From Reactive to Proactive and Selective Control: Developing a Richer Model for Stopping Inappropriate Responses

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A better understanding of the neural systems underlying impulse control is important for psychiatry. Although most impulses are motivational or emotional rather than motoric per se, it is research into the neural architecture of motor response control that has made the greatest strides. This article reviews recent developments in the cognitive neuroscience of stopping responses. Most research of this kind has focused on reactive control—that is, how subjects stop a response outright when instructed by a signal. It is argued that reactive paradigms are limited as models of control relevant to psychiatry. Instead, a set of paradigms is advocated that begins to model proactive inhibitory control—that is, how a subject prepares to stop an upcoming response tendency. Proactive inhibitory control is generated according to the goals of the subject rather than by an external signal, and it can be selectively targeted at a particular response tendency. This may have wider validity than reactive control as an experimental model for stopping inappropriate responses.

Key Words: Basal ganglia, cognitive control, executive function, impulse control, prefrontal cortex, response inhibition, working memory

Many psychiatric disorders involve problems with controlling urges. These problems include urges for movement (as in Tourette syndrome and some forms of attention-deficit/hyperactivity disorder), compulsive urges (e.g., for handwashing or hair-pulling as in obsessive-compulsive disorder [OCD] or trichotillomania), and craving for drugs and gambling. A better understanding of the etiology, risk factors, treatment, and outcome for these disorders would be aided by neurocognitive markers that relate to symptoms such as "impulsivity" and are also rooted in neuroscience and genetics (1).

Evaluating cognitive markers requires developing computerized tests in the laboratory that have "ecological validity" for the disorder of interest but are also amenable to neuroscience approaches in humans. This is a particularly challenging problem for emotion and motivation control. Although behavioral paradigms for emotion control do exist (2–4), the mapping to neural circuits is incomplete. The same can be said for the control of motivational urges, especially in humans, although there have been advances in understanding, for example, how craving may be resisted (5). Thus, much research has focused on the easier question about the stopping of motor responses, in which behavior can be better operationalized and the target of the stopping (the motor system) is better understood. Here, "stopping" refers to the behavioral outcome when a subject halts an incipient response tendency. Behavioral stopping has its counterpart in a psychological stopping process, and this may be implemented in the brain by a set of functions and circuits including inhibitory control, attentional monitoring and detection, and working memory.

It is acknowledged that the stopping of motor responses, no matter how sophisticated the model, will only be relevant for impulse control some of the time. Even when the focus is on disorders of movement such as Tourette syndrome, it is likely that successful real-world control relies on strategies such as anxiety reduction, mindfulness, and cognitive-behavioral training (6) as much as or probably more than a voluntary, top-down, process of movement control. Nevertheless, mechanisms for the top-down stopping of initiated response tendencies are important as well.

This article reviews the cognitive neuroscience of stopping. It begins by focusing on paradigms in which subjects stop a response outright when instructed by a signal. This is referred to as "reactive stopping." Although clearly useful as a beginning point for mapping the neural architecture of cognitive control, it is argued that reactive stopping is limited as a model. Instead, behavioral paradigms are advocated that model how a subject prepares to stop an upcoming response tendency (i.e., "proactive stopping"). Proactive stopping is developed according to the goals of the subject, rather than being simply triggered reactively by an external signal. Moreover, proactive stopping allows the inhibitory control to be more selective. As will be shown, this bears stronger face validity to the problems faced by psychiatric patients.

The Cognitive Neuroscience of Reactive Stopping

Behavioral Paradigms

Many experimental paradigms exist for studying how people—and, in some cases, experimental animals— control their response tendencies. These include stop signal, go/no-go, antisaccade, Eriksen flanker, Stroop, Simon, Wisconsin card sort, continuous performance, reversal learning, and many others. All require control over a prepotent response tendency. Here we consider the first three in brief detail.

The stop signal test requires people to stop an already initiated response (7). On each trial, the subject is presented with a (Go) signal, such as, "press the left button for a leftward pointing arrow, or the right button for a rightward pointing arrow." On a minority of trials, a Stop signal is presented after the Go signal. The subject is instructed to respond as fast as possible on Go trials, and to do his or her best to stop the response when the Stop signal occurs (Figure 1A). If the delay between Go and Stop signals is short, the subject is more likely to stop, whereas if the delay is long, the subject is less likely to stop. Using information about the probability of stopping at various delays and reaction time on non-Stop signal (i.e., Go) trials, it is possible to calculate the internal speed of stopping, that is, stop signal reaction time (SSRT) (8).

In a typical go/no-go paradigm the subject is presented with a stream of letter stimuli and is required to respond quickly to all

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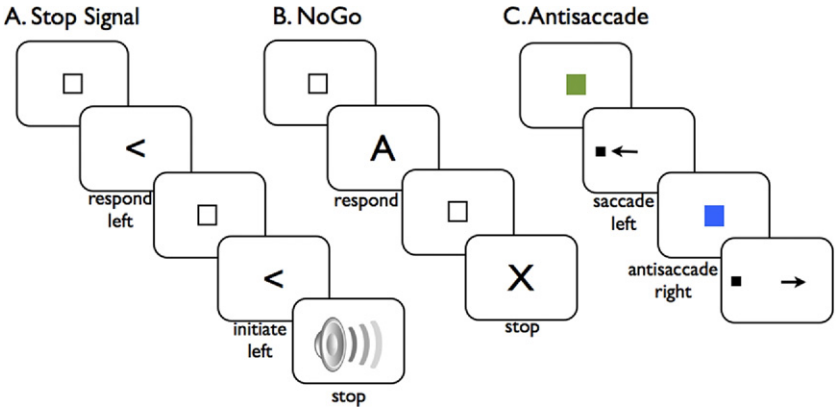

Figure 1. Three behavioral paradigms for measuring stopping. **(A)** The stop signal test. A ready signal (small box) is presented, followed by a go signal (left-pointing arrow). The subject initiates and executes a left button press (go trial). The next trial begins in the same way; however, a stop signal (auditory) is presented at a delay (e.g., 200 msec) after the go signal. The subject stops the response (stop trial). **(B)** The go/no-go test. Typically this is done with a stream of letters. The subject responds to all except the letter X. **(C)** The antisaccade test. The central eye fixation signal is a colored box. Here, green means "make a saccade" in the direction of the upcoming target, and blue means "make a saccade in the opposite direction to the upcoming target." On the antisaccade trial shown here, the target triggers an automatic saccade to the left, but the subject overrides this to move her eyes to the right.

letters except the letter X (Figure 1B). Thus, the stop signal and go/no-go paradigms are different in several respects. In the stop signal paradigm, the experimenter has tight control over when Go and Stop processes begin on each trial, whereas in the go/no-go paradigm, one cannot be sure when the Go and Stop processes begin. In go/no-go tests with rapid stimulus presentation and a low probability of no-go, the Go process could be "preactivated" on each trial, and therefore stopping on a no-go trial may be similar to stopping on a stop trial in a stop signal paradigm. However, in other go/no-go studies with lower prepotency, successful stopping may be more about deciding not to go than countermanding an initiated response. By contrast, in the stop signal paradigm, the response is already underway (on that particular trial) when the control signal occurs. Hence, the control is unlikely to reflect mere restraint of the movement plan (9), or the generation of an alternative plan (i.e., no response) or the activation of antagonist muscles; instead, the control needs to be targeted at those parts of the motor system that are already activated (10,11).

Another paradigm that requires stopping a response that is already underway is the antisaccade test (reviewed by Munoz and Everling [12]) (Figure 1C). On each trial, a cue indicates whether the trial will require a saccadic eye movement to an upcoming spatial target or an antisaccade (i.e., eye movement in the opposite direction of the target). When the target occurs, a reflexive eye movement is generated (visible in increased firing of neurons in the eye movement circuitry); thus, correct performance on antisaccade trials requires inhibiting the reflexive tendency and generating a new saccade.

Although the level of prepotency in stop signal and antisaccade tasks may supersede that in other paradigms (such as go/no-go, Eriksen Flanker, and response/task switching) these other paradigms often also require rapid action control. Consistent with this, functional magnetic resonance imaging (fMRI) activation for stop signal, no-go, antisaccade, and response switching or reversing reveals partly overlapping circuits (13,14–20) (see Figure 2A for some examples). Thus, evidence from some of these other paradigms will also be considered when motivating a model of the neural circuitry underlying stopping.

Overview of Neural Systems for Reactive Stopping

The neural systems underlying reactive stopping in the stop signal paradigm have been reviewed elsewhere (16,21–24). Here some of the key data are summarized, especially concerning humans, and evidence is updated in light of recent developments. In brief: sensory information about the stop signal is quickly relayed to the prefrontal cortex, where the stopping command is presumably generated. Two broad regions of the prefrontal cortex are apparently critical for stopping behavior—the right inferior frontal cortex (rIFC) and the dorsomedial frontal cortex (especially the presupplementary motor area, preSMA). These two regions appear to work together to send a Stop command to intercept the Go process, via the basal ganglia (Figure 3). The consequence could be suppression of basal ganglia output with downstream inhibitory effects on the primary motor cortex (M1).

In many task and real-world scenarios, this "stopping network" is probably highly integrated with valuational and mnemonic functions in other sectors of the prefrontal cortex, such as orbital frontal, and dorsolateral sectors, in both the right and left hemispheres; however, it appears that the standard (and simple) stop task may not require the integrity of these other sectors. This is perhaps because it represents a relatively "pure" version of inhibitory control.

The Right Inferior Frontal Cortex

The right rIFC referred to here corresponds to areas of lateral prefrontal cortex that are anterior to the precentral sulcus and inferior to the inferior frontal sulcus (Figure 3A). This encompasses

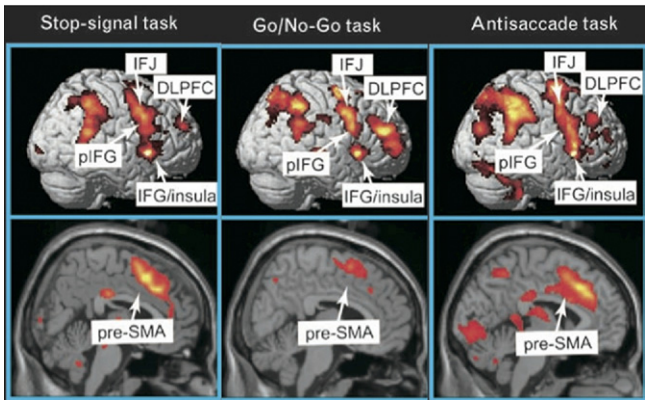

Figure 2. Functional magnetic resonance imaging studies of stop signal and related paradigms. The "stopping network" in the cortex is activated by different control tasks and is predominantly right-lateralized including the presupplementary motor area (preSMA), and the right inferior frontal cortex (rIFC). Right IFC activity is broadly distributed and may reflect an inferior frontal junction (IFJ) component, a more ventral posterior inferior frontal (inferior frontal gyrus, pIFG; putatively implementing inhibitory control), and an insula region of unknown function. Maps of the activation during performance of go/no-go, stop signal, and antisaccade tasks were revealed by contrasting no-go versus frequent-go, stop versus go, and antisaccade versus baseline-saccade trials, respectively, see Chikazoe (16) for further details. Reprinted with permission from Chikazoe J (2010): Localizing performance of go/no-go tasks to prefrontal cortical subregions [published online ahead of print March 10]. *Curr Opin Psychiatry* (33).

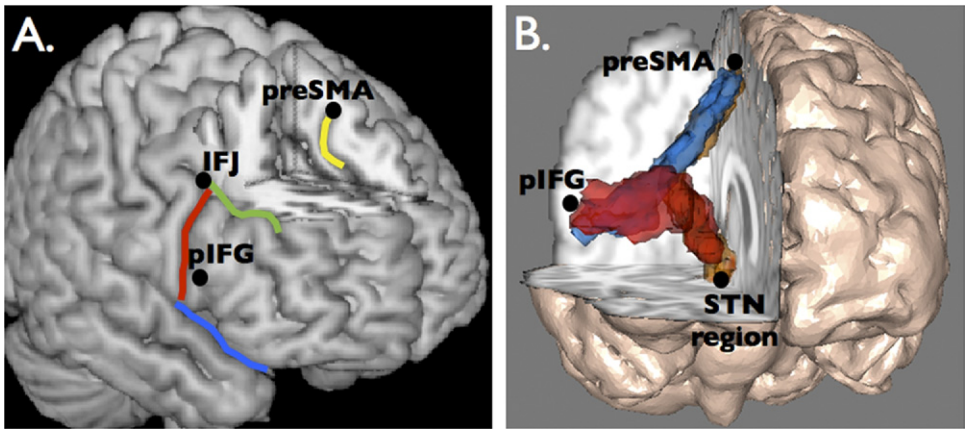

Figure 3. The brain network for reactive stopping. **(A)** Regions that are critical for stopping in the standard stop signal paradigm. Two regions within the inferior frontal cortex (IFC) are the inferior frontal junction (IFJ) and the posterior (p)IFG. The presupplementary motor area (preSMA) is in the medial surface. **(B)** White matter tractography using diffusion tensor imaging reveals a three-way network in the right hemisphere between nodes that are critical for stopping action. Reprinted with permission from (31).

pars triangularis, pars opercularis, and some of pars orbitalis and is coextensive with Brodmann areas 44, 45, and 47. In one study, damage to the rIFC in humans impaired stopping, whereas left hemisphere damage did not (25) (see also Rieger *et al*. [26], but see Swick *et al.* [27] for evidence that left frontal damage can affect go/no-go performance). The importance of the rIFC for stopping in the stop signal task has been confirmed by three studies with transcranial magnetic stimulation (TMS) using the "virtual lesion" approach (i.e., disruptive stimulation followed by behavioral testing) (28–30).

Although the rIFC is evidently important for the behavioral act of stopping, its functional role remains to be clarified: it might be critical for inhibitory control itself—for example, by projecting directly, or indirectly, to the basal ganglia to block the incipient response (31,32), or it may be critical for attentional detection of the stop signal (33–35). A recent study used TMS to test directly the inhibitory versus attention accounts (30). TMS was used to disrupt the rIFC posterior inferior frontal gyrus (pIFG) region and, in a different session, a more dorsal IFC region known as the inferior frontal junction (IFJ) (Figure 3A). Although disruption of both regions affected the speed of stopping (SSRT), it did so by affecting different processes. The results suggested that the right IFJ implements attentional detection, whereas the more ventral sector of rIFC (the posterior inferior frontal gyrus region) implements the inhibitory control. This is highly consistent with a recent fMRI study (36). Thus, different sectors of right IFC could implement both attentional detection and inhibitory control functions. This makes sense on the view that a subject needs to detect a signal in the environment to stop motor output. Thus, a putative right ventral frontoparietal circuit breaker for stimulus-driven attention (37) could be closely coupled with a mechanism for rapid inhibitory control.

Other recent evidence supports an inhibitory control function for the rIFC. Electrocorticography recordings from the surface of the brain revealed activity increases in the inferior frontal gyrus at approximately 150–300 msec following the stop signal, especially in the beta frequency band (18–30 Hz) (32). Notably, this beta-band response was greater for successful than failed stop trials. The timing of the response is consistent with an inhibitory control function that occurs within the time scale of the behavioral stopping process (SSRT). The observation of increased activity in the beta band is consistent with the possibility of long-range functional coupling with the basal ganglia to implement the stop (discussed later).

Other recent evidence for the importance of the rIFC for inhibitory control comes from studies with a paired-pulse TMS paradigm. In this technique, one coil was held over the rIFC and another over the hand area of M1. On each trial, there was either an M1 pulse alone (with the motor-evoked potential recorded from the hand muscles with electromyography) or an M1 pulse preceded by an rIFC pulse (with a very short delay, e.g., 8 msec). If the rIFC has an inhibitory effect on M1, then the size of the motor-evoked potential recorded from the hand should be smaller when rIFC stimulation precedes M1, than when there is M1 stimulation alone. This is what was found in two studies in which subjects needed to cancel an initiated action in favor of making another (13,38). These results are difficult to reconcile with an attention-only account of rIFC function.

In monkeys, lesions, microstimulation, and recording with the related go/no-go task all point to the importance of a possibly homologous region (the inferior frontal convexity) for inhibiting motor responses (39–42). These results complement a classic finding that macroelectrode stimulation of the right inferior frontal gyrus produces motor arrest (43).

Taken together, these studies clearly show that the rIFC's role in behavioral stopping cannot simply be interpreted in terms of an attentional function. Instead, the literature continues to support the proposition that the rIFC implements an inhibitory control function, likely in addition to attentional monitoring and detection (which could be a function of the more dorsal IFJ region in IFC).

In what follows, it is shown that reactive stopping likely "targets" the basal ganglia—specifically, the subthalamic nucleus. However, under some circumstances, stopping could be implemented via inputs to the striatum, and perhaps directly to M1 (38). The pathway used may relate to whether action control is purely reactive to an environmental change or proactive, as with anticipating the need for control.

The Dorsomedial Frontal Cortex

Many studies in humans (lesion, TMS, and fMRI) and monkeys (recording and stimulation) also point to a role for the dorsomedial frontal cortex, especially the preSMA region, in stopping behavioral responses in the stop signal, go/no-go, and other, related, behavioral paradigms (14,35,44–49); also see reviews by Chambers *et al.*, Mostofsky and Simmonds, and Nachev *et al.* (21,50,51). The preSMA is a region of dorsomedial frontal cortex. It is in the medial wall of

the superior frontal gyrus, dorsal to the anterior cingulate and anterior to the supplementary motor area proper (Figure 3).

Connectivity studies, using tract tracing in the monkey and diffusion tensor imaging in humans, show that the preSMA is connected with the rIFC and also with the basal ganglia input nuclei—the striatum and subthalamic nucleus (31,52,53) (Figure 3B). The findings about the functional importance of both preSMA and rIFC and their structural connectivity complements classic macrostimulation studies in humans describing this "anterior SMA" region as a "negative motor area"—a region at which stimulation produces arrest of manual movements and speech (43,54).

Yet the precise functional role of preSMA and its relation to rIFC in these forms of behavioral control is still unclear. A recent recording study in monkeys performing a manual stop signal task concluded that neurons in the preSMA/SMA may represent the motivation for specification actions rather than controlling whether or not the movement is made (11). Moreover, preSMA activation is evident in fMRI studies examining preparation to stop rather than stopping reactively, suggesting it may be more "set" related (55,56).

There have been numerous conceptual accounts for the functional role of the preSMA, including "selecting superordinate sets of action-selection rules" (57), motivation (11), conflict resolution and monitoring (14,58), and modulating response thresholds (59). These accounts might predict that preSMA generates a control signal and rIFC implements the inhibitory control. Indeed, a recent study using paired-pulse TMS found evidence for this (38). When a TMS pulse was delivered over preSMA, an excitatory effect on M1 was observed at 125 msec after a signal to control action behaviorally, whereas when a TMS pulse was delivered over rIFC, an inhibitory effect on M1 was observed at 175 msec. However, a study using Granger Causality Analysis of fMRI data came to the reverse conclusion—that is, that rIFC precedes the preSMA (35). Yet such causality methods are not well-validated with fMRI data. Indeed, a recent combined intracranial recording and fMRI study in rodents concluded that because hemodynamics varied so much between regions, the question of the relative timing of recruitment of regions was unanswerable with fMRI functional connectivity (60).

The Subthalamic Nucleus

The subthalamic nucleus (STN) input structure of the basal ganglia is a good candidate for a neural system for stopping action. First, the STN receives direct input (no intervening synapses) from the cortical foci reviewed earlier—namely, preSMA and rIFC (31,52). This means that the cortical regions could quickly activate the STN via a so-called hyperdirect pathway (61) with cortical-STN effects occurring in less than 10 msec (62,63). Second, the STN broadly excites the globus pallidus pars interna, which increases the neural inhibition on thalamocortical output. Thus, it has been conjectured that a massively connected STN leads to "widespread pulses" that could inhibit basal ganglia output and the motor system generally (64). This broad effect of the STN on basal ganglia output has motivated the view that the hyperdirect pathway is recruited as part of movement preparation to "clear" the response system briefly so that the appropriate movement can then be made through direct pathway selection (65).

Functional–behavioral studies also point to the STN as important for stopping. In a high-resolution fMRI study, activation of the STN region was found on successful stop trials ([66]; see also [67]). Modulation of the STN with deep brain stimulation in patients with Parkinson's disease affects SSRT, no-go commission error rates, and antisaccade performance, although not always in consistent directions (68–72). A single unit recording study found neurons in monkey STN that increased their response on both switch and no-go trials (73). In a rodent study, lesions to the STN produced a generalized stopping impairment for the stop signal task (74); see review by Eagle and Baunez (75). A local field potential recording study from the STN in human patients showed increases in the beta frequency band for no-go compared with Go trials (76). This is especially interesting insofar as enhancement of beta-band power was observed in the right IFC for stop trials (32) (as discussed earlier). Taking these results together, it is possible that inhibitory control is mediated via a right IFC–preSMA–STN structurally connected functional circuit operating in the beta band (~ 16 Hz). Consistent with this possibility, simultaneous cortical and STN recording studies in humans have shown "entrainment" of STN neurons by the cortex in the beta band (77).

Other, indirect, evidence for the importance of the STN in stopping comes from the observation that when reactive stopping occurs, it has global effects on the motor system. For example, when subjects stopped a thumb movement, there was significant, below baseline, suppression of corticomotor excitability of the tibia muscles of the leg (78). As the leg was not relevant for task performance, this implies there is a brain mechanism for stopping that has global effects on the motor system (such as the STN with its massive output to the globus pallidus pars interna [GPi]). Similarly, behavioral studies have shown that stopping one effector leads to long delays when continuing with another (79,80), also consistent with a global stop command.

The Striatum

Another way that reactive stopping could be implemented is through inputs to the striatum. This is a frontostriatal system for control rather than a frontosubthalamic one.

For the stop signal task, fMRI studies do show striatal activation (31,66). However, this could reflect the slower speed of the Go process on Stop than Go trials (66), feedback concerning a successful outcome, or preparation for stopping. Consistent with the last possibility, an fMRI study that examined activation on Go trials in a stop signal task found a parametric increase of striatal activation the more stopping was anticipated (81). This points to the possible importance of the striatum for proactive rather than reactive stopping and is discussed further later in the article. Other studies have observed that patients with basal ganglia damage are slow to stop their responses (26), but this could relate to generalized damage (including to the STN). Similarly, patients with Parkinson's disease are slow to stop (82), but this is also likely to reflect alterations in general basal ganglia function. Lesions to the medial striatum in rodents did lead to overall longer SSRT, but the results were complex with better stopping at earlier delays, increased Go reaction time (RT), and increased omissions errors (83). Two stop signal studies of patients with manifest Huntington disease did not reveal any deficit in stopping (84), yet at that stage of the disease, up to 50% of the striatum has been lost.

The striatum has been implicated in other paradigms such as go/no-go and antisaccade tests. For example, many functional and structural MRI studies point to a frontostriatal "circuit" underlying response inhibition in the go/no-go paradigm (85–87). In a neurophysiologic experiment, striatal activity was recorded while monkeys performed a go/no-go task (88) (Figure 4A). Each trial began with the animal holding down a lever. A red (no-go) or Go stimulus then appeared. The animal had to wait several seconds for a subsequent trigger stimulus before movement (Go) or continued nonmovement (no-go) led to reward. Two important types of neural response were observed on no-go trials: "preparatory" activity between the no-go cue and the trigger stimulus (Figure 4B); and sustained activity after the trigger stimulus (Figure 4C). These two

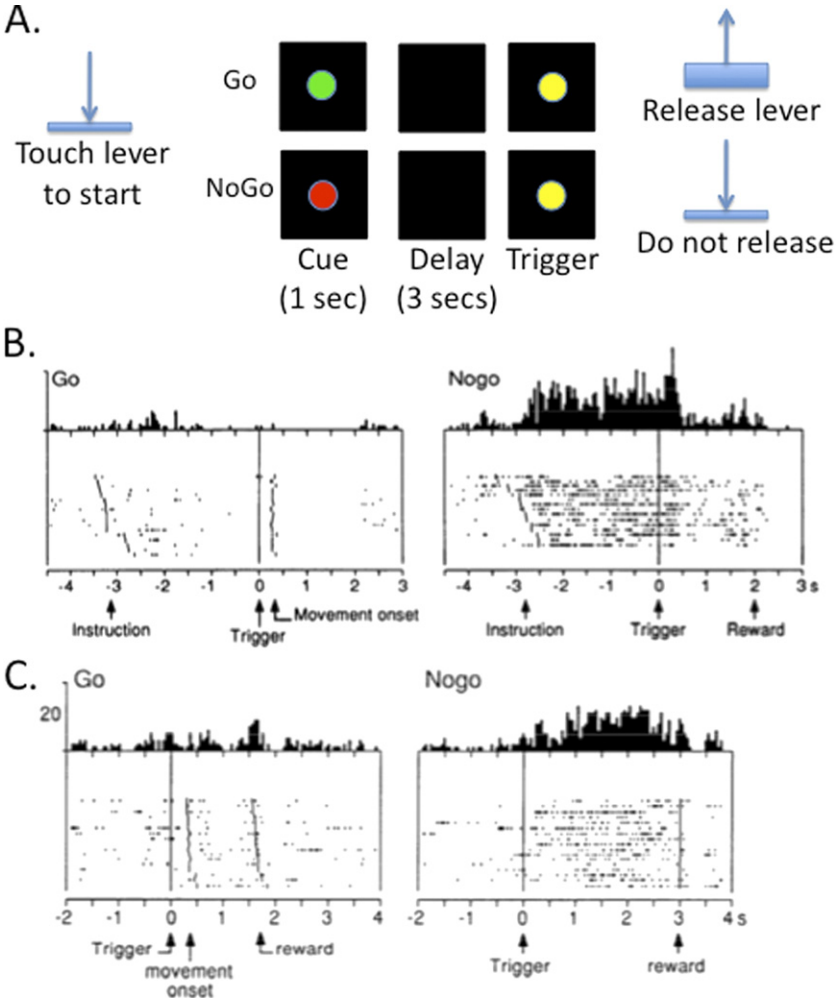

Figure 4. Neurophysiologic recording from the striatum shows the signature of proactive inhibitory control. **(A)** Monkeys were studied with a symmetrically reinforced delayed go/no-go task (88). The trial began with a lever press. A go or no-go cue was then presented. After an interval of 2.5–3.5 sec, a trigger stimulus was presented, requiring the animal to either release the lever or not release it to get reward. **(B)** Some neurons in the striatum showed a pattern of sustained activity between the no-go instruction and the trigger stimulus (perhaps involved in preparing to inhibit movement). **(C)** Other neurons showed sustained activity between the trigger stimulus and the reward (perhaps implementing the movement inhibition itself). Used with permission from The American Physiological Society (88).

kinds of neural responses suggest that the striatum could be important for preparing to stop a response (under working memory) and then implementing inhibitory control over a sustained period (perhaps selectively, as discussed later). These findings are complemented by studies showing that neurons in the caudate nucleus are active on antisaccade trials (89) and that microstimulation of caudate neurons improves antisaccade performance (90). These latter two studies are informative because these antisaccade conditions require selectivity—the subject must inhibit the reflexive saccade to the target and issue a new antisaccade. Later in the article, it will be argued that the striatum may be especially important for selective rather than global stopping.

Taken together, these studies point to the importance of the striatum for stopping. However, the scenarios in which the striatum is engaged seem more related to proactive or selective control (or both) rather than reactive and global stopping.

The Primary Motor Cortex

The primary motor cortex is the last cortical site before movement commands descend the corticospinal tract. The pyramidal cells in Layer 5 that generate the corticospinal volleys are embedded in a network of local connections, including many gamma-aminobutyric acid (GABA)ergic inhibitory interneurons. Generating a movement requires driving the pyramidal cells as well as removing the GABAergic inhibition (91).

In behavioral stop signal or go/no-go studies, the impending response on Go trials can be "visualized" as a ramping up of corticomotor excitability, measured using TMS of the primary motor cortex and concurrent electromyography (92,93). The impending response is also evident in desynchronization in the alpha–beta frequency band of local field potential recordings from electrocorticography (32,94). Stopping the initiated response also has observable effects on M1 (reviewed by Stinear *et al.* [95]). For example, TMS studies using a paired-pulse protocol reveal the signature of increased GABAergic inhibition of the M1 effector representation on stop or no-go trials (92,93,96). Further, electrocorticography of M1 shows a reduction of alpha–beta desynchronization (i.e., a relative increase of synchronization) on stop trials (32).

In standard stop paradigms it appears as if reactive stopping leads to a "global" effect on the motor system. As noted earlier, a TMS study with the stop signal paradigm showed that stopping a finger movement was associated with a suppression of the task-irrelevant leg (78); also see Coxon *et al.* and Sohn *et al.* (92,96). This could be the "TMS signature" of a stopping command generated by inputs to the STN with global downstream effects on M1.

Conclusions

Reactive stopping depends on a fronto–basal ganglia network in the right hemisphere. The network includes the preSMA, the IFC, the basal ganglia, and M1. Within the IFC, two regions seem impor-

Figure 5. Hypothetical fronto–basal ganglia circuits for global and selective stopping. **(A)** When the subject's hand is at rest, the GPi is tonically inhibiting thalamocortical output to hand representations so that these are only weakly active (small filled circles). In contrast, one primary motor cortex (M1) representation—for example, for the speech system, is strongly active (large yellow-filled circle). **(B)** The subject initiates a hand movement using the *direct pathway*. The PMC activates the putamen, and the putamen inhibits the GPi; this removes inhibition from the thalamus and increases drive to the hand area of M1. **(C)** The IFC sends input to the STN via the *hyperdirect pathway*. The STN has a broad effect on GPi, leading to global suppression of thalamocortical programs, including hand and speech systems. **(D)** Proactive selective control may be set up via the *indirect pathway*. The DLPFC activates a specific channel of the caudate, the caudate inhibits a specific channel of the GPe, the GPe inhibits a specific channel of the GPi (directly or via the STN), and inhibition of a particular thalamocortical channel is prepared (but perhaps not triggered until stopping is needed). **(E)** Action initiation occurs as for Panel B, except it occurs with the proactive selective control system activated. This could lead to slower response emission. **(F)** The indirect pathway may be triggered by the IFC when a stop signal occurs. This leads to suppression of one, but not all, representations in M1. Note: The preSMA is not shown here for simplicity. CAUD, caudate; DLPFC, dorsolateral prefrontal cortex; GPi, globus pallidus pars interna; GPe, globus pallidus pars externa; IFC, inferior frontal cortex; M1, primary motor cortex; PMC, premotor cortex; PUT, putamen; STN, subthalamic nucleus; THAL, thalamus.

tant: the IFJ and the posterior pIFG. When a stop signal occurs, the IFJ may implement an attentional detection function, whereas the pIFG may implement inhibitory control. The pIFG may implement inhibitory control via inputs to the basal ganglia. The relative functional roles of the preSMA versus pIFG in reactive stopping are not yet clear. Some evidence suggests the preSMA is recruited before the pIFG, so it may be involved in setting up or triggering the IFG response. Further research is necessary.

Reactive stopping has global effects on the motor system. This may be because it uses the fast hyperdirect pathway via the STN, with broad effects (Figure 5A–5C). The striatum may be more important for preparing to stop, and for stopping selectively, than stopping reactively with global effects. However, as discussed subsequently, reactive stopping may also be selective, and the striatum could be implicated in this form.

This relatively simple right hemisphere network may be all that is required for reactive stopping in standard stop signal, go/no-go and other paradigms. However, when stopping is complicated by adding conditional rules ("stop if this happens but not if that"), or by adding the requirement to prepare to stop, or by adding the need to stop selectively, this basic network may be augmented by other brain systems, as discussed subsequently.

The Limitations of Reactive Stopping as a Model of Control

Reactive Stopping Is a Useful Endophenotype for Psychiatry

Clearly, much has been learned about the neural architecture of reactive stopping. The convergent findings from different methods and species have motivated the stop signal task and related paradigms as endophenotypes for psychiatric disorders, as reviewed by various authors (21,23,97,98,99). To take some examples, many studies in patients have shown case–control increases in SSRT, as well as functional activation or structural integrity differences within regions such as the rIFC and dorsomedial frontal cortex. These differences are seen in methamphetamine addicts, cocaine addicts, and people who abuse alcohol, as well as in ADHD, OCD (including trichotillomania), and eating disorders (see the reviews cited earlier in the paragraph). In ADHD, for example, meta-analysis shows that the SSRT effect size is one of the largest for executive function tasks (100).

Although reactive stopping in these paradigms is generated in artificial laboratory conditions, it evidently has relevance to these real-world problems. How can this be? Three explanations are considered. First, a common symptom in psychiatric disorders is impulsivity—and one form of impulsivity relates to motor disinhibition (101). Accordingly, someone with poor reactive stopping ability who feels a motoric urge that is inappropriate may not suppress that urge very well. Second, reactive stopping in the motor domain may use overlapping circuitry with stopping in nonmotor domains, such as emotion and motivational control. Good control of emotion and motivation, even by means of a rapid and global mechanism, could be useful. Consider that an emotionally salient stimulus could trigger a chain of neural and bodily events that may cascade and be self-sustaining—for example, increased heart rate could exacerbate one's anxiety. Having a mechanism to interrupt the chain rapidly could be of high psychiatric relevance (Note: thanks to Josh

Berke for making this point). Although a review of the neural circuitry underlying emotional and motivational stopping is beyond the scope of this article, there is evidence for overlapping motor and autonomic stopping systems insofar as stopping a motor response has concurrent effects on heart rate (102,103). It is also important to recognize that the basal ganglia have different processing circuits with similar organizational principles. Each of the the striatum, the STN, and the pallidum have different sectors for sensorimotor, associative (cognitive) and limbic processing (104). Thus, in the same way that prefrontal input could lead to fast motor stopping via the basal ganglia, it could also lead to fast limbic control. A third explanation for the relevance of reactive motor stopping to psychiatry is that reactive stopping taps into brain regions such as the rIFC and preSMA that have much more general-purpose functions in decision making and intelligent behavior (105). Accordingly, hypoplasia or damage to these regions could affect many cognitive domains. This will contribute to psychiatric problems, just as it relates to poor reactive stopping.

When Do We Stop Reactively in the Real World?

Reactive stopping may be important in everyday life. One example is preventing oneself from stepping into the street when the light changes color. Another is in sports requiring fast action control, such as stopping and switching movements in response to changing environmental signals. Reactive stopping may even have evolved in a context when stopping and freezing was a key requirement to avoid danger. However, the number of scenarios requiring fast stopping, and especially stopping that has global effects on the motor system, is probably limited. Moreover, with the possible exceptions of motor disinhibition and the interrupting-the-chain example (discussed earlier), these scenarios bear limited relation to the kind of control problems in impulse control disorders. It seems doubtful that a child with a premonitory urge to tic is using a brain mechanism that reactively stops responses in a global fashion. Tic suppression, if it involves top-down control at all, is likely to be extended over time and also selectively targeted at a particular urge. The same goes for the control of urges in the context of substance abuse, such as cigarette smoking. Thus, a brain mechanism for rapid, stimulus-driven, reactive stopping of response tendencies, with global effects, seems limited as a model of control. It would be better to enrich the model of stopping so it captures core cognitive processes that are more related to real-world demands.

Stopping Reactively Versus Holding Your Horses?

One possibility is that the neural architecture for reactive stopping could be recruited during decision making to prevent incorrect response output. This is different from reactive stopping because the control is partial—the response is kept at bay until the decision is made. One theory of decision-making proposes that, in the case of conflict between response tendencies, a control system is used to "hold the horses" on motor output until the decision is made (106). This could prevent impulsive (overhasty) decisions. Evidence that such a mechanism might depend on stopping-related circuitry came from a study in patients with Parkinson's disease (107). On each trial, patients were presented with high- or low-conflict decisions. It was found that modulation of the STN with deep brain stimulation changed the error rate in the high-conflict situation. Apart from "hold-your-horses," this kind of mechanism has also been referred to as "braking" (64), "proactive control" (108), and "conflict-induced slowing" (31). Thus, within a particular trial, the presence of conflict could require a hold-your-horses mechanism to withhold response emission temporarily rather than to stop it reactively and completely.

Holding Your Horses Is Still Spur of the Moment

However, the foregoing example still requires control on the spur of the moment. The control may not require reactive stopping, but it does require a punctate process to withhold responding for a fraction of a second while a decision is made. This may somewhat extend the range of real-word scenarios that could require such a mechanism, but not by much. When a trying-to-abstain nicotine addict is confronted with a stimulus-driven urge to reach for a cigarette, the urge–action control is probably not applied in a one-off punctate fashion. It is likely applied tonically, or at least repeatedly over time, but presumably not in a way that has global effects, because that would interfere with ongoing thought, action, and feeling. Similar observations apply for the example of trying to control the urge to tic. Thus, the success of such forms of control seems to depend on keeping one's goals in mind and using them to target a particular tendency. Insofar as cognitive neuroscience can develop translational behavioral models for impulse control, and insofar as models of motor response control will fit the bill, it appears that such models would be enriched by at least two additional requirements: 1) proactivity or advance preparation and 2) selectivity, or control that is targeted at particular response tendencies. The remainder of this article focuses on paradigms of stopping which address these criteria.

Proactive Inhibitory Control—Preparing to Stop

Reactive stopping requires completely countermanding the initiated response. By contrast, hold-your-horses is a hypothesized mechanism through which subjects put a "brake" on response tendencies when conflict is detected. Another type of control is referred to here as "proactive inhibitory control." This involves a preparatory step before the response tendency is triggered. This can occur trial-by-trial in response to control cues (109), at the level of blocks of trials (110), or in a strategic sense when accuracy is favored over speed (59). For example, behavioral performance can be compared in blocks of mixed Go and no-go trials compared with pure blocks of Go trials. The behavioral manifestation of proactive inhibitory control is that response times are slower in the mixed blocks. The neural basis of proactive inhibitory control has been investigated with several paradigms (108,111,112). Here, research with stop signal and go/no-go tests are considered.

One study addressed proactive control using a conditional stop paradigm (56). Subjects were given a rule that if they initiated (for example) a right button response and a stop signal occurred, then they would have to stop (critical direction), but if they initiated a left button response and a stop signal occurred, they could ignore it (noncritical direction). Thus, as soon as the Go (choice) signal occurs, and it is the critical direction, subjects can potentially use proactive control to prepare to stop. It was found that RT was longer for Go critical than noncritical trials, and those subjects who slowed more were able to stop more quickly. Using fMRI, it was found that a network for "reactive stopping" (i.e., rIFC, preSMA, and the STN region) was more activated the greater the degree of slowing on Go critical trials. These results thus suggest that the brain network for reactive stopping could be "prepared" in advance—that is, control is proactive. Similar findings of proactive activation of the "stopping network"—including some or all the preSMA, rIFC, and the STN region—have been reported for variants of the stop signal task (81,109,113), and the go/no-go task (114). Notably, in some of these studies, there was also dorsolateral prefrontal cortex (DLPFC) and striatal activation. This likely reflects the increased working memory demands when preparation is needed. The striatal activation could also reflect use of an indirect fronto–basal ganglia pathway for proactive selective stopping. This will be considered subsequently.

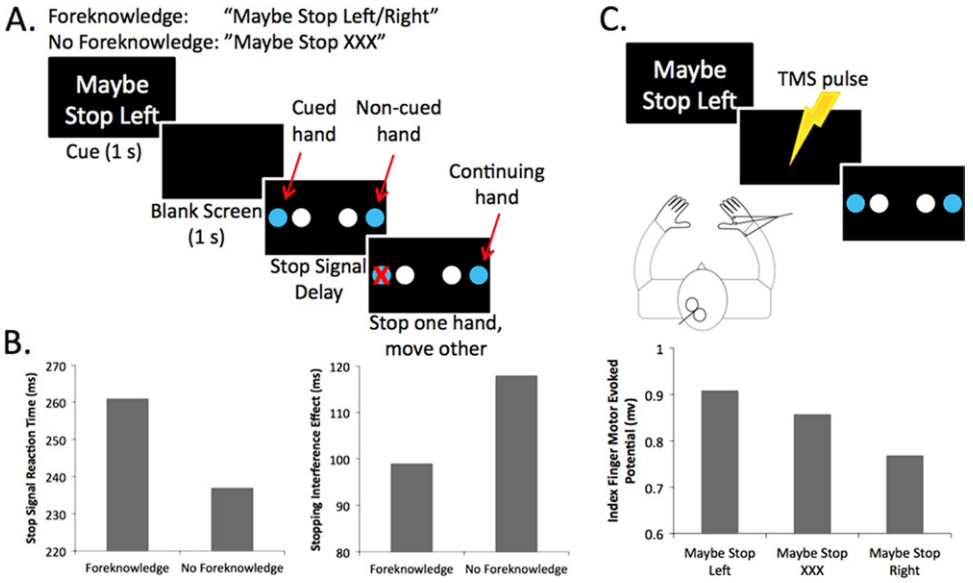

Figure 6. Behavioral and transcranial magnetic stimulation (TMS) studies of selective stopping. **(A)** The selective stopping task has stopping goal and no stopping goal conditions. Each trial begins with a cue providing a stopping goal (foreknowledge) or none (no foreknowledge). This was followed by a blank screen. A go stimulus was then presented, requiring the subject to initiate a bimanual response with index fingers or middle fingers of each hand. On a minority of trials, a visual stop signal (red X) occurred, and the subject tried to stop the indicated hand while continuing with the other hand. **(B)** When a stopping goal is provided (foreknowledge), the speed of stopping—stop signal reaction time—is longer, whereas the degree of slowing of the continuing hand is less (79). Taken together, this pattern of data suggests that stopping without a stopping goal (or with less information about what to stop) may recruit a mechanism with more global effects but that is also quicker. **(C)** For the same paradigm, TMS was delivered to left primary motor cortex (M1) with electromyography recorded from the right hand. The level of corticomotor excitability was significantly less when subjects anticipated they would have to stop the right hand, consistent with the possibility of proactive selective inhibitory control (126).

Other evidence for the neural systems underlying proactive control came from a study examining STN stimulation in humans (68). They key behavioral index was the difference in RT for mixed blocks of Go and no-go versus pure blocks of Go trials. When the patients were on stimulation, this slowing (or braking) effect was found to be smaller and rIFC activation was less than when patients were off stimulation. Thus, STN-stimulation may have altered the "stopping network," leading to a poorer ability to apply proactive inhibitory control. These findings could possibly explain the increased impulsivity that comes with STN-deep brain stimulation (DBS) in some patients (115).

Considered together, these studies suggest that regions important for reactive stopping, including the preSMA, the rIFC, and the STN, are also activated in situations in which no-go or Stop signals are anticipated. Because recruitment of this stopping network is also often accompanied by slowing of response emission (55,56,81,113,116,117), the possibility exists that the stopping network can act as a "brake" on motor output (without stopping it completely). Further, if the "stopping network" is preactivated by preparing to stop, then stopping should be quicker when it is needed. Two studies have shown that this is, in fact, the case (56,109).

Is proactive inhibitory control global or selective? The foregoing examples probably relate mainly to the global case, chiefly because selectivity is not required. For example, if Go trials require a choice response, and a subject slows down in a run of mixed Go and Stop trials, then the slowing down presumably reflects a general effect on response tendencies rather than on a particular response tendency. Indeed, some computational theories of the speed–accuracy trade-off propose that increased accuracy can be achieved by modulating cortical input to the STN, as reviewed by Bogacz *et al.* (59). However, proactive selective inhibitory control may also be possible, as seen in examples that follow.

Summary

The brain network that is used for reactive stopping—the preSMA, right IFC, and the STN—may also be used to prepare to stop. The behavioral consequence of proactive inhibitory control is that subjects slow down, and if stopping is required, they may stop more quickly. It is not yet clear whether proactive inhibitory control for these sorts of paradigms has global or selective effects on the motor system.

Selective Inhibitory Control

Distinguishing Selective from Global Mechanisms for Stopping

We saw that the STN is involved in both stop signal and no-go paradigms. We also saw that the STN may lead to widespread pulses that could inhibit basal ganglia output generally. Behavioral studies and TMS studies with the stop signal paradigm are consistent with the idea that such global suppression has functional consequences in the motor system. Other evidence, reviewed earlier, points to a role for the STN in "hold your horses" and also in proactive inhibitory control. However, a widespread pulse from the STN appears unsuitable for situations in which the subject is required to stop selectively.

It is important to distinguish selective stopping in the behavioral sense from the mechanistic sense. Behaviorally selective stopping could be achieved by stopping one response and continuing to make another, yet this could be implemented with a global stop mechanism followed by a restart of the new response. Rather than this, is mechanistically selective stopping possible?

We tried to dissociate mechanistically global and selective stopping with a novel version of the stop signal paradigm (79) (Figure 6A). On each trial, participants initiated a coupled response with fingers of both hands, and then, when a stop signal occurred, they

tried to stop one response while continuing with the other one. This design allowed a measurement of the selectivity of the stopping in terms of the degree of interference that is produced in the alternative (nonstopped) response; we refer to this as the "stopping interference effect." We compared a condition in which a stopping goal was provided of which response(s) may need to be stopped compared with a condition in which no stopping goal was provided. To do this, we presented a cue with the stopping goal ("Maybe Stop Left" or "Maybe Stop Right") or a cue without a specific stopping goal ("Maybe Stop XXX"). When a stopping goal was provided, the stopping interference effect was reduced, and stop signal reaction time was increased (Figure 6B). Thus, when the stopping goal was provided, reactive stopping was more selective, but stopping was also slower. The slower stopping may relate to use of the so-called indirect pathway of the basal ganglia, which has more synapses than the hyperdirect pathway.

Another paradigm in which mechanistically selective stopping may occur is the antisaccade test (in which a reflexive saccade must be stopped while a new saccade is generated). In this task, there is simply not enough time to stop all response tendencies and then initiate a new one. Mechanistically, selective stopping could also be used in other paradigms such as the Eriksen flanker and Simon tests, but the evidence for this is less clear.

Selective Stopping Via the Indirect Pathway of the Basal Ganglia

Mechanistically, selective stopping may be implemented by the indirect pathway of the basal ganglia. One form of this is a projection from the striatum to the globus pallidus pars externa (GPe) and then to the GPi (118). The termination pattern of striatal neurons onto the GPi, and from GPe to GPi, has a focused effect (unlike, e.g., the effect of the STN on the GPi, which is very diffuse). Thus, the striatum–GPe–GPi pathway offers a means to selectively control a particular response tendency, consistent with many conceptualizations (65,119). A puzzle, however, is that the other (more standard) form of the indirect pathway is a projection from the striatum to the GPe to the STN and only then to the GPi—and, notably, this standard form itself includes the STN. If the STN sends a widespread pulse to the GPi, this would appear to be ill suited to selective stopping. It is possible that the standard pathway is not used in the circumstance when selective stopping is required or that it corresponds to a more specific set of STN neurons with more specific effects on GPi than does the cortico–STN–GPi pathway (for review of these complex issues about the indirect pathway of the basal ganglia (see Smith *et al.* [120]). Regardless of the precise way in which selective stopping may be implemented in the basal ganglia, circuitry considerations motivate the indirect pathway via the striatum as a more selective control mechanism than the cortico–STN one.

To reprise some functional evidence for the importance of the striatum for selective control: in one study, neurophysiologic recordings were made from the caudate nucleus during an antisaccade task (89). This showed that some neurons specifically increased their firing rates for antisaccades but not for prosaccades. It was postulated that the suppression of the eye movement on antisaccade trials was due to activation of the indirect pathway of the basal ganglia, with suppressive effects on the superior colliculus. For a similar result using microstimulation in the caudate, see Watanabe and Munoz (90). These findings make the prediction that lesions to the indirect pathway of the basal ganglia should lead to saccade suppression deficits. One way this idea can be tested in humans is to study patients with early-stage Huntington disease because they may primarily have lost striatal-pallidal projections in the indirect pathway (121,122). Indeed, such patients have striking deficits on antisaccade trials (123,124).

Top-Down Frontostriatal Input for Proactive Selective Inhibitory Set

What determines whether one stops using a putative global/hyperdirect pathway versus a more selective one? One factor may be the amount of information one has about what to stop. Another factor could be whether one is required to use that information. In a typical stopping experiment, the stop signal is infrequent, and it appears after the response has been initiated. Thus, stopping is an emergency. The easiest thing for a subject to do would be to use the putative hyperdirect pathway. If this does have a global effect on the motor system, it will not matter. However, in circumstances in which the subject has more time or when selectivity of stopping is a key performance requirement, the selective stopping pathway could be used.

Using the selective stopping system may be especially likely if the selective stopping pathway has been primed. Such "priming" could correspond to a prefrontally mediated imposition of inhibitory set over the striatum. For this top-down biasing to occur the subject must have specific information in working memory of what to stop and the subject must use this information. This concept of "top down inhibitory set" complements earlier conceptions of the functional role of the striatum in "response set." For example, Robbins and Brown (125) wrote: "the striatum functions at an early stage of response selection to constrain, or weight, potential response tendencies. We refer to this process as 'response set' which we have previously defined as the prior assignment of the probability of selection from the repertoire of available responses" (page 201).

Here the notion of "response set" is extended to "inhibitory set." Accordingly, when particular response tendencies may need to be controlled, the striatum could function to weight, or constrain, potential tendencies—not just by "priming" those response channels that may need to be activated but by suppressing those channels that might need to be stopped.

We studied how such stopping goals are set up and how they are proactively deployed to target specific response tendencies using TMS and concurrent electromyography (126) (Figure 6C). TMS has the great advantage that it can reveal changes in the motor system before any behavior is initiated. As before, we used a design in which subjects were given a stopping goal (cue) "Maybe Stop Left" or "Maybe Stop Right" followed by a Go stimulus (move two hands together), followed sometimes by a stop signal (requiring them to stop one hand and to continue with the other). We delivered TMS over left M1 and recorded motor-evoked potentials from the right hand. Importantly, we measured the excitability of the right hand in the interval between the cue (stopping goal) and the Go response. We found that corticomotor excitability for the right hand was reduced when the cue indicated it might need to be stopped ("Maybe Stop Right") compared with when it would not need to be stopped. This shows that having a goal of what response may need to be stopped in the future is accompanied by applying advance control onto a specific motor representation.

A Speculative Model of Proactive Selective Inhibitory Set

At a neural systems level, proactive and selective inhibitory set may be instantiated by a frontostriatal circuit (Figure 5D–5F). The evidence implicating the striatum was reviewed earlier. Regarding the frontal cortex, the key region may be the DLPFC—specifically the middle frontal gyrus in humans. What is the evidence for this?

First, the DLPFC is key for working memory (127,128–130). Sec-

ond, stopping goals are a form of working memory—and consistent with this, there is DLPFC activation in stop signal or go/no-go paradigms with increased working memory load (56,109,131). There is also preparatory set activity in DLPFC in an antisaccade task (132,133), and pharmacologic manipulation of this region (with noradrenergic antagonists) impairs response inhibition (134), just as it does working memory (135). Third, monkey tract tracing and human diffusion tensor imaging show that the DLPFC is connected with the head of the caudate via a so-called associative frontostriatal-pallidal-thalamic loop (136,137).

It is proposed that the DLPFC–caudate frontostriatal circuit is used to stop selectively via the indirect pathway. Specifically, the subject's goal of what to stop may be implemented, at the neural level, in a signal from the DLPFC, which is sent to the striatum to inhibit the GPe, which then removes inhibition from the GPi (via the STN or directly) and finally increases inhibition of particular cortical response representations (e.g., in M1). In situations in which the subject prepares to stop in the future, this top-down inhibitory set could be established over the indirect pathway without actually being implemented (in the sense of affecting motor output; Figure 5D). This would correspond to a cortical bias over the striatum (top-down inhibitory set). Subsequently, a change in the environment could trigger the inhibitory control, so that it does affect particular response initiation–execution, in a selective way (Figure 5F).

This conception of a cortical bias followed by a trigger is motivated by a fronto–basal ganglia model of eye movement initiation (138). It is also motivated by striatal recording studies showing that no-go striatal responses occur in both a preparatory phase and a trigger phase (Figure 4) (88). This system for top-down selective inhibitory set could be implemented to stop a movement reactively, or it could be done in partial mode (leading to selectively slower response emission without cancelation; Figure 5E).

Although this model of how the stopping goal is used to prepare to stop selectively is speculative, it makes testable predictions about the locus and timing of activity in PFC, striatum, pallidum, STN, and M1 during specific behavioral conditions. For example, the model predicts that mechanistically selective stopping will activate the indirect pathway (including the striatum) more than does standard (global) stopping. The model also predicts that whereas standard stopping requires the integrity of a relatively simple cortical network (i.e., preSMA and rIFC), proactive inhibitory control (especially with a selectivity requirement) will additionally recruit DLPFC. In studies of lesion patients, one might find that although damage to DLPFC does not affect standard (global) stopping (compare Aron *et al.* [25]), it does affect selective stopping because the stopping goal will be disrupted (139).

Summary

If selective stopping is required by the behavioral paradigm, then subjects may be able to use a selective mechanism to do it. This selective mechanism could engage the indirect pathway of the basal ganglia rather than the hyperdirect pathway that is putatively used in the standard case. Proactive selective stopping may also be possible if subjects use stopping goals to prepare the indirect pathway system in advance. This proactive selective control may be setup via an influence of DLPFC over the caudate nucleus, external pallidum, and so forth. Thus, a proactive inhibitory set could be used partially (when selective slowing is required), or it could be triggered completely.

Conclusions and Further Questions

Cognitive neuroscience has made progress with behavioral paradigms that require reactive stopping. Accumulating evidence from many research groups clearly points to the critical importance of right IFC, the dorsomedial frontal cortex (esp. preSMA), and the basal ganglia, with downstream effects on M1 (16,21–24). The identification of this network is leading to efforts that characterize its subcomponents. For example, what are the relative roles of different nodes in the network such as the preSMA versus the right IFC (38) and the STN versus the striatum (59)? How do attention and inhibitory control functions map to the network (30,49)? The cognitive neuroscience advances in this area have also provided some useful endophenotypes for psychiatric research in terms of candidate behavior, brain regions, and genetics (21,98,99,140).

Notwithstanding these fruitful developments, several considerations suggest that reactive stopping is limited as a model for control in everyday life and in psychiatric disorders. First, there are scenarios in which a rapid, punctate stopping process appears ill suited—for example, when someone has to control his or her urge to tic tonically. Second, whereas reactive stopping appears to have global effects on the motor system, many scenarios require selectivity. Third, in everyday life, control is specified according to one's goals, which are monitored over seconds, minutes, or longer and periodically retrieved from long-term memory in particular contexts. Thus, the control must be setup in advance and extended across time, and it must be targeted endogenously rather than

Table 1. Types of Control and Stopping Mechanisms Discussed in the Review

	Type of Control	
Stopping Mechanism	Reactive	Proactive
Global	BG circuit: hyperdirect Behavior: fast SSRT/high interference WM: low Example paradigms: standard stop signal, some types of go/no-go	BG circuit: hyperdirect Behavior: slowed RT when going (with global effects) WM: high Example paradigms: conditional stop signal, mixed go/no-go vs. pure Go
Selective	BG circuit: indirect Behavior: slower SSRT/lower interference WM: high Example paradigms: selective stop signal, Antisaccade? Ericksen? Simon?	BG circuit: indirect Behavior: slowed RT when going (selective effects) WM: very high Example paradigms: selective stop signal

Interference indicates a measure of selectivity of stopping. Question marks indicate uncertainty as to whether these tasks engage these processes.
BG, basal ganglia; RT, reaction time; SSRT, stop signal reaction time; WM, working memory.

exogenously at particular tendencies as these emerge. This article motivates a model that meets these two additional requirements by including proactivity (i.e., advance preparation) and selectivity (i.e., control that is targeted at particular response tendencies). Adding these two features creates several kinds of stopping paradigms, the features of which are summarized in Table 1.

It appears that some forms of proactivity, such as preparing to stop in stop signal or go/no-go paradigms, or favoring accuracy over speed, engage the same brain network that is used for reactive stopping (viz. the preSMA, right IFC, and the STN)— but in a partial mode (leading to response slowing) (56,59,109). Further studies are needed to verify these findings and to understand the relative roles of the STN versus the striatum.

Other research suggests that mechanistically selective stopping is possible. When subjects are given a stopping goal and they use this to prepare to stop a particular response tendency, they can stop one response and continue making another with little interference (79,126). Further research is required to examine the neural basis of selective stopping. It is predicted that it will engage the striatum and the indirect pathway, and it is predicted that it is made possible by a top-down influence from DLPFC. This creates a proactive selective inhibitory set. When reactive selective stopping is needed, it could be implemented by the same cortical regions that are important for standard reactive stopping, but with a striatal rather than STN target.

The research summarized here has focused on motor response control. However, there are fronto–basal ganglia circuits with a highly similar organization for limbic control (104,141–143). It is likely that the circuitry principles that govern proactive and selective inhibitory control will also extend to the limbic domain. For example, top-down inhibitory set could be used to implement stopping goals for motivation. The circuitry for this could be highly similar to that for implementing stopping goals for action. Such implementation could occur via the (limbic) indirect pathway, including the ventral striatum–ventral pallidum, or via the hyperdirect pathway, including the ventral-medial sector of the STN (144). Testing this idea requires developing behavioral paradigms for proactive and selective control of motivation.

Overall, recent findings motivate a richer model of how people control their inappropriate response tendencies. The model provides greater insight into why control could fail in psychiatric or neurologic disorders. This may happen for several reasons—for example because people cannot maintain their stopping goals, because they cannot implement the inhibitory set, or because they cannot trigger inhibitory control when it is needed. As argued here, these functions may be dissociated to different brain systems. Validating this could have important implications for classifying patients according to different symptoms and for determining treatment.

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