distinct for different contexts, with reliable neural changes coinciding with



changes in task structure or behavioral responses (Caracheo et al., 2018; Durstewitz et al., 2010; Rich & Shapiro, 2009). Again, similar results have been observed within PL (Hasz & Redish, 2020a; Powell & Redish, 2016), suggesting a potential commonality between these two subregions. Thus one hypothesized role of dorsal mPFC is to establish, maintain, and utilize an internal representation of external environmental states (Fuster, 1997; Seamans & Yang, 2004; Sharpe & Killcross, 2015; Sharpe, Wikenheiser, Niv, & Schoenbaum, 2015). Such a function would support involvement in both Deliberative and Procedural decision systems as both rely on a coherent state signal and reliable transitions between states.

Unfortunately, considerably less data exist as to the potential inner workings of IL. What has been shown is that IL is involved in Procedurally driven goal-independent responding (Killcross & Coutureau, 2003), its activity develops with and is critical to the extinction of Pavlovian associations (Milad & Quirk, 2002), and during Procedural responding IL ensembles exhibit punctate bouts of firing at trial initiations (Smith & Graybiel, 2013). While the exact nature of these bouts is unclear, their developmental time course, striking similarity to striatal activity patterns, and the impact of IL manipulations on behavior all point to a role in Procedural decision processing.

There currently exists ample, though incomplete, evidence to support a prominent role for mPFC in decision processing. Furthermore, some evidence points to functionally distinct roles of ACC, PL, and IL. Yet there remain several wrinkles in this explanation that require consideration.

Firstly, while links have been drawn between PL and dorsal hippocampus (Deliberation) and between IL and dlStr (Procedural actions), neither pair share direct anatomical connections (Beckstead, 1979; Heilbronner, Rodriguez-Romaguera, Quirk, Groenewegen, & Haber, 2016; Sesack, Deutch, Roth, & Bunney, 1989; Vertes, 2004). For Deliberation, intermediary structures such as ventral hippocampus, entorhinal cortex, or nucleus reuniens could serve as relays (Adhikari et al., 2010; Hoover & Vertes, 2007; Ito et al., 2015; Jay & Witter, 1991; Swanson, 1981). For Procedural actions no obvious anatomical pathway exists. Infralimbic sends direct projections to PL which subsequently projects to dorsal striatum (Friedman, Homma, et al., 2015; Friedman, Jomma, et al., 2015; Heilbronner et al., 2016; Vertes, 2004), though given the strong association between PL and Deliberation it represents an unlikely relay point for Procedural information. Alternatively, IL could send information to the ventral striatum where internal ascending spiral loops then facilitate relay to dlStr (Haber, Fudge, & McFarland, 2000; Montaron, Deniau, Menetrey, Glowinski, & Thierry, 1996). A third option is that IL and dlStr serve complementary roles in Procedural actions.

While dlStr executes motor commands, IL may act to establish a general brain state that is permissive to the execution of habits (Smith, Virkud, Deisseroth, & Graybiel, 2012). In this way, the two brain regions could work in parallel to support Procedural decisions, but require no means of direct information transfer.

A second consideration surrounding the role of mPFC in decision processing involves how the different subregions interact. Anatomically ACC, PL, and IL are interconnected, implying functional interaction and influence across the subregions (Heidbreder & Groenewegen, 2003; van Aerde, Heistek, & Mansvelder, 2008; Vertes, 2004). Indeed results from a variety of studies that examined directed manipulations of PL and IL point to opposing roles and mutual competition between the pair (Killcross & Coutureau, 2003; Mukherjee & Caroni, 2018; Sierra-Mercado et al., 2011; Smith et al., 2012; Vidal-Gonzalez, Vidal-Gonzalez, Rauch, & Quirk, 2006). Most notably, PL lesions bias rats away from Deliberation and toward Procedural systems, while IL lesions appear to eliminate Procedural responding and instead force animals into goal-directed strategies, as would be expected in the case of direct competition between the subregions.

In actuality, competition between PL and IL, and by proxy the underlying Deliberative and Procedural decision systems, is indicative of a larger question for decision-making and the role of mPFC in it. A decision maker built from multiple independent subsystems can find itself in conflict, yet it must ultimately coalesce into a single unified action. Deconstructing this decision maker into computational and neural components has proven essential, but we must also reassemble these parts to ask how they interact in the pursuit of action-selection. Given its long established role in cognitive functioning and decision-making, along with its anatomical position as a hub for integration and processing of information, we believe that the rodent medial prefrontal cortex likely plays a central role in moderating the brain's multiple decision systems.



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## 4. Theories for decision system integration

Current theories of decision system integration have identified three main candidate proposals of how Pavlovian, Deliberative, and Procedural decision systems converge to a single action. To this set of three candidates we add a fourth novel proposal for future consideration:

Theory 1. An independent central executive could act to delegate responsibility between the three decision systems.

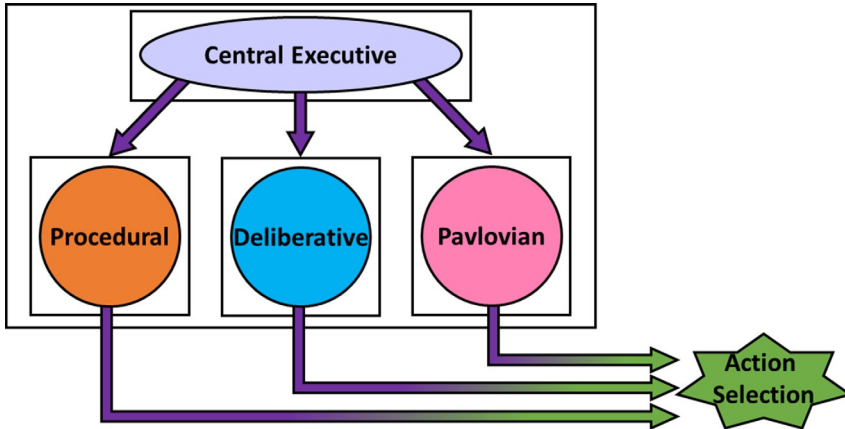
- Theory 2. Downstream motor control mechanisms could receive input from the three systems in parallel, with the final action reflecting the input of the most internally self-consistent signal.
- Theory 3. The Deliberative system could occupy a privileged position to exert an override and/or arbitrator role over both the Pavlovian and Procedural systems.
- Theory 4. The three decision systems could operate in a hierarchical structure reflecting their maturation over the course of an agent's experience with the world. In this fourth theory, actions are initially driven by ingrained Pavlovian processes, which are superseded by Deliberation as an understanding of the world develops. Deliberation is then superseded by Procedural responding as extensive training gives rise to well developed action chains.

Critical to each of these four theories is the computational structure describing how three distinct, competing decision systems interact to produce a single behavioral action. Furthermore, direct neurobiological predictions can be made from each computational theory into the nature and interactions of the medial prefrontal cortex.

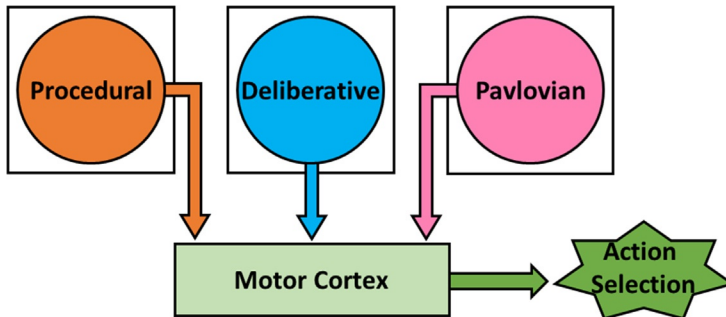
#### 4.1 Theory 1: Independent central executive

Many theories postulate that decision systems function in isolation, only coming together at a final stage to compete for behavioral control. Building from this conceptualization has led to the idea that an additional stand-alone executive system is necessary to effectively manage multiple decision systems (Freud, 1923; Fuster, 2008; Hofmann, Schmeichel, & Baddeley, 2012; Plato, 2008). Importantly, this central executive would be computationally and physiologically distinct from the other decisions systems, delegating which system directs behavior and guiding information flow, but not actively engaging in any individual system's computational processing. Specifically in the context of conflicts arising between the three decision systems (Pavlovian, Deliberative, and Procedural), the central executive model posits that a fourth entity empowers a single neural decision circuitry (amygdala, hippocampus, or dlStr) to influence action-selection (see Fig. 1).

Given its role, the requirements of this central executive suggest that it would need to contain representations of strategy while also remaining dissociated from the computational inner workings of any specific decision system. This makes neuroanatomical identification of a separate central executive challenging, though mPFC has been proposed to fulfill such a role (Fuster, 2008; Otto, Gershman, Markman, & Daw, 2013).



**Fig. 1** Theory 1: Central executive. Procedural, Deliberative and Pavlovian systems function in parallel (black boxes) to one another with their own discrete mechanisms of action-selection (purple/green arrows). A separate central executive acts upon the three subsystems to delegate which of the three mechanisms influences action-selection (purple arrows).



**Fig. 2** Theory 2: Multiple experts. Procedural, Deliberative and Pavlovian systems function in parallel (black boxes) and use their own internal mechanisms to alter their self-consistency. Each system sends a stream of information (orange, blue, pink arrows) to downstream motor centers that produce the action (green arrow) signaled by the most self-consistent input.

## 4.2 Theory 2: A multiple experts model

A second theoretical approach points to a conflict resolution hypothesis that has neither a central executive nor a hierarchy. Rather, this heuristic model claims that each decision system is individually responsible for driving downstream structures according to changes in their own self-consistency (van der Meer et al., 2012) (see Fig. 2). Because neural representations are

distributed (Hertz, Krogh, & Palmer, 1991; McClelland & Rumelhart, 1986; Rumelhart & McClelland, 1986), the output of each decision system can contain information about an array of actions, not just the best choice (Zemel, Dayan, & Pouget, 1998). Thus, measurement of the distribution breadth, or the representation's self-consistency (Jackson & Redish, 2003; Johnson, Jackson, & Redish, 2008), points toward the certainty of a particular action, a feature commonly proposed to drive behavior (Daw et al., 2005; Keramati, Dezfouli, & Piray, 2011).

This idea relies on the principle that each decision system acts independently, in parallel, and that within each system there exist internal dynamics that determine the self-consistency of the neural signal. These parallel decision systems then relay their neural information to a single downstream motor center where conflicts are resolved in a competitive winner-take-all process according to the input stream whose information is most self-consistent. Mechanistically, several theories have proposed that internal neural coherence can change the effectiveness of structure-to-structure connectivity, providing a means for self-consistency to regulate neural drive (Engel, Fries, & Singer, 2001; Fries, 2005; Hyman et al., 2010).

Conceptually, this second theory is related to mixture models and multiple experts models of machine learning (Bishop, 2006; Mitchell, 1997). In these models, specialized agents address subspaces of a problem. Each agent provides its best answer along with a confidence signal. Agents applying their specialized knowledge to appropriate components of the problem provide more confident answers, allowing a macro-agent to determine and utilize the most appropriate specialized sub-agent and outperform a single generalist approach.

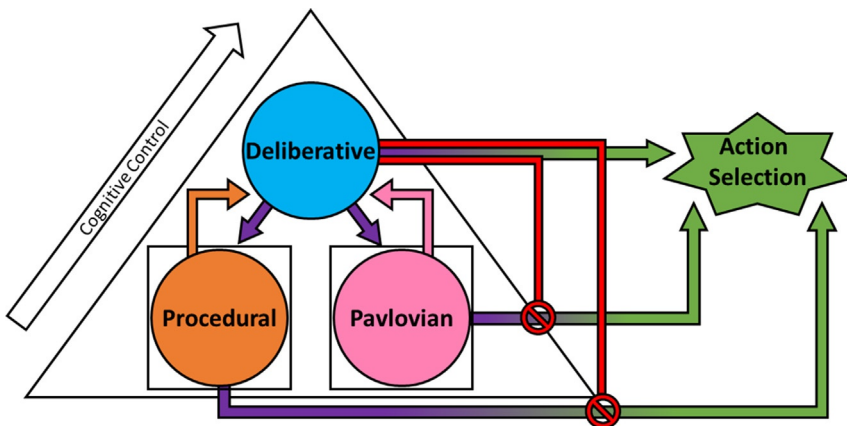
Both the multiple experts and central executive theories are rooted in the assumption that each subsystem functions in parallel, only coming together at an upstream executive (central executive) or downstream effector region (multiple experts). In contrast, the next two theories entail direct interactions between the systems themselves.

### 4.3 Theory 3: Deliberative override

Deciding between decision systems when internal conflicts arise is often viewed as an executive responsibility that requires flexibility. When the brain is presented with external conflicts requiring flexible evaluation of options, Deliberation is typically utilized (Kahneman, 2011; Mischel, 2014; Redish, Schultheiss, & Carter, 2016; Regier & Redish, 2015).

Accordingly, the Deliberative decision system has long been proposed to function as an arbitrator among internal decision processing (Augustine of Hippo (Saint Augustine), 1972; Gazzaniga, 2011; Haidt, 2006). Lending credence to this proposal, Deliberative decisions are slow, computationally intensive, and thus could reflect executive overhead, a stark contrast to the impulsive and inflexible nature of Pavlovian and Procedural responses.

Classic dual-system theories oriented systems hierarchically, with simpler systems functioning autonomously and complex (deliberative, cognitive) systems monitoring ongoing activity and overriding as needed (Bechara & van der Linden, 2005; Eagleman, 2011; Evans, 2008; Gray, 2004; Haidt, 2006; McClure & Bickel, 2014; Mischel, 2014; Redish, 2013). Extending this dual-system story to our three-system story, the resultant hybrid structure retains Deliberative processing atop the hierarchy where it adopts an executive role delegating between Pavlovian and Procedural systems (see Fig. 3). This proposed interaction has been a reigning hypothesis among behavioral economists studying intrapersonal and intertemporal choice models of self-control (Bechara & van der Linden, 2005; Bernheim & Rangel, 2004; Frederick, Loewenstein, & O'Donoghue, 2002; Loewenstein, 1996, 2000; McClure & Bickel, 2014; McClure, Laibson, Loewenstein, & Cohen, 2004; Mischel, 2014).



**Fig. 3** Theory 3: Deliberative override. Procedural and Pavlovian systems function in parallel (black boxes) with their own mechanisms for influencing action-selection (upward purple/green arrows). The Deliberative system acts as an executive over the other two by either actively permitting their action (purple arrows) or overriding it (red stops). Lower systems can also alert the Deliberative by “popping-up” (orange and pink arrows) to take over in emergency situations.

From a neurobiology perspective, deliberative-override presents concrete mechanisms of interactions between decision systems that contrast with the two earlier theories. In particular the interactions between subsystems suggests three distinct mechanisms by which “lower-order” Pavlovian and Procedural systems could drive behavior:

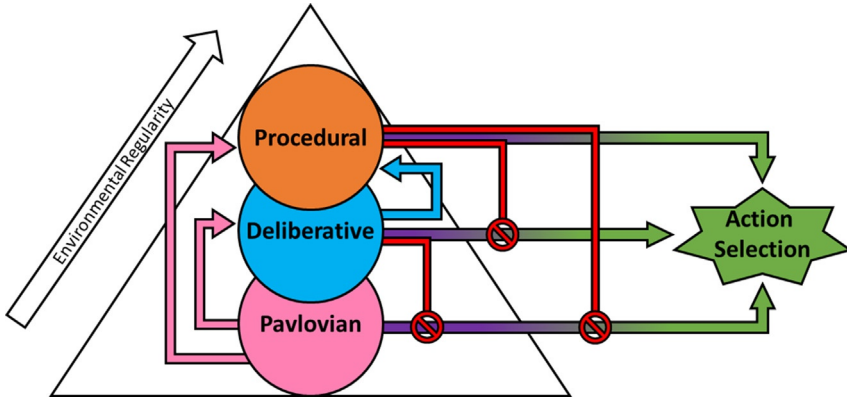
1. The Deliberative executive could actively permit a lower system to function, such as in the case of indulging a craving for sweets.
2. The Deliberative executive could attempt to override a lower system but fail to do so, perhaps due to fatigue. Such a scenario may explain the feeling of “zoning-out” while driving and finding oneself inadvertently reverting to a well-worn route.
3. An emergency or highly unexpected situation could occur, such as a deer darting across a road, inducing a fast lower-order system to actively take control of decision-making and “pop-up” to overpower the Deliberative executive.

Importantly, these mechanisms provide distinct implications for the type of neural activity expected under different decision conflict scenarios, a topic which we will explore in the final section.

Despite its introspective support, the deliberative-override theory possesses notable shortcomings. In particular, the theory lacks sufficient explanation for the relationship between Pavlovian and Procedural decision-making. Are these two systems independently parallel or is there direct competitive interaction between them? Are conflicts between the two fast systems always filtered through the slow Deliberative system, even if Deliberation is otherwise not required or making a rapid decision is critical? The deliberative-override theory also rests on the premise that a decision hierarchy depends on the level of behavioral flexibility of the decision systems at the moment of action-selection.

#### **4.4 Theory 4: Hierarchical override according to environment familiarity**

Even in a completely novel situation, the ingrained nature of Pavlovian responses allow them to drive behavior. With more experience, an agent gradually learns enough about the world to develop an internal cognitive map. At this point Deliberation becomes useful for pursuing an optimal outcome based on abstract or changing goals. Under certain conditions, the same situations necessitate the same actions to reach the same outcomes. Learning these situation-action associations through repetition solidifies Procedural responding and allows for fast decision-making with low effort.



**Fig. 4** Theory 4: Environmental regularity override. The three systems have their own mechanisms for influencing action-selection (purple/green arrows) that develop as environmental regularity is learned. The systems take on a hierarchical structure with Pavlovian processes driving responses under high uncertainty then Deliberative and Procedural systems override lower tiers (red stops) with increasing regularity. Instances where regularity in the environment diminishes, lower systems “pop-up” (pink and blue arrows) to take over.

This natural progression of experience with the external world and the corresponding maturation of the different decision systems suggests a novel (fourth) theory for integrating multiple decision systems: that decision systems operate in a hierarchical setting whereby Procedural action sits atop the hierarchy where it can override Deliberative processes, Deliberation sits above Pavlovian responding which it can override, and Pavlovian systems reside at the base (see Fig. 4). This theory is reminiscent of subsumption architecture, which may provide clues to its neural instantiation (Brooks, 1986). Importantly, in this theory, systems are only applicable in some scenarios, and so come online over time as experience and familiarization with the world drives the maturation of higher level decisions.

Of course even once habits are established, Pavlovian and Deliberative decision systems can drive behavior when situations change and a new world state must be learned. Additionally, unique scenarios can cause the decision systems to seemingly break their hierarchy. In a sudden moment of surprise or fear, behavior becomes driven by the Pavlovian system, ignoring any ongoing Deliberative or Procedural responses. Similarly, even during strongly ingrained habits, Deliberative precommitment can intervene to deviate from the default response. Much as in the case of the deliberative-override theory, these instances of “pop-up” whereby a lower hierarchical system dictates behavior can provide decision-making with additional flexibility to deal with rapid environment changes.



Mechanistically similar to the deliberative–override theory in its reliance on override by higher level systems and pop-up from lower ones, this new theory presents a key conceptual distinction. Deliberative–override centers on the highly flexible and energetically costly Deliberative system adopting a secondary executive role. In contrast, this new theory instead posits that interactions between decision systems are reflective of how these systems naturally adapt to and operate in new situations. Importantly, these two override based theories differ in their predictions for the underlying neurobiology of decision systems, particularly in regard to the role of mPFC. Discussion of predictions that arise from each of the four theories and how they can direct future study of mammalian decision-making are the focus of the final section.



## **5. Prefrontal cortex and combining decision systems**

Given its long perceived role in high level cognitive functioning and executive control, it seems likely that mPFC has a central role in resolving conflicts among the brain's decision systems. However, which of the above strategies underlies how conflicts among the decisions systems are resolved has remained a difficult topic to study. By the very nature of complex decision-making, and the subtleties between the proposed conflict-resolution theories, only a small number of studies have provided good evidence to support any one idea over others, and no solid conclusions can yet be drawn. To gain significant traction in understanding how decision systems come together, and mPFC's role in this process, we believe future work must approach decision-making through the lens of multiple systems. This is a complex undertaking, but we identify several predictions of mPFC functioning that can begin to shed light on how decision systems may interact to produce a singular action. Although we believe these predictions can provide a starting point, they should be recognized as exactly that—simplified starting points that are sure to evolve and mature as data emerge.

Most notably, we believe future work into decision-making should adopt one of two approaches.

Either, behavioral tasks should aim to engage only a single decision system (Pavlovian, Deliberative, or Procedural) as relevant to performance, creating situations where the remaining two systems are explicitly irrelevant for the task. A valuable test in such circumstances would be to completely remove a central component hypothesized to be important to one or more

of the systems and identify that the behavior is affected if and only if the system in question is involved. As it will be nearly impossible to construct behavioral tests that truly access only a single system, specialized behavioral analyses will likely be necessary to segregate decision systems. Classic work utilizing different training paradigms in the Morris Water Maze (Day, Weisend, Sutherland, & Schallert, 1999; Eichenbaum, Stewart, & Morris, 1990; McDonald & White, 1994; Redish, 1999) or localized lesions in the plus maze (Packard & McGaugh, 1992; Yin, Knowlton, & Balleine, 2002) may provide a good template. If such an approach can be successfully employed, it would allow for direct study of a single decision system's inner workings without the need to consider how multiple systems may influence or conflict with each other.

Alternatively, behavioral tasks should aim to engage two or even all three decision systems, ideally with discrete moments in which conflicts occur and behavior is directly reflective of the dominant decision system. Such tasks would present critical time points during which neural activity could be evaluated or manipulated and compared to a definable behavioral output (Gläscher, Daw, Dayan, & O'Doherty, 2010; Hasz & Redish, 2018; Papale, Stott, Powell, Regier, & Redish, 2012; Schmidt, Papale, Redish, & Markus, 2013; Sweis et al., 2018; van der Meer, Johnson, et al., 2010; van der Meer, van der Meer, et al., 2010).

We can identify three ways in which mPFC activity could differentially support the above theories for decision integration:

First, one could look for distinct physiologic signatures of individual decision systems localized to distinct subregions or subpopulations within mPFC.

- Theory 1. The central executive theory predicts that segregated decision information should not be observed as the executive reflects an entity independent of the three decision systems.
- Theory 2. The multiple experts theory predicts that independent streams should exist within mPFC, that these streams should be constitutively active, but that each should only provide reliable action-selection information when driving behavior.
- Theory 3. The deliberative-override theory identifies that independent streams of decision processing should exist among distinct subpopulations within the mPFC, but that there should be interactions such that the Deliberative stream can suppress the other two.

Theory 4. A hierarchical structure based on behavioral and environmental regularity predicts that independent streams should exist within mPFC and that hierarchical systems are actively engaged with higher systems becoming more active with more familiarity and behavioral regularity as lower systems fade away.

Current data may point toward distinct processing streams within mPFC (Killcross & Coutureau, 2003; Powell & Redish, 2016; Rich & Shapiro, 2009; Smith & Graybiel, 2013, 2016), though examples of a single region involved with processing of multiple decision systems can also be inferred (Do-Monte et al., 2015; Kim et al., 2018; Quirk et al., 2000; Sierra-Mercado et al., 2011).

Second, one could evaluate how manipulations of mPFC impact a decision response. We will address conflict resolution later; here, we address situations in which only a single system is engaged.

Theory 1. The central executive theory predicts that when behavior is driven by a single active system, the central executive would not be required and thus lesions or other experimental manipulations of mPFC would have no impact on behavior.

Theory 2. The multiple experts model predicts that the effect of manipulations to mPFC should be both dependent on which decision stream is impacted, and on the nature of the manipulation. If the qualitative nature of the neural signal were changed it would be expected to change the nature of the behavioral response, but if instead only the signal variability were altered it would have no behavioral consequence in the case of only a single active decision system.

Theory 3. The deliberative-override theory predicts that the impact of mPFC manipulation should be highly dependent on which subpopulation of mPFC is altered and which decision system is active. Substantive impacts on behavior should only occur when the affected subpopulation is the one involved in the decision system of interest.

Theory 4. Similar to deliberative-override, a regularity-based hierarchy predicts that impacts of mPFC manipulations should be highly dependent on the specific subpopulation affected and the respective decision situation.

Third, one could evaluate how manipulations of mPFC impact neural decision representations in other brain areas (amygdala, hippocampus, and dorsolateral striatum).

- Theory 1. The central executive theory predicts that manipulation of mPFC would have no impact on downstream processing in other brain regions when only a single decision system is engaged, as the central executive is not needed.
- Theory 2. The multiple experts theory also predicts mPFC manipulations should not influence processing in other brain regions. However, this is because other brain regions exist upstream from mPFC in decision processing in this theory.
- Theory 3. The deliberative–override theory predicts (though not necessarily requires) that manipulation of mPFC would produce measurable impacts on decision representations elsewhere in the brain. Furthermore, this interregional impact would be localized within mPFC where specific subpopulations only impact specific brain regions.
- Theory 4. A regularity–driven hierarchy would likewise predict any impacts from mPFC manipulations on other brain regions should be localized, and should depend on which subpopulation was affected.

To date, the prediction common to theories 3 and 4 has the best experimental support (Guise & Shapiro, 2017; Hok et al., 2013; Ito et al., 2015; Killcross & Coutureau, 2003; Rich & Shapiro, 2009; Schmidt et al., 2019; Smith et al., 2012).

Each theory also provides a set of predictions for multiple decision systems in conflict (see Table 1).

**Theory 1.** Under conditions in which multiple decision systems compete to drive behavior, the central executive theory relies on a single critical location (here proposed to be mPFC) actively relaying instructions directly to each decision system. Additionally, under this theory, the identities of the decision systems in conflict would determine which structures the central executive would be expected to communicate with. These premises elicit three prominent predictions.

First, activity in the central executive and different decision systems should be temporally linked, perhaps indicated by LFP coherence between mPFC and amygdala, hippocampus, dlStr (Adhikari et al., 2010; Benchenane et al., 2010; Hyman et al., 2010; Jones & Wilson, 2005; Kim et al., 2018).

Second, if the timing of connections between mPFC and an individual decision system were disrupted it would produce deficits in appropriately utilizing the respective system.

**Table 1** Key features and predictions summary for future mPFC decision system experiments.

Theory features	Key predictions
<p>1. <i>Central executive</i>            Physiologically distinct executive system            Information flow is guided by empowering a single decision system to influence action            All conflict resolution relies on the central executive</p>	<p>No independent streams of decision system information would be observed in mPFC            mPFC manipulations should not impact single decision behavior or downstream processing in other brain regions            Any mPFC perturbation should lead to breakdowns in decision-making during internal conflict resolution</p>
<p>2. <i>Multiple experts</i>            Decision systems are individually responsible for driving downstream structures            Information flow is guided by changes in each stream's self-consistency            A winner-take-all process determines action based on the stream whose information is most self-consistent</p>	<p>Parallel streams exist within mPFC that are consistently active and converge on a downstream target            Impact of mPFC manipulation should depend on the altered subregion and the qualitative nature of the signal            mPFC perturbation should not impact representations in other brain regions and should not result in total breakdown of conflict resolution</p>
<p>3. <i>Deliberative override</i>            The deliberative decision system functions as a central executive by delegating between Pavlovian and Procedural systems            Information flow is guided by deliberative override and lower-system pop-up mechanisms</p>	<p>Information streams should exist within mPFC and are not consistently active            Impact of mPFC manipulation should depend on the affected subregion and active decision system            There should be interactions between streams that show override, but not pop-up signatures of the deliberative system to suppress the lower other two</p>
<p>4. <i>Regularity-based hierarchy</i>            Decision system hierarchy exists with Procedural at the top followed by Deliberative then Pavlovian at the base            Experience and familiarization with the world drives the maturation of decisions up the hierarchy and overrides lower system function            Unique scenarios can cause lower systems to pop-up and break the natural hierarchy</p>	<p>Independent streams should exist within mPFC and higher systems become more active with more environmental familiarity            Impact of mPFC manipulation depends on the affected subregion and the respective decision situation            There should be interactions between streams that show both override and pop-up signatures of the Deliberative system to suppress lower Pavlovian and overcome higher Procedural systems</p>

Distinguishing physiological and behavioral predictions that are implied by the main computational features of each conflict-resolution theory.

Third, given that all conflict resolution relies on the central executive, any perturbation of the mPFC itself should produce a breakdown in all decision-making scenarios in which conflicts arise.

**Theory 2.** In the multiple experts model, distinct streams of decision processing should be present concurrently and should project to a single common source where the final action-selection can be derived based on the relative self-consistency of the streams. Accordingly, we present three predictions for experimental data.

First, distinct streams of decision information should be observable among mPFC subpopulations that share a common downstream target, and these representations should occur concurrently. Thus the requisite self-consistency information would arrive at a downstream premotor/motor center to be directly contrasted.

Second, the decision system that drives an agent's action should be directly predictable by comparing the internal self-consistency between these parallel information streams, a premise that has found experimental support (Lee, Shimojo, & O'Doherty, 2014).

Third, fine scale experimental manipulations of different aspects of decision representations within mPFC should produce different behavioral consequences. Specifically, altering the general nature of a decision signal while concurrently maintaining its overall level of self-consistency would be predicted to impact the specific action taken, but not the decision system that produced it (e.g., tweak to the Deliberative action but still a Deliberative approach). Alternatively, if an intervention reduced the self-consistency of a single system, perhaps through the addition of noise, it would decrease the likelihood of the affected decision system driving behavior.

**Theories 3 and 4.** Both of the proposed override-based theories resolve decision conflicts using similar mechanisms described here as *override* and *pop-up*. One prediction common to these two theories is that interactions between pairs of decision systems should be characterized by one of two fundamentally distinct physiologic signatures.

First, an "override" mechanism should be observable in which a higher status system exhibits prolonged activation, leading to suppression of activity within the corresponding lower status system.

Second, a "pop-up" mechanism should be observable in which the lower status system hijacks control. While we do not know how this pop-up would manifest physiologically, we expect it to be a relatively anomalous event that coincides with external stimuli that may indicate an emergency or signal the need for a dramatic change in decision processing.

Theories 3 and 4 differ largely in their utilization of override and pop-up mechanisms and in the implications for manipulations of individual decision systems.

Theory 3 predicts that Deliberation should override both Pavlovian and Procedural systems, while both Pavlovian and Procedural systems could pop-up over Deliberation. Expanding on this framework, behavioral actions linked with the Deliberative system would always be expected to coincide with elevated activity within Deliberative subpopulations of mPFC. Both behaviorally and physiologically, pop-up signatures should never be observed in association with Deliberative approaches. In parallel, instances of either Pavlovian or Procedural responding should coincide with a weak, and thus insufficient, override signal within the Deliberative system or in special circumstances with a pop-up signature in respective mPFC subpopulations. In regards to localized manipulations of individual decision systems, this theory predicts that disruption of Pavlovian or Procedural systems would have a restricted impact, affecting only the respective system. However, manipulations to the Deliberative executive could have profound consequences particularly during conflicts between the Pavlovian and Procedural systems. In such a case, lack of an override mediator would lead to a fundamental breakdown in general decision-making.

Theory 4 predicts that the occurrence of behavioral and physiological override and pop-up would match the hierarchical relationships among decision systems. Deliberation would override Pavlovian responding and the Procedural system would override both other decision systems. In parallel, Deliberation could be observed to pop-up over Procedural actions while Pavlovian responding could pop-up over both other systems. Importantly, override signatures would never be expected within the Pavlovian subpopulation of mPFC whereas pop-up is never expected from the Procedural subpopulation. Due to this hierarchical structure of interactions, disruption of any one decision system would be predicted to impair its ability to drive behavioral responding either in isolation or during conflict situations, but critically would have no substantive impact on the functioning or interactions of any remaining decision systems.



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## 6. Conclusions

Decision-making is a central feature of how animals interact with their external environment. There are multiple decision systems that are computationally and neurally distinct. Though separable circuitry houses each

decision system, current theories suggest that the rodent medial prefrontal cortex plays a central role in how these multiple systems come together to produce a single, unified action. Many theories have been developed to explain how integration occurs between multiple decision systems, and what structures may be involved in this process. Having clear, computational definitions for each decision subsystem has helped to derive mechanistic insights that link the psychological theories of decision-making to predictions about the underlying neurobiology particularly of the rodent medial prefrontal cortex. These predictions can frame experimental data and act as a guide for the future work necessary to fully understand how decisions are made and how mPFC activity relates to behavior. These competing theories have direct implications for what mPFC is doing for individual systems as well as multiple system integration. These theories point to different neurophysiological and behavioral predictions for which data can be collected and used to provide greater insight into mPFC's role in rodent action-selection, and thus into the internal dynamics of the decision process itself.

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