Review

The Urge to Decide and Act: Implications for Brain Function and Dysfunction

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Abstract

Humans and other animals are motivated to act so as to maximize their subjective reward rate. Here, we propose that reward rate maximization is accomplished by adjusting a context-dependent "urgency signal," which influences both the commitment to a developing action choice and the vigor with which the ensuing action is performed. We review behavioral and neurophysiological data suggesting that urgency is controlled by projections from the basal ganglia to cerebral cortical regions, influencing neural activity related to decision making as well as activity related to action execution. We also review evidence suggesting that different individuals possess specific policies for adjusting their urgency signal to particular contextual variables, such that urgency constitutes an individual trait which jointly influences a wide range of behavioral measures commonly related to the overall quality and hastiness of one's decisions and actions. Consequently, we argue that a central mechanism for reward rate maximization provides a potential link between personality traits such as impulsivity, as well as some of the motivation-related symptomology of clinical disorders such as depression and Parkinson's disease.

Keywords

reward rate, decision making, urgency, vigor, motivation, basal ganglia, personality, impulsivity, depression, Parkinson's disease

Introduction

Animal behavior is fundamentally motivated by the pursuit of rewards, including primary reinforcers such as food as well as secondary goods such as money. The prospect of reward thus governs our decisions about the actions we take as well as the effort we invest in those actions. Understanding how the brain weighs rewards and efforts and how it adjusts behavior accordingly are therefore critical topics of research for understanding cognition and action.

However, the value of an individual reward is rarely the sole variable of interest. That is because any time an animal engages in a given activity—no matter how rewarding—it also necessarily foregoes other potential activities that may also be rewarding. A large coconut that takes 2 minutes to crack may taste good but might not ultimately be the best choice in the presence of some grapes that would take merely seconds to eat. Thus, the real subjective value of a given activity is related to a multitude of factors linked not just to the immediate rewards and efforts associated with that activity but also to the amount of time invested in it and the prospective value of any latent alternatives. Therefore, what is ultimately most adaptive is to choose actions that maximize one's global *reward rate*, relative to the other potential courses of action that one could pursue instead.

Reward rate depends on many factors, including the subjective payoff (*utility*) of a potential outcome, the *probability* of obtaining that outcome by performing a given action, the *cost* (e.g., biomechanical effort) of the action, as well as the total time invested—which includes the *deliberation time* taken to make the decision, the *handling time* required before the chosen action yields the reward, and the *intertrial interval* (ITI) before one can try again (Fig. 1). Optimizing one's performance in any scenario involving the serial collection of rewards over time therefore requires that each of these factors be taken into account when determining how to think and act.

The interrelationships among the multiple variables that jointly determine reward rate necessarily give rise to a number of fundamental trade-offs. For example, while taking more time to deliberate generally improves one's probability of successfully choosing the action

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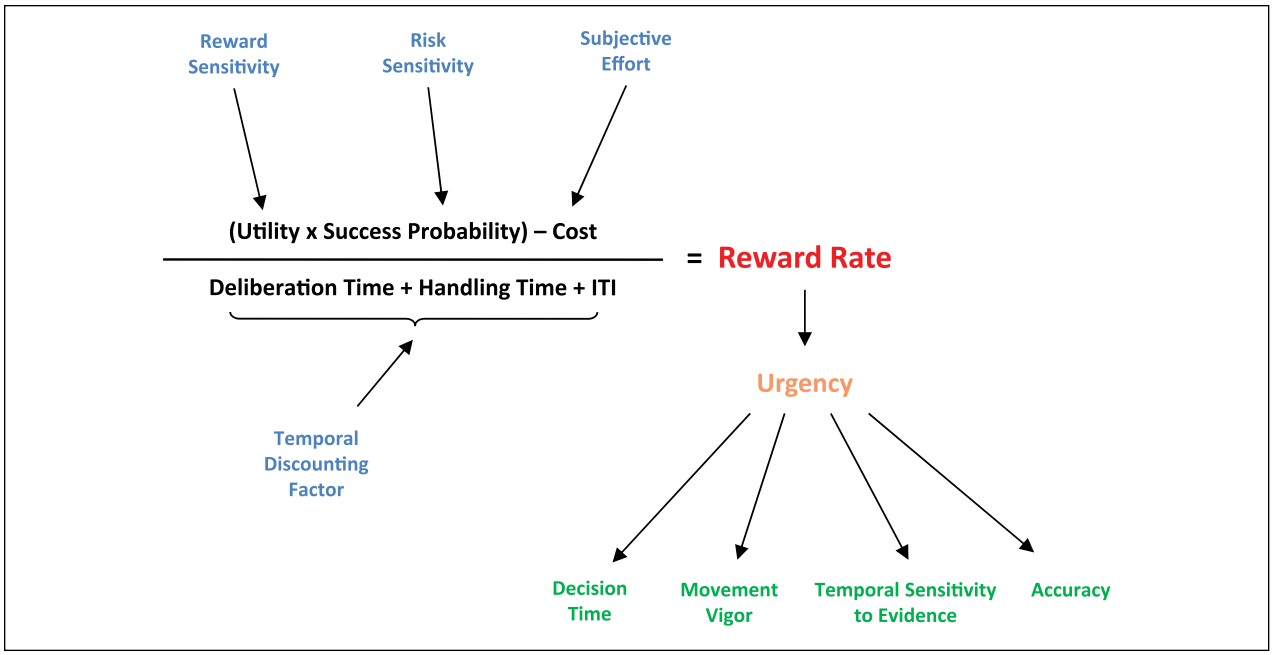


Figure 1. Schematic view of how multiple subjective factors (blue text) and situational variables (equation, black text) jointly influence an individual's estimate of reward rate. ITI = intertrial interval. We propose that the resulting estimate of reward rate is used to control an "urgency signal," whose setting produces systematic shifts in a variety of "downstream" behaviors (green text). The joint coordination of multiple behavioral dimensions by a single underlying mechanism thereby provides an efficient mechanism for maximizing reward rate across a broad range of settings.

that yields a reward, doing so also delays that reward, as well as reduces the amount of time that one can potentially spend pursuing other possibilities. By extension, costs in any one dimension—such as increased deliberation time—may be compensated for in another, for example, by increasing the speed of the movements used to implement the outcome of that deliberation so that the next opportunity can be encountered more quickly.

Because of the inherent complexity of these interrelationships, even relatively subtle differences among any single task factor can significantly affect how one should best spend their time, and there is therefore no single decision policy that is guaranteed to maximize reward rate across all contexts. Instead, many diverse cognitive and behavioral variables must be flexibly coordinated within each new setting in order to exploit these interdependencies in an optimal manner. Consequently, nearly all decision scenarios present decision makers with a fundamental *speed-accuracy trade-off* (SAT) that constrains how they adjust their behavior to a given environmental context. Indeed, a wide variety of studies have shown that both animals and humans are highly sensitive to the context-dependent trade-offs between hasty versus conservative behavior (Heitz 2014) and will often flexibly sacrifice one for the other when doing so can improve their overall rate of reward (Balci and others 2011; Bogacz and others 2010a). However, the precise neural mechanisms by which this context-dependent behavioral flexibility is achieved remain largely unknown.

In what follows, we review theoretical arguments, as well as behavioral and neural data, suggesting that an "urgency" signal provides the central underlying mechanism by which multiple aspects of behavior are jointly coordinated in the service of maximizing reward rate. We first present the theoretical motivation for positing the existence of the urgency signal, and review data suggesting that it is controlled by projections from the basal ganglia to a wide set of cognitive and sensorimotor regions of the cerebral cortex. This neural signal grows over the course of deliberation, continually "pushing" decision-related neural activity toward the threshold required for choice commitment as time elapses. Importantly, the rate at which this signal grows is strongly modulated by task context, and directly influences multiple behavioral parameters that are each intrinsically related to reward rate maximization, such as the amount of time required for committing to an action choice and how quickly ("vigorously") that action is performed.

Next, we review data suggesting that both animal and human decision makers exhibit considerable variability in their "baseline" level of urgency, and thus that urgency may be usefully conceptualized as an individual "trait" (Berret and others 2018; Reppert and others 2018). For example, consider an identical task performed by two individuals who differ solely in their relative sensitivity

to the value of rewards (Fig. 1, blue text). This would yield two different subjective estimates of reward rate, culminating in a suite of behavioral differences across multiple measures commonly related to the overall "hastiness" of their decisions and motor behavior (Fig. 1, green text). By acting as a common mechanistic pathway linking various ("lower-level") aspects of reward processing and motivation to overt behavior, we argue that individual variability in urgency may potentially provide a link between decision making and the hallmark cognitive and behavioral manifestations of broader personality traits, such as impulsivity.

Finally, we conclude by reviewing a range of clinical findings that suggest the potential of an urgency mechanism to provide a unified account of the etiology and symptomology of a number of clinical disorders, focusing in particular on depression and Parkinson's disease. In this view, pathophysiological alterations within a variety of neural mechanisms centrally related to reward processing may lead to chronically elevated or diminished levels of urgency, thereby contributing to some of the defining symptoms of these disorders. Overall, therefore, we aim to illustrate how a highly general and evolutionarily conserved mechanism—one that is at the core of animals' ability to adapt their behavior to the reward contingencies across many different behavioral contexts—may have important ramifications for understanding individual differences in human personality, and may even constitute a novel "trans-diagnostic" mechanism for understanding multiple heterogeneous forms of clinical pathophysiology.

Reward Rate and Urgency

We begin with a simple demonstration of why control of urgency is useful for maximizing reward rates. Consider a scenario in which an agent is making a series of simple decisions between mutually exclusive actions on the basis of information that is gradually collected over time, and in which the agent is free to decide how much time to allocate toward information gathering before committing to a choice. After the choice is made, there will be a certain probability of successfully receiving a reward, the likelihood of which tends to be higher if more time was spent collecting information about which choice is correct. However, each choice also necessarily incurs costs—including the effort of movement as well as the total time invested in deliberation, handling, and ITI—which at least partially offset the gains in reward rate available from investing additional decision time.

In general, the local reward rate for a given action can be mathematically expressed using the equation shown in Figure 1, which is plotted in Figure 2A (red curves) for trials of different difficulty. Because prolonging deliberation improves accuracy (Fig. 2A, green curves)—and thus increases the probability of reward—the reward rate (red curves) initially increases as a function of time. However, as the marginal improvements in accuracy level off, the investment of additional time begins to outweigh the value of further deliberation, and the reward rate function begins to decrease. Thus, during any given decision, there is a moment in time at which reward rate is maximal (purple dots), which thereby defines the optimal time at which to commit to an action.

Interestingly, the mathematical solution for the optimal time of commitment has the same mathematical form as Charnov's *marginal value theorem* (Charnov 1976), a law in foraging theory that describes how long animals tend to harvest a given "resource patch" in their environment before leaving to find another. In a foraging scenario, the quantity being maximized is the global harvest rate from patches that each yield diminishing returns over time, whereas what is maximized here is the reward rate from trials in which the value of further deliberation yields diminishing returns over time. Nonetheless, in both cases there are diminishing returns with longer duration (of either foraging or deliberation)—and one therefore obtains the same mathematical form of the solution for the optimum duration. A wide variety of studies have shown that animals ranging from insects to humans generally follow the marginal value theorem (Hayden and others 2011; Stephens and Krebs 1986; Yoon and others 2018), though of course their behavior may also be influenced by other factors such as exploration, fatigue, sudden threats, and so on.

Thura and others (2012) have shown that under a wide range of conditions there is a simple policy for finding the ideal moment in time when reward rate is maximal. Stated briefly, one needs to commit at the moment when one's estimate of the probability of success reaches a threshold ("accuracy criterion") that *decreases over time* (Fig. 2A, purple line). This follows directly from the equation in Figure 1, but it also expresses a very intuitive heuristic: If you're confident right away, go ahead and act. If you're not, then think a little more and/or wait to see if the world provides you with more information. But as time passes, lower your criterion of accuracy so that you don't wait forever.

How might the brain implement such a decision-making policy at the neural level? One possible mechanism is to estimate the evidence in favor of a given choice and compare it with a decreasing threshold (Fig. 2B). Another is to combine the evidence with a signal that rises over time and compare the result to a fixed threshold (Cisek and others 2009), as shown in Figure 2C. As reviewed below, neural data currently favors the latter mechanism, and suggests the existence in the brain of a context-dependent "urgency" signal that grows over time, thereby continually "pushing" neural activity toward a fixed firing rate threshold for committing to an action.

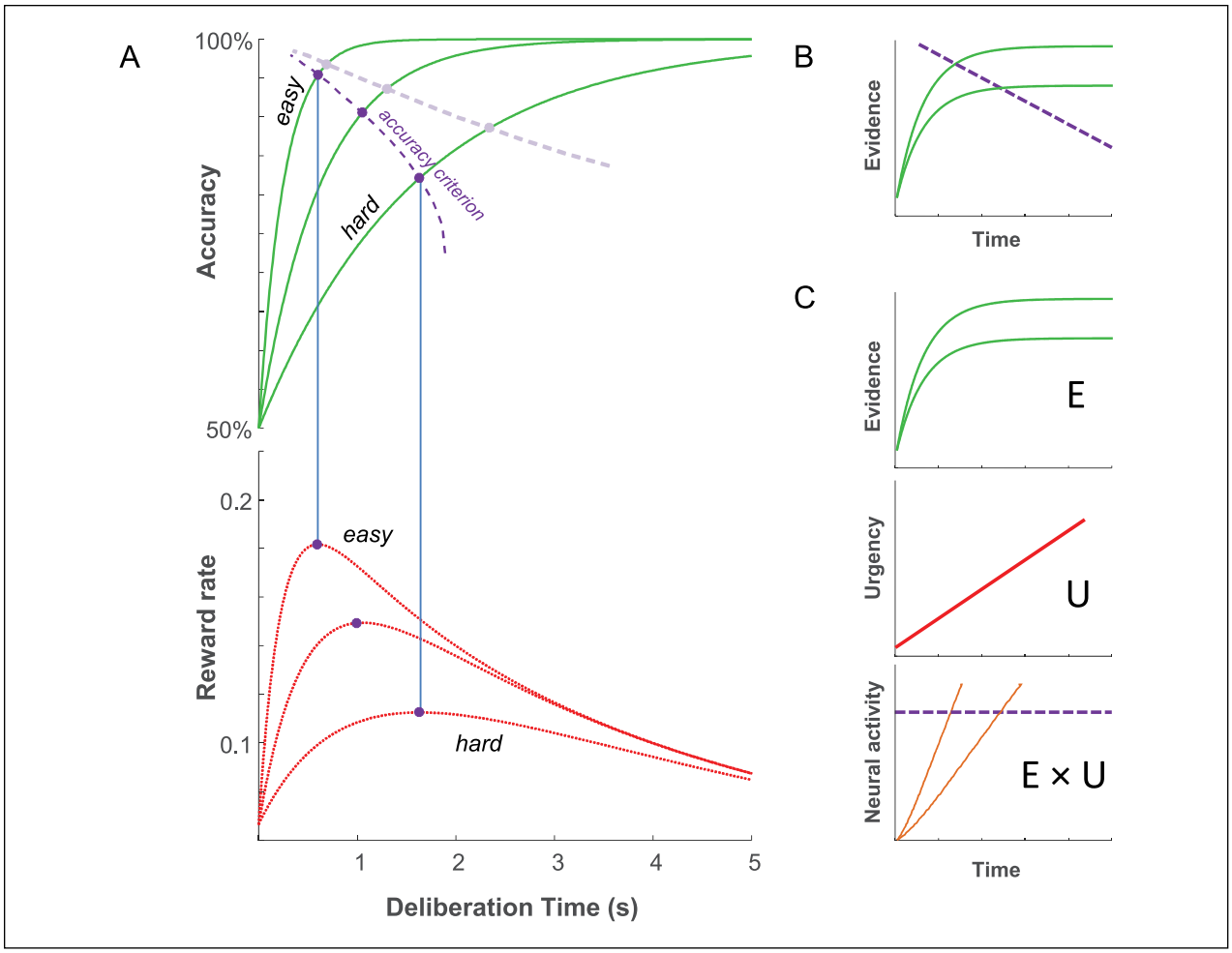


Figure 2. (A) Theoretical motivation for the use of an urgency signal in decision making. The plot at the top shows the probability of being correct (solid green lines) as a function of deliberation time for three trials that differ in difficulty (strength of evidence). The plot at the bottom shows the reward rate (red lines) obtained for those trials, again as a function of deliberation time (here calculated assuming that handling time + ITI = 3 seconds (ITI = intertrial interval), and that the cost of the movement used to report the decision is proportional to 30% of the value of the reward at stake). Purple dots (at the peak of each reward rate function) indicate the mathematically optimal moment at which to commit. Note that these moments define a decreasing criterion (dashed purple line) in the accuracy plot above. The precise rate at which this ideal accuracy criterion decreases is also dependent on a variety of other factors, such as the cost of the movement (see Fig. 1), and would therefore decrease more slowly under conditions in which the movement used to report the decision outcome is more costly (50% of reward; light purple). (B) Optimal decision-making can be implemented by calculating evidence (green) and comparing it to a decreasing threshold (purple). (C) Alternatively, evidence (green) could be combined with a growing "urgency" signal (red) to produce neural activity that grows over time (orange) until it reaches a fixed commitment threshold.

Neural Mechanisms of Decision Making

Over the past two decades, neurophysiological investigations in non-human primates have led to the hypothesis that when a decision involves the selection of an action, it is computed in the same circuits that guide the preparation and execution of that action (for reviews, see Cisek and Kalaska 2010; Gold and Shadlen 2007). Indeed, regions of the brain traditionally labelled as "sensorimotor areas" possess neurons whose action-related activity often covaries with non-motor decision factors such as expected utility, reward probability, elapsed time, and many other variables. Based on such observations, it has been proposed that during interactive behavior, sensorimotor areas of the brain simultaneously specify the actions currently available in the environment and select between them through a dynamic, distributed competition that is continuously influenced by a variety of biasing inputs. Such inputs may include salience (Foley and others 2014), expected utility (Platt and Glimcher 1999), reward probability (Pastor-Bernier and Cisek 2011; Yang and Shadlen 2007), or motivational significance

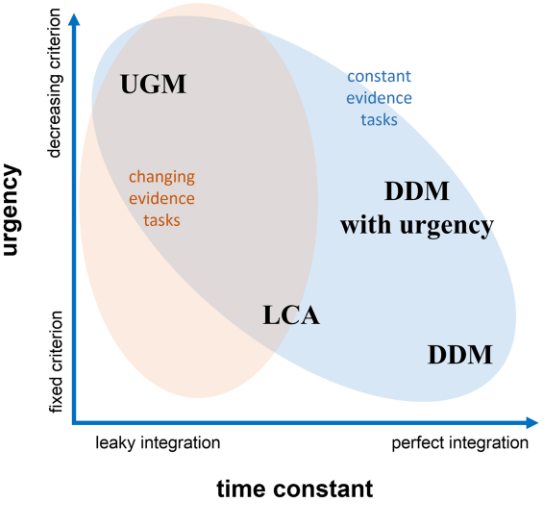
(Leathers and Olson 2012)—in short, any factor relevant for resolving the competition between potential actions (Cisek 2007; Cisek and Pastor-Bernier 2014; Shadlen and others 2008).

Interestingly, many studies have shown that during the process of deliberation, neural activity in these sensorimotor structures gradually builds up at a rate related to the strength of sensory evidence, reaching a final firing rate at the time of commitment that is approximately the same across trials (Gold and Shadlen 2007; Hanes and Schall 1996; but see Heitz and Schall 2012). Such neural activity patterns have typically been interpreted as the temporal integration of sensory evidence to a fixed accuracy threshold, in line with a class of theories called *bounded integrator* or *drift-diffusion models* (Gold and Shadlen 2007; Ratcliff 1978). However, an alternative explanation is that such neural build-up is due to the combination of sensory evidence with an "urgency" signal that grows over the course of deliberation (Fig. 2C) (Cisek and others 2009; Ditterich 2006). Importantly, such a mechanism would not only explain the timing of decisions but would also reduce the effective amount of evidence required for commitment as time progresses, thereby simultaneously implementing the decreasing accuracy criterion that is necessary for optimal behavior (Drugowitsch and others 2012; Thura and others 2012).

Whether the build-up of neural activity is caused by evidence integration or urgency is currently under debate (see Box 1). It is difficult to discriminate these explanations on the basis of most existing data; and because bounded integration models are so well-known in the field, most studies still tend to interpret neural activity build-up as evidence integration. However, studies specifically designed to discriminate between these models favor the existence of an urgency mechanism and suggest that it may be responsible for most of the build-up observed during decision making (see references cited in Box 1). If that is the case, then it is important to consider what the conceptual and practical ramifications of the existence of such a signal might be. First, however, it is important to ask whether we can identify such a signal in the brain and characterize how it influences the neural mechanisms of decisions and actions.

Box 1.

A classic model of perceptual decision making—the *drift-diffusion model* (DDM)—posits that during deliberation the brain continuously accumulates sensory evidence until the total reaches a fixed threshold, whose setting acts as an accuracy criterion (Ratcliff 1978). Based on this popular framework, the build-up of neural activity reported during many decision-making studies is commonly interpreted as the neural correlate of the evidence accumulation process (Forstmann and others 2016; Gold and Shadlen 2007). However, several observations cast doubt upon this interpretation. For example, numerous studies have demonstrated that the time window used by the brain to integrate incoming evidence is substantially shorter than the duration of decisions (Cook and Maunsell 2002; Ghose 2006; Ludwig and others 2005; Luna and others 2005; Stanford and others 2010; Uchida and others 2006; Yang and others 2008), and shorter than the duration of build-up activity. Furthermore, build-up activity is observed even when no genuine decision-related evidence is present (Churchland and others 2008), suggesting that this activity may instead be related simply to the passage of time itself (Ditterich 2006; Janssen and Shadlen 2005; Thura and Cisek 2014). Conversely, build-up activity is significantly weaker—or even entirely absent—during decision-making tasks in which the time of response is externally controlled (e.g., by a "GO" cue; see Roitman and Shadlen 2002; Shadlen and Newsome 2001), or before information is provided about the action that must be performed (Bennur and Gold 2011). In short, the presence or absence of build-up activity appears to be less related to the processing of sensory information and more related to motor-preparatory processes, especially when animals are free to trade-off speed versus accuracy to maximize their reward rate.



Based on these observations, we have suggested two modifications to the classic DDM (Cisek and others 2009; Thura and others 2012). First, we propose that integration of sensory evidence is fast, in line with the data cited above, with Bayesian optimality, and with the ecological necessity of remaining sensitive to sudden changes in the world. Second, we propose that the build-up of neural activity is largely caused by a growing urgency, which as noted above is important for maximizing reward rates (Drugowitsch and others 2012; Thura and others 2012). The result is called the *urgency-gating model* (UGM).

The UGM and DDM are not completely different models. Both involve integration of sensory information (DDM with a long time constant, UGM with a short one) and both compare the result to an accuracy criterion (fixed in the DDM, decreasing in

the UGM). Therefore, they can be seen as two corners of a two-dimensional space of models, whose axes are defined by the length of the time constant and the slope of the urgency signal (see figure). Other models—such as the *leaky competing accumulator* (LCA) (Usher and McClelland 2001)—also lie within that space, and the challenge for researchers is to devise experiments that help to narrow down which part of that space is most compatible with the data.

Importantly, almost all the studies used to support the DDM have used behavioral tasks in which the information contained in the stimulus is constant over time in each trial. Under such conditions, the DDM and UGM make nearly identical predictions regarding the patterns of neural activity build-up and the resulting behavior. In other words, data from constant-evidence tasks (blue) is compatible with many models in this space and does not exclusively support any one type of model. For this reason, attempts to determine which model provides the best fit to data from such tasks (Chandrasekaran and others 2017; Hawkins and others 2015a; Hawkins and others 2015b; Murphy and others 2016; Palestro and others 2018) have not provided a consistent answer, with results sometimes favoring one model and sometimes the other, and sometimes yielding different answers even for individual subjects in an identical task. In contrast, distinguishing the models is much easier using data from tasks in which the information contained in the stimulus changes over the course of an individual trial, because in such conditions, the models make very different predictions regarding how the decision process is influenced by a given sample of evidence at a given moment. These studies have consistently favored the assumptions of the UGM (Carland and others 2016; Cisek and others 2009; Gluth and others 2012; Malhotra and others 2017; Thura and others 2012). In particular, one recent study from our lab (Carland and others 2016) presented human subjects with a version of the classic random-dot motion discrimination task often used to support the DDM, but with a crucial difference: we inserted brief and subtle "pulses" of motion information at different times during the trial and tested what effect these pulses had on behavior. We found that a given motion pulse influenced behavior only if it fell within a relatively short temporal window that depended on a given subject's tendency to respond quickly or slowly in a given condition. This is exactly what was predicted by the UGM and is incompatible with any version of the DDM—regardless of parameter settings—because it directly contradicts the assumption that all sensory information is integrated until the threshold is reached.

Consequently, while we recognize the important role that the DDM has played for many years in advancing our understanding of decision making, we believe that some of its original assumptions must be modified in light of recent neural and behavioral data. This is controversial, and we refer interested readers to our earlier papers in which we provide a more complete account of why we favor the UGM (Carland and others 2015; Carland and others 2016; Thura and others 2012). In the present article, we focus instead on exploring what potential additional insights the concept of an urgency signal may offer into neural mechanisms and behavioral phenomena in both health and disease.

To directly investigate these questions at the neural level, we trained rhesus monkeys in a probabilistic guessing paradigm we call the "tokens task" (Fig. 3A), which we previously used with human subjects (Cisek and others 2009). In each trial, 15 small circular tokens are distributed one by one, every 200 ms, from the central circle to one of two potential lateral targets, and subjects have to complete a reaching arm movement to select the target they believe will contain the most tokens by the end of the trial. Importantly, this decision can be made at any time, and once a target is selected the remaining token movements shorten to either 150 ms (in "slow" blocks of trials) or 50 ms (in "fast" blocks). Thus, the subject is faced with a trade-off between improving their reward rate either by emphasizing *accuracy* (i.e., increasing their likelihood of success by taking more time to collect information on individual trials) or emphasizing *speed* (i.e., by guessing more quickly to increase their total number of opportunities for reward). Importantly, the best setting of this trade-off differs between the blocks, as the significantly reduced ITI in the "fast" blocks means that the subject stands to gain more benefit from making faster, less-accurate decisions, thereby shifting the balance in favor of a hastier decision policy.

As predicted, we found that our subjects effectively formed their decisions on the basis of progressively less evidence as time elapsed in a given trial. Moreover, we also observed that the way in which their decision criteria decreased over time differed significantly between the "fast" and "slow" blocks, indicating that the subjects were indeed sensitive to the context-specific trade-offs afforded by each task condition. Finally, we showed that the monkeys' reaction time and accuracy distributions for each block type could be modeled using a simple linear urgency signal with just two parameters (slope and intercept; Fig. 3B). Together, these findings are consistent with the proposal that decision policies are governed by an urgency signal which continually "pushes" the subjects to make decisions as time elapses, and that this signal is higher when hasty behavior becomes increasingly advantageous (Thura and others 2014).

Interestingly, our studies also revealed an unexpected interaction between decision urgency and movement kinematics: in blocks of trials favoring hasty decisions, the monkeys' reaching movements were faster than similar movements performed during blocks of trials favoring slower, more accurate decisions (Fig. 3C). This block-dependent effect of urgency on movement execution did not appear to be effector-specific, as it also affected to some extent the speed of saccadic eye movements (despite the fact that oculomotor behavior was not constrained in the task and did not affect reward rates). Furthermore, an

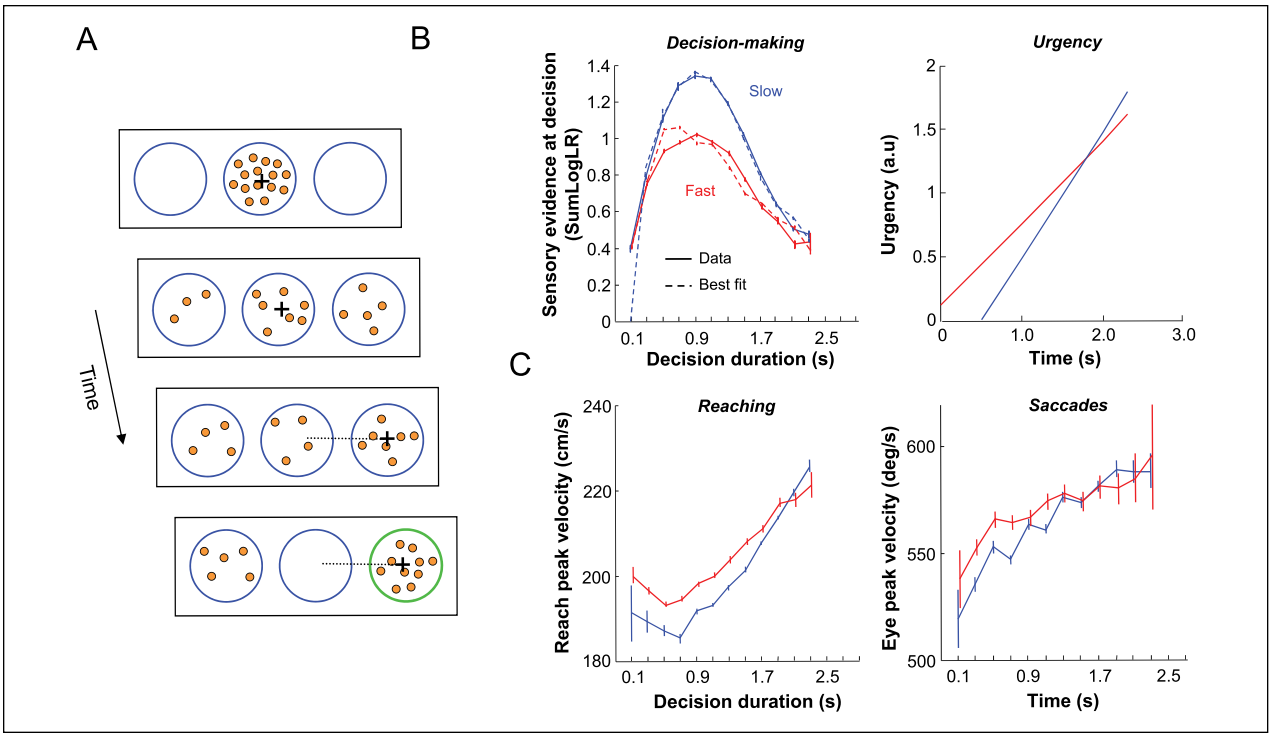


Figure 3. (A) The "tokens" task. During each trial, 15 tokens jump sequentially from the center to one of the outer targets every 200 ms. The monkey's task is to move the cursor (cross) to the target that he believes will ultimately receive the majority of tokens (green circle) and is free to make this decision at any time during a trial. After his choice is made, the speed at which the remaining tokens are distributed into the targets is increased either to 50 ms (in "fast" blocks) or 150 ms (in "slow" blocks). Because the benefits of early decisions are significantly greater in "fast" blocks, each block type encourages different speed-accuracy trade-off (SAT) policies, causing the monkeys to respond with relatively hastier or slower decisions in each condition. (B) The behavior of Monkey S in the tokens task. The left panel shows the quantity of sensory evidence (computed as the sum of log-likelihood ratios), available to the monkey at the time of commitment as a function of decision duration and SAT context, that is, trials in which slow and accurate decisions are favored (blue) or trials encouraging fast and risky decisions (red). The right panel shows the estimated shapes of the urgency functions in the two SAT conditions computed by fitting the urgency-gating model to the monkey's behavior (dashed curves in the left panel) using different values of urgency slope and intercept. (C) Monkey S's motor behavior in the tokens task. The left panel shows the peak velocity of reaching movements performed by the monkey to report his choices as a function of decision duration and SAT condition. The right panel shows the peak velocity of eye movements performed by the monkey as a function of time during deliberation and SAT condition. Reproduced with permission from Thura and others (2014).

effect of urgency was also evident *within* task blocks: earlier decisions (generally made on the basis of strong sensory evidence combined with relatively low urgency) were followed by longer, slower movements; whereas later decisions (relying on comparatively weaker sensory evidence in combination with a higher level of urgency) were followed by shorter and faster arm movements. These findings suggest not only that urgency controls the timing of decisions, but also that the *state* of the urgency signal at the time of a decision can influence the speed of the ensuing motor commands.

To test the model at the neural level, we recorded the spiking activity of individual neurons in the dorsal premotor (PMd) and primary motor cortex (M1) (Thura and Cisek 2014; 2016), two key nodes in the network controlling the selection and execution of reaching movements. In both regions, neurons active during the deliberation process exhibited activity patterns that clearly reflected how the sensory evidence provided by the tokens unfolded over time in different types of trials (Fig. 4A, left). Furthermore, in addition to the sensory evidence, these same PMd and M1 neurons were also modulated by a signal that grew over time in exactly the block-dependent manner as the predicted urgency signal (Fig. 4B; compare with Fig. 3B). Finally, about 280 ms before movement onset, these same neurons reached approximately the same fixed firing-rate threshold regardless of evidence or urgency (Fig. 4A, right), consistent with the mechanism depicted schematically in Figure 2C. In summary, deliberation in this task appeared to

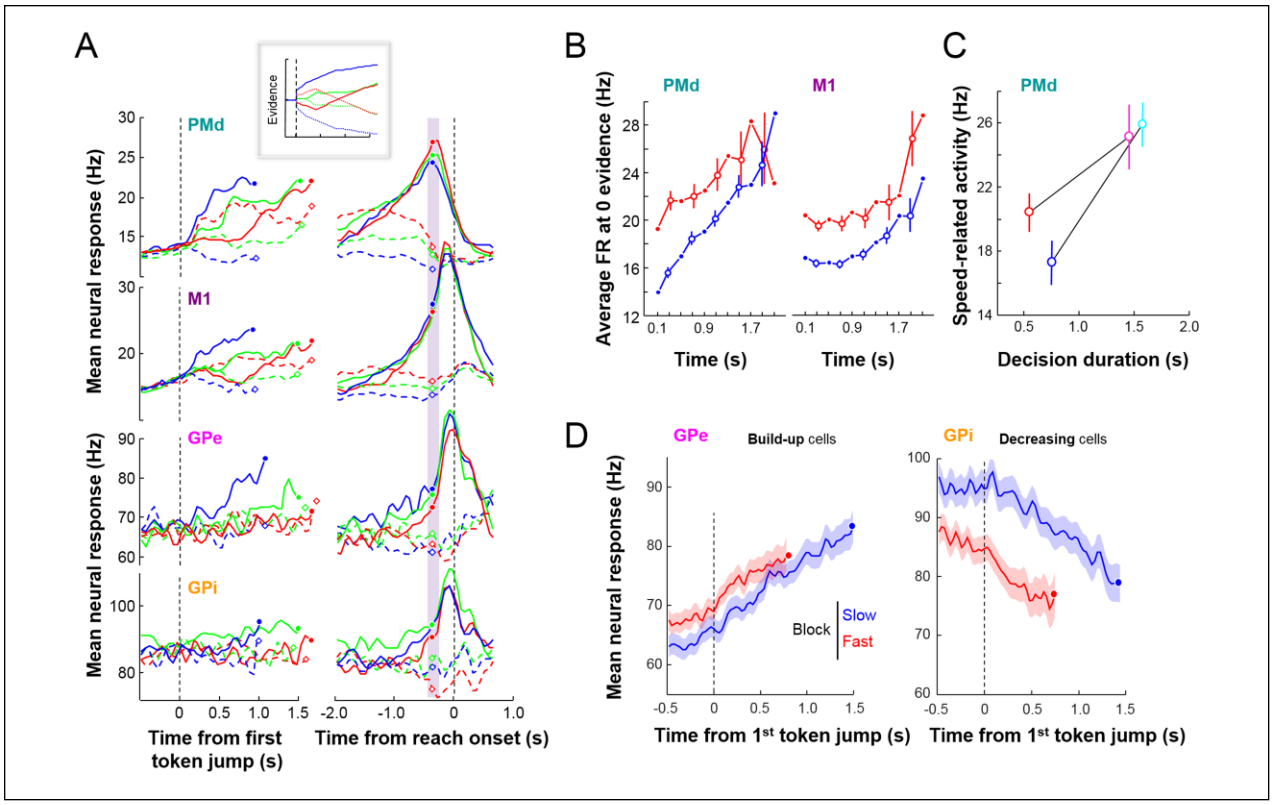


Figure 4. (A) The top-left panel shows the average activity of spatially tuned neurons recorded in dorsal premotor (PMd) during "easy" (blue), "ambiguous" (green), and "misleading" (red) trials, in which the monkey correctly chose the cells' preferred target (solid lines) or the opposite target (dashed lines). Below, we show the average activity during those same trials of spatially tuned neurons recorded in primary motor cortex (M1), external globus pallidus (GPe), and internal globus pallidus (GPi). Activity is aligned on the first token jump and truncated 280 ms before movement onset (squares and diamonds) to avoid averaging artifacts. The inset shows the evolution of sensory evidence provided to animals by successive token jumps in those same trials. Right panels: Same as left but aligned on movement onset. Circles and diamonds mark our estimate of the monkey's time of commitment. Modified with permission from Thura and Cisek (2017). (B) The left panel shows the evolution of the average activity of decision-related neurons in PMd, calculated at moments in time when the evidence is equal for each target, plotted as a function of time in either the slow (blue) or the fast (red) blocks. Right panel: Same as left for a population of decision-related neurons in area M1. (C) Average activity, at the time of commitment, of PMd neurons involved in movement execution during the tokens task. Data are sorted according to the duration of decisions preceding the reach that reports them, either the shortest (dark colors) or the longest (light colors), and as a function of the speed-accuracy trade-off (SAT) condition, the slow (blue) and the fast (red) SAT regime. B and C reproduced with permission from Thura and Cisek (2016). (D) The left panel shows the average activity (with 95% confidence intervals) of 19 "build-up" GPe cells aligned on the first token jump during the fast (red) and slow blocks (blue). The right panel shows the average activity of 11 GPi "decreasing" cells in the same SAT conditions. Activity is truncated before decision commitment (circles). Modified with permission from Thura and Cisek (2017).

involve the combination of evidence and urgency until a fixed firing rate was reached, constituting commitment to the developing choice.

Another important observation concerns the activity of other neurons in PMd and M1, which are *not* active during deliberation but are strongly implicated in movement execution. We found that their activity at the time of commitment strongly depended on the current level of the urgency signal at that time (Fig. 4C; compare with Fig. 3B). A natural explanation is that these "movement-related" neurons are recipients of the same context-dependent urgency signal that drives the animals to make their decision. If these neurons influence muscular contraction, they will therefore provide a mechanistic link between the urgency with which choices are made and the speed (or "vigor") of the chosen actions.

Although initially surprising, a link between deliberation and movement kinematics makes perfect sense in the context of reward rate maximization (Fig. 1), as reward rate is influenced not only by the time taken to decide but also by the time spent executing the movement and obtaining the reward (Haith and others 2012; Shadmehr and others 2010; Summerside and others 2018). Thus, the correlations between a monkey's level of urgency at the

time of their decision and the vigor with which actions are performed suggests that urgency exerts a compensatory influence on handling time, such that the cost of investing additional time in deliberation will be partially offset by a decrease in the duration of the movements used to report the choice. This link also provides a clue to the neural origins of the urgency signal, and hints to how it may be related to a wide variety of behavioral phenomena in both health and disease.

The Origin of Urgency in the Brain

If an urgency signal is combined with evidence-related activity of sensorimotor areas, what might be the source of this signal? Given the observations described above, an urgency signal would be expected to originate from a region that projects to a wide range of cortical areas to influence both decision-making and action execution. In this respect, the basal ganglia (BG) provide a natural candidate. At the macroarchitectural level, this set of subcortical nuclei form segregated neuroanatomical loops with nearly every part of the brain—including cortical sensorimotor regions, frontal "cognitive" regions, and subcortical limbic regions associated with emotion, to name but a few (Alexander and others 1990)—thus providing the BG with a broad connective territory appropriate for regulating many diverse forms of externally directed behavior. Relatedly, extensive study of the microarchitectural (i.e., circuit-level) properties of these loops has revealed a canonical scheme of cortical-subcortical connectivity, which has been interpreted as suggesting a common, domain-general functional purpose for these loops across the BG's broad and functionally heterogeneous set of afferent targets (Swanson 2000).

Furthermore, the basal ganglia have long been functionally associated with the regulation of motivated behavior and reinforcement learning for maximizing reward (Frank 2011; Graybiel 2005), and are strongly implicated in both the control of movement vigor (Dudman and Krakauer 2016; Turner and Anderson 1997; Turner and Desmurget 2010; Yttri and Dudman 2016) and the general ability to motivate the expenditure of energy in the pursuit of potential rewards (Mazzoni and others 2007; Niv and others 2007; Pessiglione and others 2007). Multiple lines of neurophysiological evidence suggest that effort expenditure and movement vigor are largely under the control of activity within a variety of BG structures, including the striatum, substantia nigra, ventral pallidum, and the globus pallidus (Pessiglione and others 2007; Reppert and others 2018). Neural activity in the BG is higher before movements that are more highly rewarded, with activity in multiple regions effectively scaling with reward magnitude and probability (Kawagoe and others 1998; Nakamura and Ding 2017), and transient stimulation or inhibition of these regions within a temporal window of up to ~300 ms prior to a movement affects the vigor with which the ensuing movement is executed (da Silva and others 2018; Yttri & Dudman 2016). Conversely, lesions in BG structures commonly result in an inability to modulate movement vigor in response to changes in reward (Tachibana and Hikosaka 2012). Therefore, if a unified mechanism in the brain is responsible for regulating both decision timing and movement vigor in the service of maximizing reward rate, the structures of the BG would appear to be prime candidates.

Guided by these lines of evidence, we recorded the activity of neurons in a major output nucleus of the basal ganglia, the globus pallidus (GP)—including both the external (GPe) and internal (GPi) segments—while monkeys performed the tokens task (Thura and Cisek 2017). In contrast to the activity patterns we observed in PMd and M1, the evolution of changing evidence was only weakly reflected in the activity of GPe neurons, and was virtually absent in GPi, the final output structure (Fig. 4A, bottom plots). Instead, many neurons in both GPe and GPi exhibited time-dependent activities, either building up or decreasing as a function of time during deliberation (Fig. 4D). Crucially, these time-dependent activity levels were also strongly modulated by the SAT condition in which the task was being performed: "build-up" neurons often were more active during fast blocks than in slow blocks, whereas "decreasing" cells showed the opposite pattern, as if each cell population was directly or inversely correlated with urgency. BG output activity thus appears to encode an urgency signal as well as its adjustment across different speed-accuracy regimes.

Taken together, our data suggest that unlike the cortical networks involved in arbitrating between decision options, the primary output of the BG is not involved in deliberation about which target is chosen per se, but instead provides a signal that *selectively invigorates* a given behavior (Cisek and Thura 2018), motivating the expenditure of effort toward obtaining reward. For some tasks, such as weight lifting, this signal takes the form of a tonic arousal of the cortical regions controlling the relevant muscles. For tasks in which there exists a direct trade-off between speed and accuracy, this signal takes on the form of a context-dependent ramping activity that influences both the urgency to decide and the vigor of action, because that results in maximizing reward rates. This is in agreement with previous studies that have implicated the basal ganglia in the control of the SAT (Bogacz and others 2010b; Forstmann and others 2010), as well as with similar findings showing SAT-related modulations of the baseline and gain of neural processing in oculomotor regions during decisions between saccade targets (Hanks and others 2014; Heitz and Schall 2012).

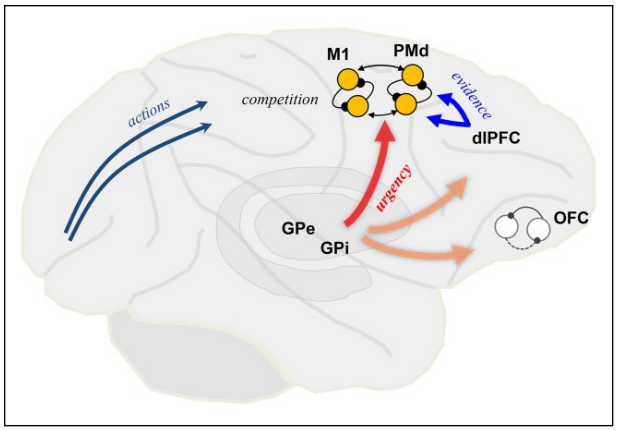


Figure 5. A proposed neural circuit mechanism for making decisions between actions. During deliberation, cortical activity (dorsal premotor [PMd] and primary motor cortex [M1]) reflects a dynamic, biased competition between candidate actions, which is gradually amplified by an urgency signal (red) from the basal ganglia's (BG's) principal output structures (external and internal globus pallidus [GPe and GPi, respectively]). The urgency determines the amount of evidence needed before the animal commits to his reach choice, while simultaneously controlling decision-related speed-accuracy trade-off adjustments as a function of a task's opportunities and constraints. Although this mechanism has been directly studied primarily in the context of decisions about perceptions and actions, the broad regional anatomical connectivity and circuit-level stereotypy of cortico-basal ganglia loops suggests the possibility that the influence of urgency may extend to other (e.g., non-motor) domains of cortical function, including "cognitive" domains such as executive function. In this view, a hypothetical "cognitive urgency" signal (orange)—possibly provided by the associative and limbic territories of the BG—could regulate the decision processes determined in prefrontal areas of the brain.

Furthermore, human neuroimaging studies have reported that emphasizing response speed increases baseline activity in the striatum, the presupplemental motor area, as well as premotor and parietal regions (Bogacz and others 2010b; Forstmann and others 2010; Ivanoff and others 2008; van Veen and others 2008). Thus, a consistent theme emerging from all studies of the SAT is that it involves modulating the local neural dynamics of a variety of cortical and subcortical decision-making networks as a function of the context in which a given task is performed (Standage and others 2014).

A Neuroanatomical Circuit for Deliberation and Commitment

To summarize, recent data support a centralized decision mechanism that jointly regulates neural activity across multiple interconnected brain structures, each of which encode specific aspects of the choice process (Fig. 5). During deliberation, cortical activity reflects a dynamic, biased competition between candidate actions, which is gradually amplified by an urgency signal from the BG that effectively determines the amount of evidence needed before the animal commits to the currently favored action target. Once the emerging cortical bias grows strong enough to engage directionally tuned activity in the GPi, a cascade of positive feedback initiates commitment to the action choice—the vigor of which is determined by the level of urgency at the time of the decision. The urgency signal thus serves as a central control mechanism for the SAT adjustment as a combined function of the multiple opportunities and constraints of a given task, thereby allowing animals to flexibly adjust multiple dimensions of cognition and behavior for the ultimate purpose of maximizing their reward rate across a wide variety of contexts (Thura and Cisek 2017).

This mechanism is well supported by neurophysiological data from monkeys making simple decisions about actions and is compatible with behavioral data from many studies in human subjects (see Box 1)—but it may have still broader implications. In particular, if urgency is the mechanism that ties together the timing of decisions and movements for the general goal of maximizing reward rates through projections from the basal ganglia to sensorimotor regions, then it might also influence many other aspects of motivated behavior through projections to other cortical regions, including prefrontal and limbic areas (Fig. 5, red and orange arrows, respectively). If so, then its regulation could influence a wide range of behaviors, perhaps thereby accounting for interindividual differences in a variety of specific traits, and possibly even some symptoms of neurological disorders.

Trait-Level Differences in Urgency

While the motivation to maximize reward rate is universal among animals, the fact that decision makers do not all behave identically in a given setting implies that the neural mechanisms involved are subject to some degree of variability across individuals. Therefore, an important question to consider is whether individuals exhibit a certain "baseline" level of urgency that remains stable over time and across contexts, and which distinguishes their performance from that of other decision makers under similar conditions. If so, then an individual's unique setting of this urgency mechanism may be sufficient to account for the resulting suite of behavioral differences that characterize an individual's typical decision-making performance.

Some direct evidence in support of a "trait-like" view of urgency is furnished by our own work with both human (Carland and others 2016) and non-human (Thura and others 2014) subjects. Behavioral data from these studies

reveals that when a subject is first presented with an unfamiliar decision-making task, the initial learning phase is followed by convergence toward a stable and idiosyncratic decision policy that governs multiple aspects of how that individual decides and acts. Consequently, each decision-maker exhibits a suite of consistent differences across multiple ensuing behavioral measures, including their gross response time distributions, their accuracy rates within different task conditions, their temporal sensitivity to incoming sensory evidence, and their movement kinematics (Fig. 1, green text). Importantly, we have also shown that the variance across these measures can be jointly accounted for by a model in which each subject is assigned a unique set of urgency parameters, the settings of which are alone sufficient to reproduce multiple "downstream" aspects of their behavior from a single set of parametric changes (Fig. 6A and B). Furthermore, the consistency of our subjects' performance over spans of time up to several months in length speaks to the considerable temporal stability of this "urgency" trait (i.e., demonstrating high "test-retest reliability").

Although relatively few other decision-making studies have explicitly considered urgency-like mechanisms when accounting for behavioral data, a number of related findings nonetheless provide additional indirect support for the trait-like nature of urgency. For example, subjects who tend to move with greater vigor also exhibit generally faster response times (Jaśkowski and others 2000; Reppert and others 2018), which is precisely what would be expected if these behavioral measures are each the result of an individual's characteristic level of urgency (Fig. 6B). Conversely, after any given amount of deliberation time, an individual with a higher "baseline" level of urgency would be predicted to issue faster movements relative to an individual whose urgency is lower (Fig. 6C). Indeed, a considerable number of studies have reported that when controlling for decision times, some

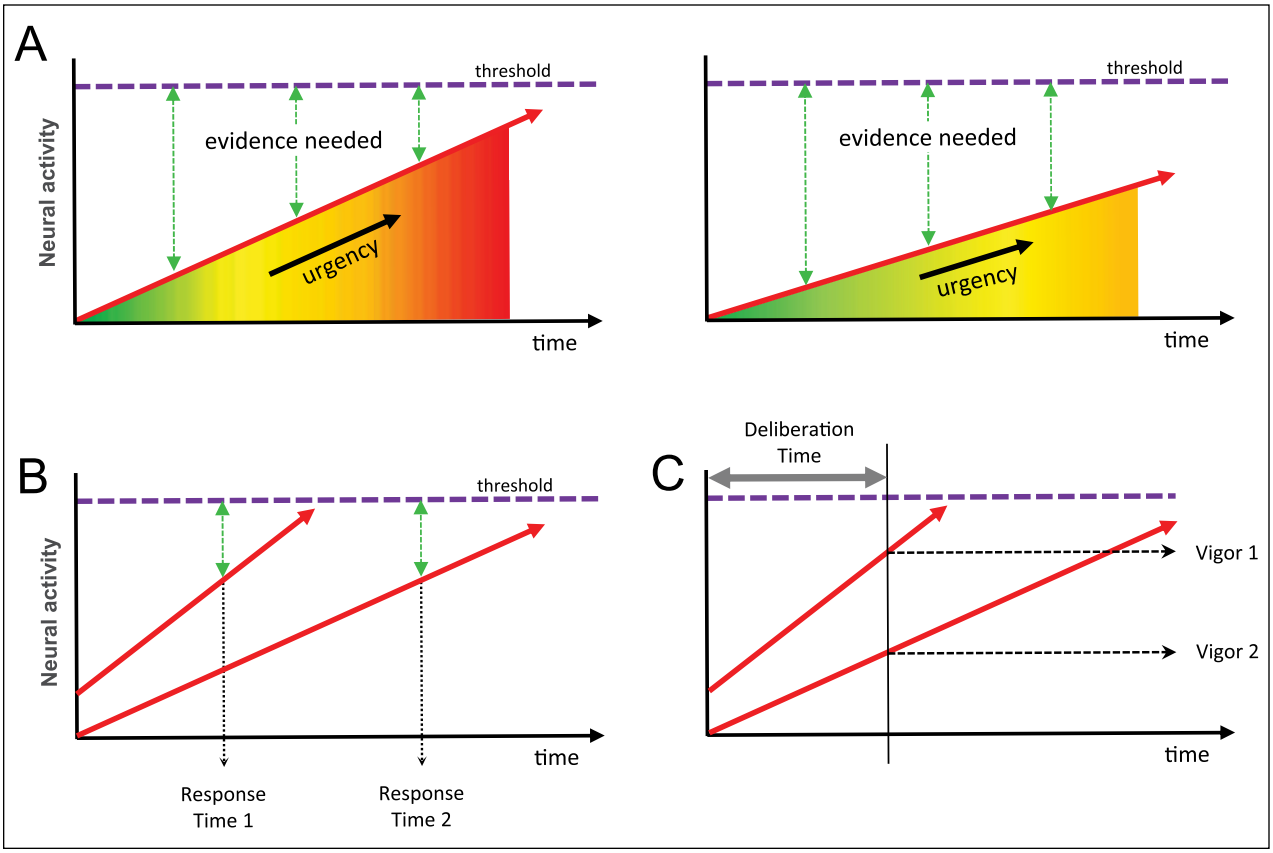


Figure 6. (A) As time passes and urgency grows, the amount of evidence needed to reach the decision threshold decreases. This occurs at a faster rate for a "hasty" individual (left) than for a more "conservative" individual (right), thereby accounting for inter-subject differences in response time distributions under otherwise-identical task conditions. (B) When free to respond at any time, an individual with low urgency will take longer to decide than a hasty individual, even when the evidence being presented (green arrows) is identical. (C) If deliberation time is externally controlled, the influence of urgency on motor execution means that the movements of an individual with relatively lower urgency will be performed with a lower level of vigor than those performed by an individual with higher urgency.

individuals consistently perform movements up to two to four times faster than others (Berret and others 2018; Reppert and others 2015; Rigas and others 2016), and that these characteristic differences in vigor remain stable when tested at intervals of up to 11 months apart (Bargary and others 2017; Choi and others 2014; Friedman and others 2017).

In light of our previous results suggesting that contextual changes in urgency affect both arm- and eye movements simultaneously (Thura and others 2014), a third prediction would be that the speed with which a given individual moves in one motor modality should be a statistically significant predictor of their speed when using other bodily effectors. Recently, Reppert and others (2018) have shown that "trait" levels of vigor appear to be shared across the skeletomuscular system, such that different individuals' characteristic motor kinematics are similar when performing orienting movements with different bodily effectors (e.g., head, neck, and arm movements). In fact, individual differences in movement vigor are sufficiently robust that several recent studies have even demonstrated that these characteristic patterns of motor behavior may serve as fairly reliable biometric markers for identifying specific individuals (Friedman and others 2017; Rigas and others 2016).

Taken together, these findings suggest that decision makers exhibit a set of systematic and consistent interrelationships between multiple indices of behavior during motor-control and decision-making tasks—each of which follow naturally from the proposal that these diverse behavioral outputs are under the control of a common mechanism whose "default" setting varies across individuals. However, because urgency is proposed to serve as the common mechanism by which subjective estimates of reward rate are effectively "translated" into behavior, additional sources of inter-individual variability within any factor that affects reward-rate estimation itself are also likely to be reflected in an individual's characteristic level of urgency. On this point, it is worth noting that robust and stable individual differences have been previously reported for a variety of decision-making and reward-related mechanisms, including reward sensitivity (Baskin-Sommers and Foti 2015), risk aversion (Chen and Kwak 2017), effort cost estimation (Treadway and others 2012a), and temporal discounting rates (Choi and others 2014; Kirby 2009)—each of which serve as inputs to reward rate estimation. Thus, it remains an open question to what extent "trait" urgency may also constitute a higher-order construct encapsulating multiple sources of variance among a variety of lower-order mechanisms commonly related to reward processing. Nonetheless, the ability to capture individual variability within a number of critical mechanisms related to reward processing, combined with its relatively direct relationship to a variety of discretely quantifiable behaviors commonly related to the speed of decisions and actions, suggests that urgency may be a particularly useful construct for conceptualizing certain phenotypic personality traits, such as impulsivity.

Urgency as a Mechanism of Impulsivity

Although not formally considered a clinical condition in and of itself, trait impulsivity is known to play a role in the development of a variety of clinical psychopathologies, including attention deficit hyperactivity disorder, substance abuse disorders and addiction, problem gambling, disordered eating, and "externalizing behaviors" such as aggression (Cyders and others 2007; Egervari and others 2018; Martin and others 2014). However, while the etiological ramifications of trait impulsivity have been relatively well mapped out over the past several decades, comparatively little remains known about the underlying cognitive, behavioral, and neurobiological mechanisms involved in the origins of impulsive behaviors (Aichert and others 2012; Cyders & Coskunpinar 2011). Consequently, the fact that the "downstream" behavioral effects of urgency are commonly related to the overall quality and hastiness of decisions raises the question of whether individual differences in urgency may be implicated in the phenotypic class of behaviors commonly recognized as trait impulsivity.

On a conceptual level, the behavioral profile of an individual with a relatively high "trait" level of urgency would be broadly consistent with many of the known cognitive and behavioral hallmarks of impulsivity. For example, the direct relationship between elevated states of urgency and faster, less-accurate decisions fits in quite neatly with the well-known tendency of impulsive individuals not to think long before deciding and acting (Burnett-Heyes and others 2012; Voon 2014). Impulsive individuals also generally exhibit greater difficulty withholding or inhibiting "prepotent" motor responses (Aichert and others 2012; Choi and others 2014), which would be expected if the same mechanism that produces shorter decision times is also fed into the motor system to place it into a higher state of readiness for action (Spieser and others 2017).

Although largely indirect and provisional, additional evidence is provided by a number of recent studies which have reported findings explicitly linking urgency-related behaviors to psychometric measures related to trait impulsivity. For example, Berret and others (2018) have reported positive correlations between movement vigor and *boredom proneness*, a construct that is related to broader trait impulsivity via an intermediary sub-factor variously termed *Sensation Seeking* or *(lack of) Perseverance* (Watt & Vodanovich 1992; Whiteside & Lynam 2001). Relatedly,

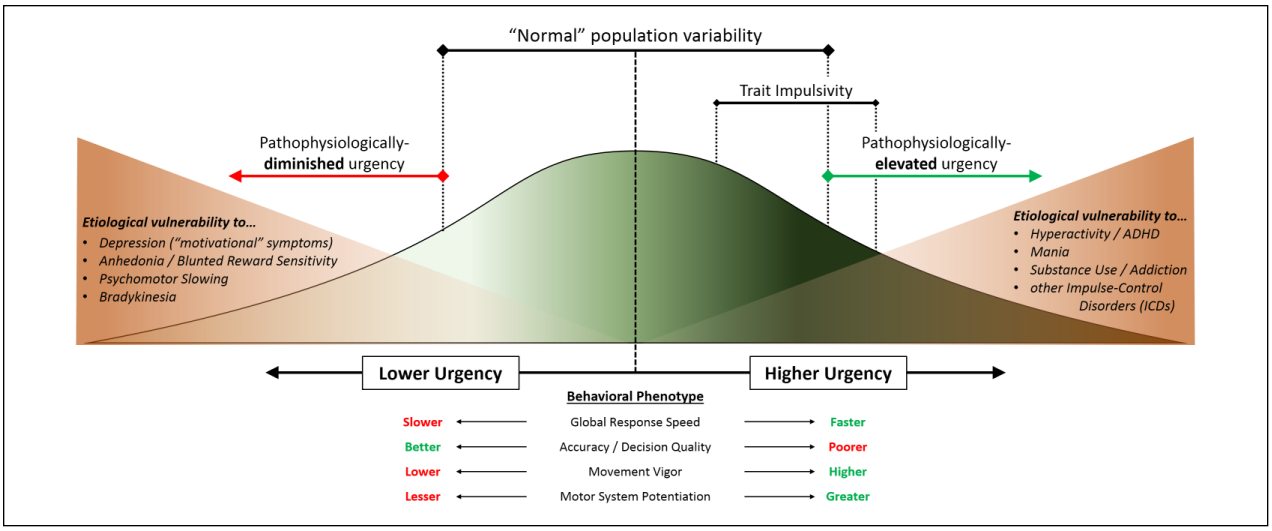


Figure 7. A "dimensional" view of trait urgency. Subjects drawn from non-clinical populations exhibit interindividual variability in decision-making behavior across a variety of quantifiable dimensions of performance (bottom), the interrelationships between which can be accounted for by the common involvement of a singular underlying urgency mechanism whose "default" or "baseline" level varies across individuals. By extension, individuals at the higher end of the population range would be predicted to exhibit a constellation of cognitive and behavioral tendencies which are broadly consistent with the core features of a general "impulsivity" personality phenotype. Further deviations from the "normal" range of variability may confer increasing etiological susceptibility to a variety of disorders by directly contributing to the emergence of symptoms related to the various behavioral functions that fall under the control of this urgency mechanism.

a study by Dalley and Robbins (2017) has shown that impulsive individuals also exhibit markedly steeper *temporal discounting* rates. Such a link would be expected given that higher urgency both shortens decision times and produces faster motor actions, each of which are effective means for minimizing reward delays, thereby partially counteracting the subjective reduction in reward rates caused by exaggerated temporal discounting policies in these individuals (Haith and others 2012; Shadmehr and others 2010; Summerside and others 2018).

Although each of these relationships between impulsivity and decision-making behavior could in principle arise from multiple distinct mechanisms, the underlying pattern of interrelationships observed across these studies are broadly consistent with—and follow straightforwardly from—a trait-like view of urgency. Taken together, the various findings reviewed above may suggest a "dimensional" conceptualization of trait urgency (Fig. 7), according to which relatively elevated levels of urgency within individuals could contribute to recognizable personality-level differences in trait impulsivity. By extension, above- or below a certain range of "normal" population-level variability, significant deviations from the population-wide average level of trait urgency may confer increased etiological vulnerability to a variety of clinical pathologies involving disordered responsiveness to reward, impaired motivation, and/or impairments in decision making—a subject to which we turn next.

The Neurobiology of Urgency as a "Transdiagnostic" Mechanism in Clinical Etiology

In light of the considerable evidence linking urgency to dopaminergic activity in the basal ganglia, clinical disorders that are known to involve disruptions in dopaminergic neurotransmission would be especially likely to interfere with the neurobiological substrates regulating urgency and its adjustment across contexts, in turn producing observable impairments in the ability to initiate, sustain, and motivate actions. Additionally, if urgency signals are broadcast widely throughout the cortex by centrally located subcortical structures within the BG, then unbalanced or dysregulated urgency output into different cortical networks could interact with the local functionality of these afferent regions to produce a variety of specific symptoms or deficits (Fig. 5). In this manner, pathophysiological alterations to a single underlying urgency mechanism could potentially account for a broad variety of symptoms across multiple diagnostic categories, thereby constituting a *transdiagnostic* etiological mechanism (Insel and others 2010). In what follows, we focus on two particularly illustrative examples—depression and Parkinson's disease—although these are only two of many potential candidate clinical disorders whose etiology may be amenable to an urgency-based perspective.

Urgency and Depression

Although typically regarded primarily as a mood disorder, the DSM-5 (*Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition) criteria for *major depressive disorder* (MDD) nonetheless include a number of non-affective symptoms related to motivation and psychomotor control (American Psychiatric Association 2013). MDD patients frequently exhibit deficits in the "activational" aspects of motivation, presenting in the form of highly-generalized symptoms such as low energy (*anergia*), apathy, and fatigue—which are in fact some of the most frequently-reported symptoms of MDD, second only to the primary mood disturbances themselves (Stahl 2002). Another prominent non-affective symptom of depression is *psychomotor slowing* (sometimes also called *psychomotor-* or *neurocognitive retardation*), a symptom that manifests as a generalized slowing of movements and cognition (American Psychiatric Association 2013). Together, these non-affective symptoms form a "motivational" symptom cluster that is a prominent diagnostic feature of all major depression syndromes, and which often proves remarkably resistant to treatment (Demyttenaere and others 2005; Fava and others 2014; Stahl 2002). The relative severity of these symptoms is also strongly associated with the number of depressive episodes, their duration, and age of disease onset (Calugi and others 2011) and is one of the single-best quantitative predictors of lack of clinical remission among MDD patients undergoing treatment (Fava and others 2014; Gorwood and others 2014).

Selective serotonin reuptake inhibitors (SSRIs) are the first-line pharmacological treatments for depression and are generally effective for alleviating the principal affective symptoms of MDD (Chekroud and others 2017). However, the non-affective, "motivational" symptoms of depression are generally resistant to treatment with first-line antidepressants (Stahl 2002; Treadway and Zald 2011), and often continue to persist even after clinical remission of the primary (affective) symptoms (Fava and others 2014; Gorwood and others 2014). Conversely, motivational symptoms appear to be responsive to drugs targeting non-serotonergic monoamines, such as the noradrenaline- and dopamine-reuptake inhibitor (NDRI) *bupropion* (Pae and others 2007; Stahl 2002; Treadway and Zald 2011; Zisook and others 2006). Similarly, drugs that selectively target dopamine (DA) transport and synaptic activity—including amphetamines (e.g., *dextroamphetamine*) and non-amphetamine stimulants (e.g., *methylphenidate, modafinil*)—have been successfully used by clinicians to treat these symptoms, despite the fact that these drugs are not typically considered to be "antidepressants" in the classical sense (Demyttenaere and others 2005; Stahl and others 2003). Together, these pharmacological dissociations suggest that the "affective" and "motivational" symptom domains likely emerge from functionally and pharmacologically independent neurobiological substrates (Argyropoulos and Nutt 2013; Nutt and others 2007; Stahl and others 2003).

Although motivational symptoms are often described by clinicians and patients alike in terms of a generalized absence of pleasure, several lines of evidence suggest that these symptoms need not necessarily arise due to a primary deficit in the ability to experience hedonic or consummatory pleasure per se (Sherdell and others 2012). Rather, the "motivational syndrome" frequently observed in depression may instead emerge as the distal result of underlying primary impairments in mechanisms related to reward sensitivity and/or effort-based decision making (Treadway and Zald 2011). For example, depressed patients exhibit behavioral patterns consistent with diminished sensitivity to the magnitude and probability of rewards compared with healthy controls (Treadway and others 2012b). Patients with MDD also appear to be subconsciously "less willing" to exert effort to obtain rewards, such that they report greater subjective difficulty in producing identical grip forces relative to healthy controls, even when reward is held constant across subject groups (Cléry-Melin and others 2011). Notably, these reward-modulation deficits generally scale in direct proportion to the severity of patients' self-reported anhedonic symptomology (Pizzagalli and others 2008) and are associated with substantially higher likelihood of the persistence of their MDD diagnosis (Vrieze and others 2013). Additionally, extensive neurophysiological work in animal models has demonstrated that surgical, optogenetic, pharmacological, and genetic disruptions of dopaminergic neurotransmission among a variety of subcortical structures implicated in effort-based decision making consistently produce alterations of behavior that are highly reminiscent of the clinical presentations of motivational symptoms in human patients (Salamone and others 2018). Consequently, the picture that is rapidly emerging from the ongoing study of reward-processing deficits in depression suggests that the motivational symptoms of MDD are likely the result of underlying impairments in the neural circuitry by which cognitive and behavioral activity is effectively "energized" by reward (Cléry-Melin and others 2011; Salamone and Correa 2012; Salamone and others 2016; Treadway and others 2012b). By extension, this could indicate an underlying impairment in an urgency-like mechanism, of which these symptoms would be secondary, "downstream" consequences.

Although the above studies have not explicitly interpreted their results in terms of urgency, a related body of behavioral studies in human depression patients reveals

specific patterns of performance that are nonetheless consistent an underlying impairment in urgency. For example, depressed patients typically take longer than healthy controls to complete laboratory tests of cognitive functioning, and commonly exhibit slower response times than controls across a wide variety of decision-making tasks (Bennabi and others 2013; Buyukdura and others 2011; Gorwood and others 2014; Rubinsztein and others 2006). Tasks that tap into urgency-related behavioral measures may even be used to inform clinical treatment, as several studies in depressed populations have reported that patients with more pronounced symptoms of psychomotor slowing have a greater likelihood of responding to treatment with pharmacological agents targeting dopaminergic and noradrenergic neurotransmission, and a correspondingly *lower* likelihood of responding to SSRI treatment (Bruder and others 2014; Stahl 2002). Conversely, faster response times in various motor, attention, and verbal fluency tasks (Gorlyn and others 2008; Taylor and others 2006), as well as increased rates of *commission errors* (i.e., urgency-driven or "impulsive" responding) in a Go/No-Go task (Crane and others 2017), are each reliable predictors of clinical response to treatment with SSRIs (possibly because these behaviors indicate a neuropharmacologically intact underlying urgency mechanism). Consequently, meta-analyses have concluded that experimental tasks that tap into urgency-related psychomotor processes are among the best neurocognitive measures for predicting the likelihood of successful clinical response to conventional (i.e., serotonergic) treatment (Voegeli and others 2017).

In summary, a considerable body of clinical and experimental evidence implicates pathophysiological alterations of dopaminergic signaling in the BG in the cluster of psychomotor and motivational deficits frequently observed in depression patients. Moreover, they further suggest that the neurobiological substrates of urgency may be plausible therapeutic targets in MDD, such that laboratory tasks designed to assess urgency may have significant diagnostic and prognostic value in informing and monitoring clinical treatment.

Urgency and Parkinson's Disease

Parkinson's disease (PD) is characterized by the progressive loss of dopaminergic cells in the nigrostriatal pathways of the BG, culminating in a variety of overt motor symptoms including resting tremors, muscular rigidity, and *bradykinesia*, a generalized slowing of movements (Albin and Leventhal 2017; Magrinelli and others 2016). Patients with *bradykinesia* experience considerable difficulty in planning, initiating, executing, and sustaining movements—highly generalized deficits which affect motor performance across multiple domains, including stride length and gait, arm movements, and speech (McDonald and others 2015).

While these symptoms have traditionally been ascribed to a central impairment of motor control, accumulating empirical evidence suggests that patients with PD may not actually suffer from an inability to perform movements per se. For example, fine-grained kinematic analyses of bradykinetic patients with PD reveal that these patients remain objectively capable of executing movements within the same range of accuracy and movement speeds as healthy controls, albeit less reliably (Mazzoni and others 2007), and that these putative "motor" impairments may instead be better accounted for by an insufficient modulation of the motor system by internal signals of reward (Pekny and others 2015). Such an interpretation is particularly well-illustrated by the phenomenon of *paradoxical kinesis*, in which the dramatic motor impairments of patients with PD can be temporarily overcome under situations of elevated or extreme "urgency" (in the colloquial sense of the term) (Ballanger and others 2008; McDonald and others 2015). This phenomenon thus provides further evidence that the central underlying deficit in PD is not explicitly "motor" in nature, but rather involves a disruption in the brain's normal ability to use internal representations of reward to motivate or "energize" actions (Ballanger and others 2008; Chong and others 2015; Kojovic and others 2016).

Interestingly, PD is also highly comorbid with depression (Koerts and others 2007)—and symptoms in the "motivational" domain (such as *anhedonia*) are the most frequently reported among depressed PD patients. Conversely, other common "affective" symptoms of MDD—such as feelings of sorrow, shame, and guilt—are disproportionately *under*-reported by depressed PD patients relative to non-PD MDD patients (Rana and others 2015). These observations suggest that the particular depressive endophenotype observed in PD patients may be directly related to the dopaminergic neurodegeneration in PD, thus implicating impaired urgency as a shared etiological mechanism across each of these clinical disorders.

The primary clinical treatment for PD is dopamine replacement therapy (DRT), which involves restoring endogenous dopaminergic neurotransmission by administering a variety of DA agonists and metabolic precursors (such as L-DOPA), which in the short-to-medium term often dramatically alleviate the cardinal motor symptoms of PD (Albin and Leventhal 2017). Pharmacological studies of the effects of DA agonists in both healthy and clinical subjects suggest that these drugs alleviate the motor impairments in PD specifically by enhancing or restoring the ability of internal signals of reward to "energize" or "invigorate" motor activity (Beierholm and others 2013; Chong and others 2015; Kojovic and others 2016). This hypothesis is consistent

with the known functionality of the BG: Because vigor scales directly as a function of dopaminergic activity in BG areas such as the striatum, the pathophysiological loss of dopaminergic cells in these regions would straightforwardly result in globally diminished urgency, thereby interfering with the modulation of externally directed behavior by internal signals of reward (da Silva and others 2018; Panigrahi and others 2015).

While the deficits observed in the typical pathophysiological course of PD are suggestive of a chronic "low-urgency" state, the consequences of long-term treatment frequently result in a coherent suite of changes in temperament, cognition, and behavior that are—conversely—highly reminiscent of a chronic "high-urgency" state. Behavioral studies of PD patients undergoing DRT have reported significantly exaggerated temporal discounting rates in these populations (Housden and others 2010), as well as other decision-making deficits broadly consistent with elevated trait impulsivity (Djamshidian and others 2014; Kojovic and others 2016). Similarly, a significant number of patients who receive deep-brain stimulation (DBS) to counteract the loss of endogenous dopaminergic neurotransmission in the BG exhibit pronounced post-treatment changes in personality that are consistent with elevated trait impulsivity (Frank and others 2007), and which can be quantitatively measured with both self-report psychometric batteries (Hälbig and others 2009) and behavioral tasks (Wylie and others 2010). Long-term treatment with both DRT and DBS has also been associated with greatly increased risk of mania (Maier and others 2014) and various *impulse control disorders* (ICDs), including hypersexuality, binge eating, compulsive shopping, and pathological gambling (Lopez and others 2017). Notably, the incidence and temporal onset of treatment-related ICDs correlates with both the duration of DA agonist treatment and escalation of dose (Maier and others 2014; Molina and others 2000; Seedat and others 2000), suggesting that the risk of impulsivity-related iatrogenic disorders is directly commensurate with the degree of therapeutic exposure to dopaminergic agents.

However, the fact that not all patients with PD develop such behavioral issues has motivated the search for premorbid risk factors that may help identify PD patients at risk for treatment-related ICDs. Consequently, several studies have noted that adverse consequences of DRT are significantly more prevalent among sub-populations of PD patients who may have been predisposed due to preexisting personality factors, such high premorbid trait impulsivity (Heiden and others 2017). The fact that similar etiological factors are also associated with the development of these behavioral disorders within the general (i.e., non-clinical) population (Johansson and others 2009) suggests that multiple temperamental and neuropharmacological factors may combine additively to increase the risk of impulsivity-related psychopathology—and thus that these various factors may share a common mechanism and/or neurobiological substrate.

In summary, the clinical course of PD suggests that the progressive loss of dopaminergic tone in key subcortical networks initially manifest as a chronic "low-urgency state," thereby resulting in the hallmark "motor" symptoms of PD as well as the potential emergence of a distinctive depressive endophenotype predominated by "motivational" symptoms. Conversely, reversal of the primary "motor" syndrome of PD via chronic administration of DRT and/or DBS may produce a shift of the underlying neurobiological substrates into a "high-urgency" state, potentially culminating in mania, elevated trait impulsivity, and the development of iatrogenic ICDs. PD thus serves as a particularly relevant example of the potential clinical relevance of urgency, as both its typical etiopathological course and the neuropharmacology involved in its treatment illustrate and recapitulate the full spectrum of urgency's hypothesized behavioral functions (Fig. 7).

Concluding Remarks

Here, we reviewed the theoretical basis and the neural and behavioral data supporting the existence of an "urgency signal," carried by projections from the basal ganglia to the cerebral cortex, which influences both the timing of decisions and the vigor of actions in the service of maximizing reward rates. We propose that a growing urgency to decide and act is largely responsible for the build-up of neural activity often observed during decision-making tasks. Furthermore, the particular setting of the urgency signal is dependent both on contextual factors as well as individual preferences and influences a wide range of behavioral measures such as reaction times, accuracy, and movement speed. Consequently, it may provide a unifying mechanistic link for explaining a wide variety of phenomena in both health and disease, ranging from personality traits such as impulsivity to some of the major symptom domains commonly observed in depression and PD. Ultimately, the emergence of urgency's effects across a diverse range of cognitive and behavioral domains stems from the fact that all these domains are pertinent to the fundamental motivation to improve what all animals care about the most: *reward rate*.

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References

Aichert DS, Wöstmann NM, Costa A, Macare C, Wenig JR, Möller HJ, and others. 2012. Associations between trait impulsivity and prepotent response inhibition. J Clin Exp Neuropsychol 34(10):1016–32.

Albin RL, Leventhal DK. 2017. The missing, the short, and the long: L-Dopa responses and dopamine actions. Ann Neurol 82(1):4–19.

Alexander GE, Crutcher MD, DeLong MR. 1990. Basal ganglia-thalamocortical circuits: parallel substrates for motor, oculomotor, "prefrontal" and "limbic" functions. Prog Brain Res 85:119–46.

American Psychiatric Association. 2013. Diagnostic and statistical manual of mental disorders (5th ed.). Washington, DC: American Psychiatric Association.

Argyropoulos SV, Nutt DJ. 2013. Anhedonia revisited: is there a role for dopamine-targeting drugs for depression? J Psychopharmacol 27(10):869–77.

Balci F, Simen P, Niyogi R, Saxe A, Hughes JA, Holmes P, and others. 2011. Acquisition of decision making criteria: reward rate ultimately beats accuracy. Atten Percept Psychophys 73(2):640–57.

Ballanger B, Thobois S, Baraduc P, Turner RS, Broussolle E, Desmurget M. 2008. "Paradoxical kinesis" is not a hallmark of Parkinson's disease but a general property of the motor system. Mov Disord 21(9):1490–5.

Bargary G, Bosten JM, Goodbourn PT, Lawrance-Owen AJ, Hogg RE, Mollon JD. 2017. Individual differences in human eye movements: an oculomotor signature? Vision Res 141:157–69.

Baskin-Sommers AR, Foti D. 2015. Abnormal reward functioning across substance use disorders and major depressive disorder: considering reward as a transdiagnostic mechanism. Int J Psychophysiol 98(2, pt 2):227–39.

Beierholm U, Guitart-Masip M, Economides M, Chowdhury R, Düzel E, Dolan R, and others. 2013. Dopamine modulates reward-related vigor. Neuropsychopharmacology 38(8):1495–503.

Bennabi D, Vandel P, Papaxanthis C, Pozzo T, Haffen E. 2013. Psychomotor retardation in depression: a systematic review of diagnostic, pathophysiologic, and therapeutic implications. Biomed Res Int 2013:158746. doi:10.1155/2013/158746

Bennur S, Gold JI. 2011. Distinct representations of a perceptual decision and the associated oculomotor plan in the monkey lateral intraparietal area. J Neurosci 31:913–21.

Berret B, Castanier C, Bastide S, Deroche T. 2018. Vigour of self-paced reaching movement: cost of time and individual traits. Sci Rep 8(1):10655. doi:10.1038/s41598-018-28979-6

Bogacz R, Hu PT, Holmes PJ, Cohen JD. 2010a. Do humans produce the speed-accuracy trade-off that maximizes reward rate? Q J Exp Psychol (Hove) 63(5):863–91.

Bogacz R, Wagenmakers EJ, Forstmann BU, Nieuwenhuis S. 2010b. The neural basis of the speed-accuracy tradeoff. Trends Neurosci 33(1):10–6.

Bruder GE, Alvarenga JE, Alschuler D, Abraham K, Keilp JG, Hellerstein DJ, and others. 2014. Neurocognitive predictors of antidepressant clinical response. J Affect Disord 166:108–14.

Burnett-Heyes S, Adam RJ, Urner M, van der Leer L, Bahrami B, Bays PM, and others. 2012. Impulsivity and rapid decision-making for reward. Front Psychol 3:153.

Buyukdura JS, McClintock SM, Croarkin PE. 2011. Psychomotor retardation in depression: biological underpinnings, measurement, and treatment. Prog Neuropsychopharmacol Biol Psychiatry 35(2):395–409.

Calugi S, Cassano GB, Litta A, Rucci P, Benvenuti A, Miniati M, and others. 2011. Does psychomotor retardation define a clinically-relevant phenotype of unipolar depression? J Affect Disord 129(1–3):296–300.

Carland MA, Marcos E, Thura D, Cisek P. 2016. Evidence against perfect integration of sensory information during perceptual decision making. J Neurophysiol 115(2):915–30.

Carland MA, Thura D, Cisek P. 2015. The urgency-gating model can explain the effects of early evidence. Psychon Bull Rev 22(6):1830–8.

Chandrasekaran C, Peixoto D, Newsome WT, Shenoy KV. 2017. Laminar differences in decision-related neural activity in dorsal premotor cortex. Nat Commun 8(1):614.

Charnov EL. 1976. Optimal foraging, the marginal value theorem. Theor Popul Biol 9(2):129–36.

Chekroud AM, Gueorguieva R, Krumholz HM, Trivedi MH, Krystal JH, McCarthy G. 2017. Reevaluating the efficacy and predictability of antidepressant treatments: a symptom clustering approach. JAMA Psychiatry 74(4):370–8.

Chen XJ, Kwak Y (2017). What makes you go faster?: the effect of reward on speeded action under risk. Front Psychol 8:1057.

Choi JE, Vaswani PA, Shadmehr R. 2014. Vigor of movements and the cost of time in decision-making. J Neurosci 34(4):1212–23.

Chong TT, Bonnelle V, Manohar S, Veromann KR, Muhammed K, Tofaris GK, and others. 2015. Dopamine enhances willingness to exert effort for reward in Parkinson's disease. Cortex 69:40–6.

Churchland AK, Kiani R, Shadlen MN. 2008. Decision-making with multiple alternatives. Nat Neurosci 11:693–702.

Cisek P. 2007. Cortical mechanisms of action selection: the affordance competition hypothesis. Philosophical Transactions of the Royal Society B: Biological Sciences 362(1485): 1585-99.

Cisek P, Kalaska JF. 2010. Neural mechanisms for interacting with a world full of action choices. Annu Rev Neurosci 33:269–98.

Cisek P, Pastor-Bernier A. 2014. On the challenges and mechanisms of embodied decision-making. Philosophical Transactions of the Royal Society B: Biological Sciences 369.

Cisek P, Puskas GA, El-Murr S. 2009. Decisions in changing conditions: the urgency-gating model. J Neurosci 29(37):11560–71.

Cisek P, Thura D. 2018. Neural circuits for action selection. In: Corbetta D, Santello M editors. Reach-to-grasp behavior: brain, behavior, and modelling across the life span. New York, nY: Taylor & Francis. p. 91–118.

Cléry-Melin ML, Schmidt L, Lafargue G, Baup N, Fossati P, Pessiglione M. 2011. Why don't you try harder? An investigation of effort production in major depression. PLoS One 6(8):e23178.

Cook EP, Maunsell JH. 2002. Dynamics of neuronal responses in macaque MT and VIP during motion detection. Nat Neurosci 5:985–94.

Crane NA, Jenkins LM, Bhaumik R, Dion C, Gowins JR, Mickey BJ, and others. 2017. Multidimensional prediction of treatment response to antidepressants with cognitive control and functional MRI. Brain 140(2):472–86.

Cyders MA, Coskunpinar A. 2011. Measurements of constructs using self-report and behavioral lab tasks: is there overlap in nomothetic span and construct representation for impulsivity? Clin Psychol Rev 31(6):965–82.

Cyders MA, Smith GT, Spillane NS, Fischer S, Annus AM, Peterson C. 2007. Integration of impulsivity and positive mood to predict risky behavior: development and validation of a measure of positive urgency. Psychol Assess 19(1):107–18.

da Silva JA, Tecuapetla F, Paixão V, Costa RM. 2018. Dopamine neuron activity before action initiation gates and invigorates future movements. Nature 554(7691):244–8.

Dalley JW, Robbins TW. 2017. Fractionating impulsivity: neuropsychiatric implications. Nat Rev Neurosci 18(3):158–71.

Demyttenaere K, De Fruyt J, Stahl SM. 2005. The many faces of fatigue in major depressive disorder. Int J Neuropsychopharmacol 8(1):93–105.

Ditterich J. 2006. Evidence for time-variant decision making. Eur J Neurosci 24(12):3628–41.

Djamshidian A, O'Sullivan SS, Lawrence AD, Foltynie T, Aviles-Olmos I, Magdalinou N, and others. 2014. Perceptual decision-making in patients with Parkinson's disease. J Psychopharmacol 28(12):1149–54.

Drugowitsch J, Moreno-Bote R, Churchland AK, Shadlen MN, Pouget A. 2012. The cost of accumulating evidence in perceptual decision making. J Neurosci 32(11):3612–28.

Dudman JT, Krakauer JW. 2016. The basal ganglia: from motor commands to the control of vigor. Curr Opin Neurobiol 37:158–66.

Egervari G, Ciccocioppo R, Jentsch JD, Hurd YL. 2018. Shaping vulnerability to addiction: the contribution of behavior, neural circuits and molecular mechanisms. Neurosci Biobehav Rev 85:117–25.

Fava M, Ball S, Nelson JC, Sparks J, Konechnik T, Classi P, and others. 2014. Clinical relevance of fatigue as a residual symptom in major depressive disorder. Depress Anxiety 31(3):250–7.

Friedman L, Nixon MS, Komogortsev OV. 2017. Method to assess the temporal persistence of potential biometric features: application to oculomotor, gait, face and brain structure databases. PLoS One 12(6):e0178501.

Foley NC, Jangraw DC, Peck C, Gottlieb J. 2014. Novelty enhances visual salience independently of reward in the parietal lobe. J Neurosci 34(23):7947–57.

Forstmann BU, Anwander A, Schafer A, Neumann J, Brown S, Wagenmakers EJ, and others. 2010. Cortico-striatal connections predict control over speed and accuracy in perceptual decision making. Proc Natl Acad Sci U S A 107(36):15916–20.

Forstmann BU, Ratcliff R, Wagenmakers EJ. 2016. Sequential sampling models in cognitive neuroscience: advantages, applications, and extensions. Annu Rev Psychol 67:641–66.

Frank MJ. 2011. Computational models of motivated action selection in corticostriatal circuits. Curr Opin Neurobiol 21(3):381–6.

Frank MJ, Samanta J, Moustafa AA, Sherman SJ. 2007. Hold your horses: impulsivity, deep-brain stimulation, and medication in parkinsonism. Science 318(5854):1309–12.

Ghose GM. 2006. Strategies optimize the detection of motion transients. J Vis 6(4):429–40.

Gluth S, Rieskamp J, Buchel C. 2012. Deciding when to decide: time-variant sequential sampling models explain the emergence of value-based decisions in the human brain. J Neurosci 32(31):10686–98.

Gold JI, Shadlen MN. 2007. The neural basis of decision making. Annu Rev Neurosci 30:535–74.

Gorlyn M, Keilp JG, Grunebaum MF, Taylor BP, Oquendo MA, Bruder GE, and others. 2008. Neuropsychological characteristics as predictors of SSRI treatment response in depressed subjects. J Neural Transm (Vienna) 155(8):1213–9.

Gorwood P, Richard-Devantoy S, Baylé F, Cléry-Melin ML. 2014. Psychomotor retardation is a scar of past depressive episodes, revealed by simple cognitive tests. Eur Neuropsychopharmacol 24(10):1630–40.

Graybiel AM. 2005. The basal ganglia: learning new tricks and loving it. Curr Opin Neurobiol 15(6):638–44.

Haith AM, Reppert TR, Shadmehr R. 2012. Evidence for hyperbolic temporal discounting of reward in control of movements. J Neurosci 32(34):11727–36.

Hälbig TD, Tse W, Frisina PG, Baker BR, Hollander E, Shapiro H, and others. 2009. Subthalamic deep-brain stimulation and impulse control in Parkinson's disease. Eur J Neurol 16(4):493–7.

Hanes DP, Schall JD. 1996. Neural control of voluntary movement initiation. *Science* 274: 427-430.

Hanks T, Kiani R, Shadlen MN. 2014. A neural mechanism of speed-accuracy tradeoff in macaque area LIP. Elife 3.

Hawkins GE, Forstmann BU, Wagenmakers EJ, Ratcliff R, Brown SD. 2015a. Revisiting the evidence for collapsing boundaries and urgency signals in perceptual decision-making. J Neurosci 35(6):2476–84.

Hawkins GE, Wagenmakers EJ, Ratcliff R, Brown SD. 2015b. Discriminating evidence accumulation from urgency

signals in speeded decision making. J Neurophysiol 114(1):40–7.
Hayden BY, Pearson JM, Platt ML. 2011. Neuronal basis of sequential foraging decisions in a patchy environment. Nat Neurosci 14(7):933–9.
Heiden P, Heinz A, Romanczuk-Seiferth N. 2017. Pathological gambling in Parkinson's disease: what are the risk factors and what is the role of impulsivity? Eur J Neurosci 45(1):67–72.
Heitz RP. 2014. The speed-accuracy tradeoff: history, physiology, methodology, and behavior. Front Neurosci 8:150.
Heitz RP, Schall JD. 2012. Neural mechanisms of speed-accuracy tradeoff. Neuron 76(3):616–28.
Housden CR, O'Sullivan SS, Joyce EM, Lees AJ, Roiser JP. 2010. Intact reward learning but elevated delay-discounting in Parkinson's disease patients with impulsive-compulsive spectrum behaviors. Neuropsychopharmacology 35(11):2155–64.
Insel T, Cuthbert B, Garvey M, Heinssen R, Pine DS, Quinn K, and others. 2010. Research domain criteria (RDoC): toward a new classification framework for research on mental disorders. Am J Psychiatry 167(7):748–51.
Ivanoff J, Branning P, Marois R. 2008. fMRI evidence for a dual process account of the speed-accuracy trade-off in decision-making. PLoS One 3(7):e2635.
Janssen P, Shadlen MN. 2005. A representation of the hazard rate of elapsed time in macaque area LIP. Nat Neurosci 8(2):234–41.
Jaśkowski P, van der Lubbe RH, Wauschkuhn B, Wascher E, Verleger R. 2000. The influence of time pressure and cue validity on response force in an S1-S2 paradigm. Acta Psychol (Amst) 105(1):89–105.
Johansson A, Grant JE, Kim SW, Odlaug BL, Götestam KG. 2009. Risk factors for problematic gambling: a critical literature review. J Gambl Stud 25(1):67–92.
Kawagoe R, Takikawa Y, Hikosaka O. 1998. Expectation of reward modulates cognitive signals in the basal ganglia. Nat Neurosci 1(5):411–6.
Kirby KN. 2009. One-year temporal stability of delay-discount rates. Psychon Bull Rev 16(3):457–62.
Koerts J, Leenders KL, Koning M, Portman AT, van Bellen M. 2007. Striatal dopaminergic activity (FDOPA-PET) associated with cognitive items of a depression scale (MADRS) in Parkinson's disease. Eur J Neurosci 25(10):3132-6.
Kojovic M, Higgins A, Jahanshahi M. 2016. In Parkinson's disease STN stimulation enhances responsiveness of movement initiation speed to high reward value. Neuropsychologia 89:273–80.
Leathers ML, Olson CR. 2012. In monkeys making value-based decisions, LIP neurons encode cue salience and not action value. Science 338(6103):132–5.
Lopez AM, Weintraub D, Claassen DO. 2017. Impulse-control disorders and related complications of Parkinson's disease therapy. Semin Neurol 37(2):186–92.
Ludwig CJ, Gilchrist ID, McSorley E, Baddeley RJ. 2005. The temporal impulse response underlying saccadic decisions. J Neurosci 25(43):9907–12.
Luna R, Hernandez A, Brody CD, Romo R. 2005. Neural codes for perceptual discrimination in primary somatosensory cortex. Nat Neurosci 8(9):1210–9.
Magrinelli F, Picelli A, Tocco P, Federico A, Roncari L, Smania N, and others. 2016. Pathophysiology of motor dysfunction in Parkinson's disease as the rationale for drug treatment and rehabilitation. Parkinsons Dis 2016:9832839.
Malhotra G, Leslie DS, Ludwig CJH, Bogacz R. 2017. Overcoming indecision by changing the decision boundary. J Exp Psychol Gen 146(6):776–805.
Martin J, Hamshere ML, Stergiakouli E, O'Donovan MC, Thapar A. 2014. Genetic risk for attention-deficit/hyperactivity disorder contributes to neurodevelopmental traits in the general population. Biol Psychiatry 76(8):664–71.
Maier F, Merkl J, Ellereit AL, Lewis CJ, Eggers C, Pedrosa DJ, and others. 2014. Hypomania and mania related to dopamine replacement therapy in Parkinson's disease. Parkinsonism Relat Disord 20(4):421–7.
Mazzoni P, Hristova A, Krakauer JW. 2007. Why don't we move faster? Parkinson's disease, movement vigor, and implicit motivation. J Neurosci 27(27):7105–16.
McDonald LM, Griffin HJ, Angeli A, Torkamani M, Georgiev D, Jahanshahi M. 2015. Motivational modulation of self-initiated and externally-triggered movement speed induced by threat of shock: experimental evidence for paradoxical kinesis in Parkinson's disease. PLoS One 10(8):e0135149.
Molina JA, Sáinz-Artiga MJ, Fraile A, Jiménez-Jiménez FJ, Villanueva C, Ortí-Pareja M, and others. 2000. Pathological gambling in Parkinson's disease: a behavioral manifestation of pharmacological treatment? Mov Disord 15(5): 869–72.
Murphy PR, Boonstra E, Nieuwenhuis S. 2016. Global gain modulation generates time-dependent urgency during perceptual choice in humans. Nat Commun 7:13526.
Nakamura K, Ding L. 2017. Parsing heterogeneous striatal activity. Front Neuroanat 11:43.
Niv Y, Daw ND, Joel D, Dayan P. 2007. Tonic dopamine: opportunity costs and the control of response vigor. Psychopharmacology (Berl.) 191(3):507–20.
Nutt D, Demyttenaere K, Janka Z, Aarre T, Bourin M, Canonico PL, and others. 2007. The other face of depression, reduced positive affect: the role of catecholamines in causation and cure. J Psychopharmacol 21(5):461–71.
Pae CU, Lim HK, Han C, Patkar AA, Steffens DC, Masand PS, Lee C. 2007. Fatigue as a core symptom in major depressive disorder: overview and the role of bupropion. Expert Rev Neurother 7(10):1251–63.
Palestro JJ, Weichart E, Sederberg PB, Turner BM. 2018. Some task demands induce collapsing bounds: evidence from a behavioral analysis. Psychon Bull Rev 25(4):1225–48.
Panigrahi B, Martin KA, Li Y, Graves AR, Vollmer A, Olson L, and others. 2015. Dopamine is required for the neural representation and control of movement vigor. Cell 162(6):1418–30.
Pastor-Bernier A, Cisek P. 2011. Neural correlates of biased competition in premotor cortex. J Neurosci 31(19): 7083-88.
Pekny SE, Izawa J, Shadmehr R. 2015. Reward-dependent modulation of movement variability. J Neurosci 35(9):4015–24.
Pessiglione M, Schmidt L, Draganski B, Kalisch R, Lau H, Dolan RJ, and others. 2007. How the brain translates money into force: a neuroimaging study of subliminal motivation. Science 316(5826):904–6.

Pizzagalli DA, Iosifescu D, Hallett LA, Ratner KG, Fava M. 2008. Reduced hedonic capacity in major depressive disorder: evidence from a probabilistic reward task. J Psychiatr Res 43(1):76–87.

Platt ML, Glimcher PW. 1999. Neural correlates of decision variables in parietal cortex. Nature 400(6741): 233-38.

Rana AQ, Ahmed US, Chaudry ZM, Vasan S. 2015. Parkinson's disease: a review of non-motor symptoms. Expert Rev Neurother 15(5):549–62.

Ratcliff R. 1978. A theory of memory retrieval. Psychol Rev 85(2):59–108.

Reppert TR, Lempert KM, Glimcher PW, Shadmehr R. 2015. Modulation of saccade vigor during value-based decision-making. J Neurosci 35(46):15369–78.

Reppert TR, Rigas I, Herzfeld DJ, Sedaghat-Nejad E, Komogortsev O, Shadmehr R. 2018. Movement vigor as a trait-like attribute of individuality. J Neurophysiol 120(2):741–57.

Rigas I, Komogortsev O, Shadmehr R. 2016. Biometric recognition via eye movements: saccadic vigor and acceleration cues. ACM Transactions on Applied Perception (TAP) 13(2):6.

Roitman JD, Shadlen MN. 2002. Response of neurons in the lateral intraparietal area during a combined visual discrimination reaction time task. J Neurosci 22(21):9475–89.

Rubinsztein JS, Michael A, Underwood BR, Tempest M, Sahakian BJ. 2006. Impaired cognition and decision-making in bipolar depression, but no 'affective bias' evident. Psychol Med 36(5):629–39.

Salamone JD, Correa M. 2012. The mysterious motivational functions of mesolimbic dopamine. Neuron 76(3):470–85.

Salamone JD, Correa M, Yang JH, Rotolo R, Presby R. 2018. Dopamine, effort-based choice, and behavioral economics: basic and translational research. Front Behav Neurosci 12:52.

Salamone JD, Yohn SE, López-Cruz L, San Miguel N, Correa M. 2016. Activational and effort-related aspects of motivation: neural mechanisms and implications for psychopathology. Brain 139(5):1325–47.

Seedat S, Kesler S, Niehaus DJ, Stein DJ. 2000. Pathological gambling behaviour: emergence secondary to treatment of Parkinson's disease with dopaminergic agents. Depress Anxiety 11(4):185–6.

Shadlen MN, Kiani R, Hanks TD, Churchland AK. 2008. Neurobiology of decision making: An intentional framework. In C. Engel & W. Singer (Eds.), Better than Conscious? Decision Making, the Human Mind, and Implications for Institutions (pp. 71-101). Cambridge, MA: MIT Press.

Shadlen MN, Newsome WT. 2001. Neural basis of a perceptual decision in the parietal cortex (area LIP) of the rhesus monkey. J Neurophysiol 86(4):1916–36.

Shadmehr R, Orban de Xivry JJ, Xu-Wilson M, Shih TY. 2010. Temporal discounting of reward and the cost of time in motor control. J Neurosci 30(31):10507–16.

Sherdell L, Waugh CE, Gotlib IH. 2012. Anticipatory pleasure predicts motivation for reward in major depression. J Abnorm Psychol 121(1):51–60.

Spieser L, Servant M, Hasbroucq T, Burle B. 2017. Beyond decision! Motor contribution to speed-accuracy trade-off in decision-making. Psychon Bull Rev 24(3):950–6.

Stahl SM. 2002. The psychopharmacology of energy and fatigue. J Clin Psychiatry 63(1):7–8.

Stahl SM, Zhang L, Damatarca C, Grady M. 2003. Brain circuits determine destiny in depression: a novel approach to the psychopharmacology of wakefulness, fatigue, and executive dysfunction in major depressive disorder. J Clin Psychiatry 64(Suppl 14):6–17.

Standage D, Blohm G, Dorris MC. 2014. On the neural implementation of the speed-accuracy trade-off. Front Neurosci 8:236.

Stanford TR, Shankar S, Massoglia DP, Costello MG, Salinas E. 2010. Perceptual decision making in less than 30 milliseconds. Nat Neurosci 13(3):379–85.

Stephens DW, Krebs JR. 1986. Foraging theory. Princeton, NJ: Princeton University Press.

Summerside EM, Shadmehr R, Ahmed AA. 2018. Vigor of reaching movements: reward discounts the cost of effort. J Neurophysiol 119(6):2347–57.

Swanson LW. 2000. Cerebral hemisphere regulation of motivated behavior. Brain Res 886(1–2):113–64.

Tachibana Y, Hikosaka O. 2012. The primate ventral pallidum encodes expected reward value and regulates motor action. Neuron 76(4):826–37.

Taylor BP, Bruder GE, Stewart JW, McGrath PJ, Halperin J, Ehrlichman H, and others. 2006. Psychomotor slowing as a predictor of fluoxetine nonresponse in depressed outpatients. Am J Psychiatry 163(1):73–8.

Thura D, Beauregard-Racine J, Fradet CW, Cisek P. 2012. Decision making by urgency gating: theory and experimental support. J Neurophysiol 108(11):2912–30.

Thura D, Cisek P. 2014. Deliberation and commitment in the premotor and primary motor cortex during dynamic decision making. Neuron 81(6):1401–16.

Thura D, Cisek P. 2016. Modulation of premotor and primary motor cortical activity during volitional adjustments of speed-accuracy trade-offs. J Neurosci 36(3):938–56.

Thura D, Cisek P. 2017. The basal ganglia do not select reach targets but control the urgency of commitment. Neuron 95(5):1160–70 e5.

Thura D, Cos I, Trung J, Cisek P. 2014. Context-dependent urgency influences speed-accuracy trade-offs in decision-making and movement execution. J Neurosci 34(49):16442–54.

Treadway MT, Bossaller NA, Shelton RC, Zald DH. 2012a. Effort-based decision-making in major depressive disorder: a translational model of motivational anhedonia. J Abnorm Psychol 121(3):553–8.

Treadway MT, Buckholtz JW, Cowan RL, Woodward ND, Li R, Ansari MS, and others. 2012b. Dopaminergic mechanisms of individual differences in human effort-based decision-making. J Neurosci 32(18):6170–6.

Treadway MT, Zald DH. 2011. Reconsidering anhedonia in depression: lessons from translational neuroscience. Neurosci Biobehav Rev 35(3):537–55.

Turner RS, Anderson ME. 1997. Pallidal discharge related to the kinematics of reaching movements in two dimensions. J Neurophysiol 77(3):1051–74.

Turner RS, Desmurget M. 2010. Basal ganglia contributions to motor control: a vigorous tutor. Curr Opin Neurobiol 20(6):704–16.

Uchida N, Kepecs A, Mainen ZF. 2006. Seeing at a glance, smelling in a whiff: rapid forms of perceptual decision making. Nat Rev Neurosci 7(6):485–91.

Usher M, McClelland JL. 2001. The time course of perceptual choice: the leaky, competing accumulator model. Psychol Rev 108(3):550–92.

van Veen V, Krug MK, Carter CS. 2008. The neural and computational basis of controlled speed-accuracy tradeoff during task performance. J Cogn Neurosci 20(11):1952–65.

Voegeli G, Cléry-Melin ML, Ramoz N, Gorwood P. 2017. Progress in elucidating biomarkers of antidepressant pharmacological treatment response: a systematic review and meta-analysis of the last 15 years. Drugs 77(18): 1967–86.

Voon V. 2014. Models of impulsivity with a focus on waiting impulsivity: translational potential for neuropsychiatric disorders. Curr Addict Rep 1(4):281–8.

Voon V, Thomsen T, Miyasaki JM, de Souza M, Shafro A, Fox SH, and others. 2007. Factors associated with dopaminergic drug-related pathological gambling in Parkinson's disease. Arch Neurol 64(2):212–6.

Vrieze E, Pizzagalli DA, Demyttenaere K, Hompes T, Sienaert P, de Boer P, and others. 2013. Reduced reward learning predicts outcome in major depressive disorder. Biol Psychiatry 73(7):639–45.

Watt JD, Vodanovich SJ. 1992. Relationship between boredom proneness and impulsivity. Psychol Rep 70(3):688–90.

Whiteside SP, Lynam DR. 2001. The Five-Factor Model and impulsivity: using a structural model of personality to understand impulsivity. Pers Ind Diff 30(4):669–89.

Wylie SA, Ridderinkhof KR, Elias WJ, Frysinger RC, Bashore TR, Downs KE, and others. 2010. Subthalamic nucleus stimulation influences expression and suppression of impulsive behaviour in Parkinson's disease. Brain 133(12):3611–24.

Yang T, Shadlen MN. 2007. Probabilistic reasoning by neurons. Nature 447(7148): 1075-80.

Yang Y, DeWeese MR, Otazu GH, Zador AM. 2008. Millisecond-scale differences in neural activity in auditory cortex can drive decisions. Nat Neurosci 11(11):1262–3.

Yoon T, Geary RB, Ahmed AA, Shadmehr R. 2018. Control of movement vigor and decision-making during foraging. Proc Natl Acad Sci U S A 115(44):E10476–85.

Yttri EA, Dudman JT. 2016. Opponent and bidirectional control of movement velocity in the basal ganglia. Nature 533(7603):402–6.

Zisook S, Rush AJ, Haight BR, Clines DC, Rockett CB. 2006. Use of bupropion in combination with serotonin reuptake inhibitors. Biol Psychiatry 59(3):203–10.