Towards real-world generalizability of a circuit for action-stopping

Ricci Hannah ✉ *and Adam R. Aron*

Abstract | Two decades of cross-species neuroscience research on rapid action-stopping in the laboratory has provided motivation for an underlying prefrontal–basal ganglia circuit. Here we provide an update of key studies from the past few years. We conclude that this basic neural circuit is on increasingly firm ground, and we move on to consider whether the action-stopping function implemented by this circuit applies beyond the simple laboratory stop signal task. We advance through a series of studies of increasing 'real-worldness', starting with laboratory tests of stopping of speech, gait and bodily functions, and then going beyond the laboratory to consider neural recordings and stimulation during moments of control presumably required in everyday activities such as walking and driving. We end by asking whether stopping research has clinical relevance, focusing on movement disorders such as stuttering, tics and freezing of gait. Overall, we conclude there are hints that the prefrontal–basal ganglia action-stopping circuit that is engaged by the basic stop signal task is recruited in myriad scenarios; however, truly proving this for real-world scenarios requires a new generation of studies that will need to overcome substantial technical and inferential challenges.

'Executive control' refers to the way we use our goals to control our behaviour and thoughts. One type of executive function is the stopping of actions and thoughts, and it works alongside other functions such as working memory to help us respond appropriately under circumstances that involve novelty or the overriding of habits[1,2]. For example, holding the goal in mind of losing weight when on a diet might lead us to stop when reaching for an extra biscuit. The potential importance of stopping is emphasized in clinical disorders characterized by problems controlling thoughts or impulses to act (for example, intrusive thinking or motor tics). Although thought-stopping and action-stopping are highly relevant to healthy human behaviour, and may even rely on analogous brain systems[3], action-stopping has received greater systematic investigation because it is easier to quantify and because we know more about the motor system. Action-stopping is therefore a stronger starting point for this Review, which broaches the question of whether our understanding of stopping, developed largely from highly controlled laboratory-based experiments, generalizes to the real world.

In the laboratory, action-stopping has been most commonly studied with the stop signal task[4,5] (FIG. 1a). This requires people to rapidly stop an initiated response when a signal occurs. Although other forms of action-stopping exist, such as proactively braking or delaying impending actions (BOX 1), as do other broader forms of behavioural control (for example, choosing not to act, or resisting interference from distraction), overall these are less understood and may even engage different processes or networks[6–8], and so here we focus on the simpler case. A prominent model (hereafter referred to as the action-stopping model) proposes that action-stopping is achieved via a prefrontal cortex (PFC)–basal ganglia–thalamocortical 'stopping' network[9] (hereafter referred to as the action-stopping network). We begin by reviewing this model, moving briefly over older results that have been covered many times[10–12] and focusing more on recent human, and in some cases non-human animal, studies since the last major review[9]. We see that key claims of the model are well supported. We then ask whether the action-stopping model applies beyond simple laboratory-based tasks that mostly use manual responses. We then review recent work that starts to tackle whether action-stopping generalizes to more naturalistic settings, and end with the application of the model to clinical movement disorders. Overall, these insights are intended to provide a road map for future research into real-world action control by highlighting the promises and challenges offered by the action-stopping model.

Neural basis of action-stopping

The stop signal task provides an estimate of the behavioural latency of action-stopping, the stop signal reaction time (SSRT; the latency of stopping a cued action). As the time at which an uninitiated action plan is stopped

Department of Psychology, University of California San Diego, San Diego, CA, USA.
✉*e-mail: rhannah@ucsd.edu*

https://doi.org/10.1038/s41583-021-00485-1

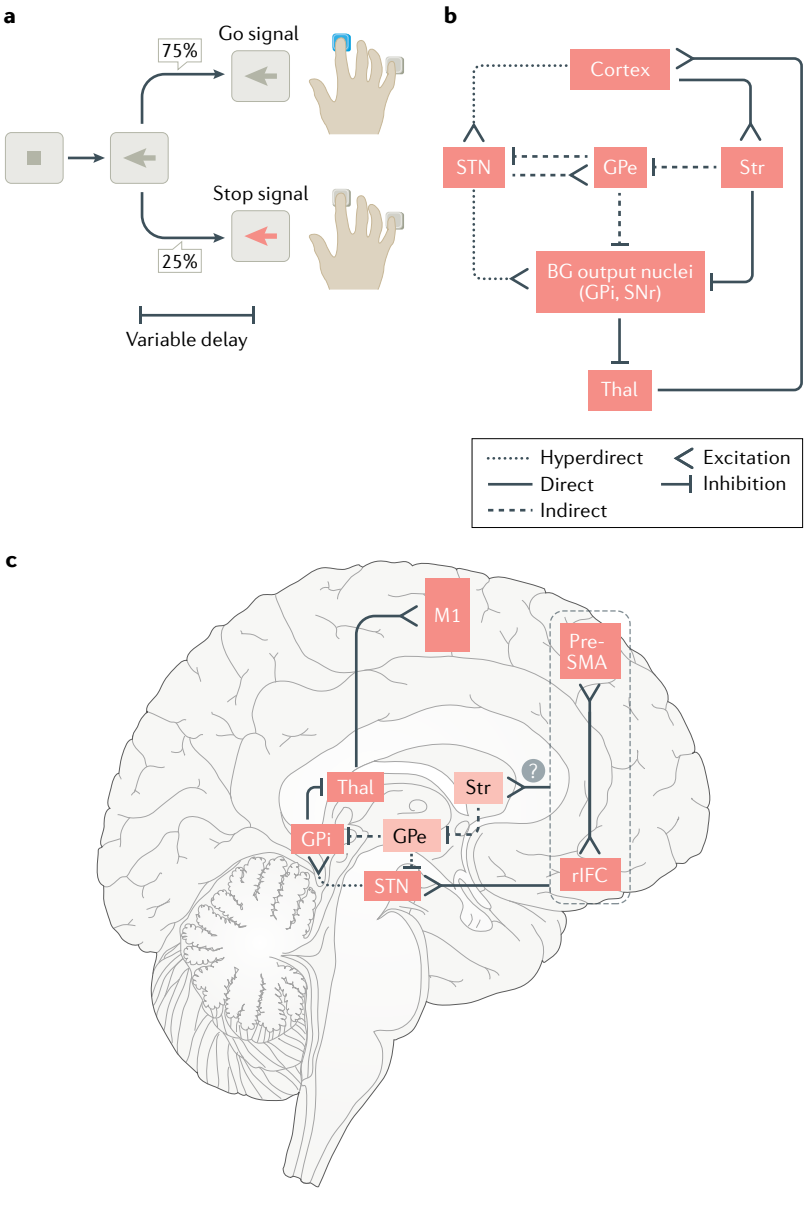

Fig. 1 | **Cortico–basal ganglia–thalamocortical networks for action control in the stop signal task. a** | In the stop signal task, a 'go' signal (here, an arrow) requiring a response (a key press indicated by the direction of the arrow) is presented on every trial. In about 25% of trials, the go signal is followed shortly by a 'stop' signal (here, the arrow turning red), and on those trials, participants must attempt to stop the impending response. The delay between the go and stop cues varies from trial to trial and, if the delay between them is short, the participant is more likely to stop. By titrating the probability of successfully stopping at various delays and examining the response-time distribution, one can estimate the latency of action-stopping, the stop signal reaction time (SSRT)[4,5]. **b** | The basal ganglia (BG) output nuclei (the globus pallidus interna (GPi) and the substantia nigra pars reticulata (SNr)) provide tonic inhibition of the thalamic outputs that facilitate motor cortical areas. A classic view is that the direct pathway, which involves striatal projections to the GPi/SNr, supports actions by inhibiting the BG output, thus disinhibiting thalamic output to the cortex[81]. Meanwhile, the indirect pathway, which involves projections from the striatum (Str) to the GPi/SNr via the globus pallidus externa (GPe), may help to suppress actions by increasing inhibitory control over BG output (for a more nuanced discussion, see REF.[172]). The hyperdirect pathway is also thought to be involved in regulating BG output[173], offering a fast route for stopping because of the short-latency, monosynaptic connections between the cortex and the subthalamic nucleus (STN)[36], and the direct access of the STN to the GPi/SNr. **c** | The prefrontal–BG–thalamocortical model of action-stopping[9,10] proposes that on detection of a stop signal, sensory information about the cue is fed forward to the prefrontal cortex, where the stop command is produced. Two prefrontal areas, the right inferior frontal cortex (rIFC) and the dorsomedial prefrontal cortex (particularly the pre-supplementary motor area (pre-SMA)), are thought send the stop command via the STN. Output from the STN excites the GPi (or SNr, for example with eye movements), which in turn inhibits thalamic excitatory drive to the primary motor cortex (M1) and thus reduces the likelihood of movement. The Str, acting via the GPe, has also been implicated in action-stopping, although its precise role is currently debated. Both the GPe and the Str have been shaded a lighter colour to illustrate the questions surrounding their inclusion in the network. Thal, thalamus.

cannot be directly observed, SSRT is derived on the basis of a mathematical model that uses reaction times and the probability of successful stopping[5]. Estimates of SSRT are therefore sensitive to violations of the model assumptions[13] and to occasional failures by individuals to trigger the stop process[14]. Notwithstanding these methodological challenges, SSRT can provide a useful constraint for research on the neural correlates: for neural activity to be involved in stopping, it must occur before this time of the stop reaction, which is typically approximately 200–250 ms for manual responses[15–18].

Two decades of action-stopping research, building on a long history of work on cortico–basal ganglia circuits (FIG. 1b), has provided motivation for a model of action-stopping that depends on PFC–basal ganglia circuits (FIG. 1c). Briefly, sensory information about a stop signal is transmitted to two key regions of the PFC — the right inferior frontal cortex (rIFC) and the pre-supplementary motor area (pre-SMA) — which generate a stop command and forward it to the subthalamic nucleus (STN). The command is then sent via the basal ganglia output nuclei to the motor thalamus, with the effect of reducing drive to the motor cortical areas and thus reducing the likelihood of movement.

We now update the evidence for this model, brain region by brain region in the order in which they seem to be activated by the requirement to stop 'reactively' ('reactive stopping' in BOX 1), noting in particular new data illustrating the timing of activity in each brain region that support the presumed temporal flow through the network see REF.[15] (FIG. 2).

Right inferior frontal cortex. It was proposed the ventral pars opercularis of the rIFC initiates the stop command[19], implying it should be active early during the stop process. Indeed, recent findings confirm the early involvement of the rIFC.

Imaging studies first identified the rIFC as a potential mediator of action-stopping[18,20–23]. Causal evidence

Offline transcranial magnetic stimulation (TMS). Non-invasive brain stimulation eliciting long-lasting after-effects. Typically delivered before a participant undergoes behavioural testing or neuroimaging.

Electrocorticography (ECoG). Invasive electrophysiological technique that uses electrodes placed directly on the exposed surface of the brain to record electrical activity from the cerebral cortex.

Hyperdirect pathway Pathway connecting cortical areas directly to the subthalamic nucleus, bypassing the striatum.

Electromyography (EMG). Electrophysiological technique that uses electrodes placed on the skin over a muscle to record its electrical activity.

came from patients with prefrontal damage[24] (pointing particularly to the pars opercularis), and then from offline transcranial magnetic stimulation (TMS) studies showing that disrupting the rIFC prolonged SSRT[25,26]. An electrocorticography (ECoG) study revealed increased oscillatory power in the beta band (13–30 Hz) in the rIFC in the period between the stop signal and SSRT[27] but lacked the temporal resolution to say more about its role in initiating the stop command. Functional imaging[18] and imaging of white-matter tracts[18,28] have suggested that regions of the rIFC and the pre-SMA that are activated following a stop signal are connected with each other and to the STN, thus pointing to a possible hyperdirect pathway.

These findings have since been buttressed by another ECoG study showing an increase in gamma-band activity in the rIFC after the stop signal[29] (earliest in the ventral pars opercularis (also see REF.[30]) relative to more anterior inferior frontal cortex (IFC) regions and the anterior insula), and by three recent studies combining electroencephalography (EEG), TMS and electromyography (EMG)[15,31,32]. The last three studies revealed four main findings. First, bursts of beta-band activity were observed in right-lateralized frontal electrodes on successful stop trials within approximately 120 ms after the stop signal[15,31,32]. Second, TMS revealed that these bursts were soon followed by a broad suppression of the motor system (a putative signature of basal ganglia recruitment, see later)[15]. Third, there was subsequently a cancellation of motor output, manifesting itself as a decline in muscle activity[15,31,32]. Fourth, behavioural stopping occurred at about 220 ms after the stop signal (FIG. 2).

Two of these studies involved TMS-induced disruption targeting the rIFC. One showed that the timing of beta-band activity correlated with that of action-stopping at the single-trial level, and that online TMS disruption around the time of this beta activity prolonged the latency of action-stopping[31]. The other showed that offline disruption, again targeting the rIFC, slowed stopping speed and reduced rIFC beta-band activity[32].

A criticism of the three EEG studies[15,31,32] is that the low spatial resolution of EEG precludes knowing whether beta-band activity truly emanated from the rIFC[33]. However, evidence from a combined functional MRI (fMRI)–magnetoencephalography (MEG) study, offering greater spatial resolution, replicated the timely increase in beta that was specific to the rIFC not the left IFC (lIFC)[34]. Together, these studies begin to address previous concerns about the specificity of rIFC activation (including its laterality) and its involvement in action-stopping per se[35]. For example, both the time-locking of beta-band activity to action-stopping[31], rather than to the stop signal, and the elevation of beta specifically after a stop signal[34], rather than any infrequent or unexpected signal, are more consistent with a role for the rIFC in stopping than simply monitoring or attentional capture.

A recent study in individuals with Parkinson disease provided high temporal resolution evidence of a functional rIFC–STN hyperdirect pathway for action-stopping[36]. First, stimulation of the STN (specifically the ventral part, as implicated in the action-stopping model[37]; see later) evoked short-latency potentials (occurring about 2 ms after stimulation) in ECoG electrodes over the rIFC, consistent with a monosynaptic connection[36]. Second, event-related potentials in the rIFC associated with stopping preceded those in the STN, consistent with the temporal primacy of the rIFC. Last, individuals with greater functional correlation between these regions stopped faster than did individuals with less co-activity between these regions.

Overall, these studies are broadly consistent with the idea that the rIFC plays a key role early in the stop process and that effects on putative basal ganglia and muscle occur later.

Pre-supplementary motor area. The pre-SMA was also thought to have a critical role in implementing the stop command, and recent findings support that. However, its functional role in relation to the rIFC is still unclear.

The right pre-SMA is activated in fMRI studies of action-stopping[18,20,38,39]. ECoG indicated that successful stopping is associated with increased beta-band and gamma-band (30–90 Hz) oscillatory power before the SSRT in the pre-SMA[27]. There is also some causal evidence of pre-SMA involvement in stopping from individuals with large lesions[40,41] and from TMS studies[39,42,43].

Box 1 | **Modes of action control**

Several different modes of action-stopping have been described. Each may be called upon in different situations, and although some seem likely to depend on a shared neural architecture, others may engage different pathways.

Reactive stopping
Reactive stopping is triggered in response to an unpredictable cue, as in the standard stop signal task, and reflects emergency-like stopping. Although this form of stopping is most widely studied, in real life it is probably called upon only sometimes — for example, stopping oneself from stepping into the road when a car suddenly approaches. It is thought to rely on the action-stopping network (FIG. 1c).

Proactive control
Proactive control refers to preventing actions or slowing them down, and can occur in two ways. First, it can be set up in advance of an overt need to stop, and not implemented until that time. Laboratory tests of this scenario have shown that this form of proactive control recruits the pre-supplementary area (pre-SMA), striatum and pallidum, suggestive of indirect pathway recruitment[74,177,178] (see also below). Second, it can act like a brake, recruited partially when you anticipate having to stop[72,76,179]. The subthalamic nucleus (STN)[55,87,90] and a pre-SMA–striatal pathway[72,77] have both been implicated in this form of proactive control[72,77].

Selective stopping
Selective stopping in a behavioural sense refers to stopping one action without affecting other ongoing actions. This is often tested in tasks where participants initiate bilateral hand movements but are then told to stop with one hand and continue with the other[16,180]. They can do so, but the response time of the continuing hand is delayed compared with typical responses. This implies the use of a global, STN-mediated[64,67], mechanism. However, a mechanistically selective mechanism can be used if one can proactively prepare to stop selectively[177,178] (but see REF.[86]), and this may involve the prefrontal–striatopallidal (indirect) pathway[16,74].

Stop–change and switching
Stop–change and switching are when the stopping of one action is immediately followed by the initiation of another: a football player cancels a pass to one teammate when they see a defender nearby, and quickly passes to an unmarked teammate. Neuroimaging[181,182], neurophysiology[48,70,183] and brain stimulation[183,184] studies suggest there is overlap in the systems involved in stop–change and switching with the action-stopping network, although this overlap probably depends on the type of switching task[41,70].

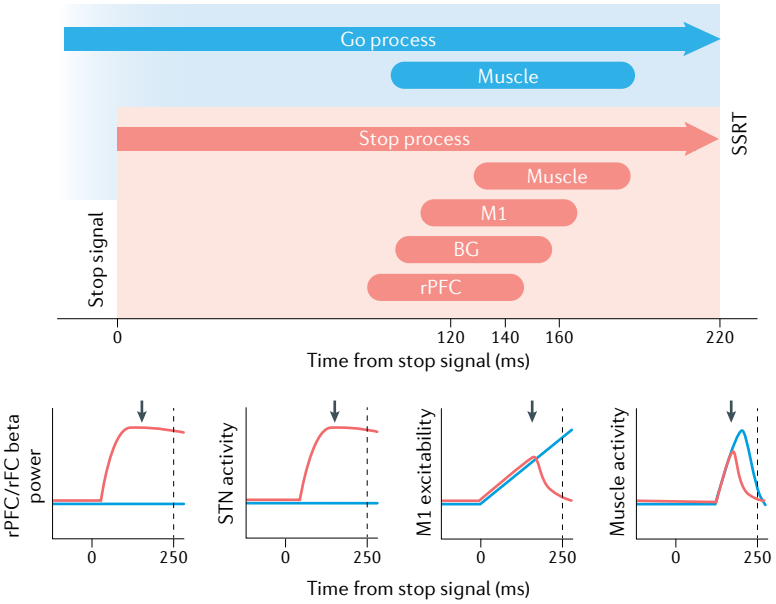

Fig. 2 | **Timing of events in the action-stopping network.** The top panel illustrates the approximate timing of events, and the bottom panel shows a schematized version of changes in neural activity at different sites, with arrows representing the same key time points as in the main text and the different coloured lines representing neural activity on go (blue) and stop (red) trials. This example is for stopping a manual response in relation to a salient stop signal. Following a go signal, a putative go process (blue) is initiated and proceeds over time. After some delay, typically about 200 ms, a stop signal is presented, prompting the initiation of a stop process (red) that races to completion with the go process. Physiologically, the generation of the stop command is reflected by activity in the right prefrontal cortex (rFPC) and the right frontal cortex (rFC), particularly the right inferior frontal cortex and the pre-supplementary motor area, within approximately 120 ms after the stop signal[15,31]. This is followed by activity in the basal ganglia (BG), starting with the subthalamic nucleus (STN), which receives hyperdirect input from the rPFC shortly after[36,48]. We presume activity in the BG precedes a global suppression of the primary motor cortex (M1) that occurs from about 140 ms after the stop signal[15,82]. In the meantime, muscle activity related to the go process may already have been initiated, but has not developed sufficiently to produce an overt response. A stop-related suppression of any ongoing muscle activity is evident in the electromyogram within approximately 160 ms[15,31,32,86]. Assuming that this occurs soon enough — that is, that the stop process reaches completion before the go process — behavioural stopping as indicated by the stop signal reaction time (SSRT) occurs within about 220 ms. These timings impose new constraints on when activity in a brain region must occur by to be included in the network model. For example, recent work suggested that the parietal cortex might functionally contribute to stopping[174]. However, the timing of its supposed role, which comes after the cancellation of muscle activity, argues against its inclusion in the action-stopping network and instead hints at a role in action-execution[175] (for example, ensuring the timely release of actions). Nevertheless, there remains a degree of uncertainty in the timing of the neurophysiological events described here. For example, some brain processes may take time to develop following the initial receipt of a signal from another brain region and may not be immediately detectable in currently available neurophysiological measures. There is also variability in how timings are reported, wherein, for example, beta-band burst timings are measured from the peak of activity, whereas electromyogram suppression is taken from its onset. Adapted with permission from REF.[15], CC BY 4.0 (https://creativecommons.org/licenses/by/4.0/).

Online TMS
Non-invasive brain stimulation eliciting short-lived after-effects. Typically delivered while a participant undergoes behavioural testing or neuroimaging.

The pre-SMA has been implicated in various sensorimotor functions[44], including conflict resolution (as reviewed in REF.[44]). With respect to stopping, one possibility is that monitoring-related activity in the pre-SMA identifies the need to stop, and that the pre-SMA forwards this via the frontal aslant tract to the rIFC[18,45], which implements the stop process[10]. This predicts that pre-SMA activity precedes rIFC activity during action-stopping. Alternatively, the pre-SMA could exert its influence directly on the STN via hyperdirect projections[18,45–48] and could act synergistically with any influence of the rIFC on the STN. MEG studies have provided conflicting results concerning the temporal primacy of pre-SMA activity versus rIFC activity[34,49].

A recent EEG study showed that frontocentral beta-band bursts during action-stopping[50], presumably corresponding to the pre-SMA[27], were followed shortly by beta-band bursting in sensorimotor areas, a putative signature of inhibitory activity. The temporal relationship fits with the presumed flow of the stop command from prefrontal to motor areas. However, a non-human primate EEG study questioned the functional relevance of frontocentral beta-band bursting, on the grounds that it occurs too infrequently to explain stopping and was more sensitive to stopping failures than stopping success[51].

New rodent data have provided causal evidence for a direct influence of the dorsomedial PFC (dmPFC; which in humans encompasses the pre-SMA) over the STN[52]. Tracing was used to identify subpopulations of intermixed neurons in rodent dmPFC with different projection targets, including the STN. Next, optogenetic activation and inactivation of the STN-projecting neurons in the dmPFC during a go–no-go task, as well as the STN directly, reduced and increased impulsive responding, respectively. Furthermore, stimulation of dmPFC neurons projecting to the lateral hypothalamus showed opposite behavioural effects in the go–no-go task to stimulation of dmPFC–STN projections, providing a clear dissociation of the function of dmPFC targets.

Overall, it seems there is a functional hyperdirect pathway from the pre-SMA or the dmPFC to the STN that is activated in sufficient time to affect stopping; however, research is still needed to delineate the relative roles of the pre-SMA and the rIFC in what seems to be a pre-SMA–rIFC–STN network.

Subthalamic nucleus. The ventral STN was proposed to receive the stop command from the PFC and relay it via basal ganglia output neurons to the thalamus. Recent findings provide support for a hyperdirect pathway from the PFC to the ventral STN.

The STN has been implicated in interrupting[53], delaying and 'braking'[54–56], and outright stopping of actions that have been prepared or already initiated[18,20,48,57]. Several studies have shown that deep brain stimulation of the STN in individuals with Parkinson disease changes SSRT[58–61]. Neurophysiological recordings in such individuals have suggested that STN activity increases about 100 ms or so before behavioural stopping[36,62,63] (FIG. 2). Relatedly, beta-band power increases for stopping trials in local field potentials recorded from the STN of individuals with Parkinson disease[64,65]. Trials in which beta-band activity is greater are also ones in which there is a greater global motor system suppression[64], whereby when a participant stops one effector from moving, there is a reduction in the excitability of task-irrelevant muscle representations measured with TMS over the primary motor cortex (M1)[15,66]. Stopping via the STN might therefore reflect an emergency-like system that

briefly interrupts all ongoing behaviour, which may be more efficient than identifying and stopping all active motor representations individually. These global effects may reflect the putatively broad output from the STN to the globus pallidus interna (GPi)[9,67]. However, the evidence for this idea is still weak, as tracing studies imply that STN–GPi projections are topographically and somatotopically organized[68,69].

The action-stopping model was recently updated, on the basis of monkey tract-tracing data, to suggest that the ventral part of the STN specifically is important for stopping because it receives input from the lateral PFC, including the rIFC[37]. The prediction was validated by a monkey recording study[70] and the aforementioned study in people with Parkinson disease[36]. There is also now good causal evidence of STN involvement in stopping: optogenetic studies of the rodent STN[53] and the dmPFC–STN connection[52] (mentioned earlier) show that they are important for interrupting ongoing and planned behaviours.

An interesting feature of STN activity in action-stopping is the increase of beta-band power. This is also observed in the rIFC and the pre-SMA, which has prompted the speculation that beta-band oscillations could be a property of the stopping network. One suggestion is that the bursts reflect brief periods of top-down communication from the PFC to the STN that instantiates the stopping command[37].

Potential role for the striatum. The striatum has also been implicated in stopping, but whether it should be included in the standard action-stopping network is still unclear.

fMRI studies of stopping often show striatal activation[18,20,39,71,72]. Furthermore, disruption of the pre-SMA and the rIFC with offline TMS alters SSRT, with changes in SSRT correlated with changes in the blood oxygen level-dependent (BOLD) activation in the striatum[39,73]. However, inconsistent with a striatal role in standard action-stopping, SSRT is normal in individuals with premanifest Huntington disease who have reductions in striatal volume compared with healthy controls[74,75].

Striatal BOLD activity seems to increase when one is told that the likelihood of needing to stop is high, irrespective of whether one is eventually required to stop[72,76]. This could indicate that the striatum is more involved proactively in delaying or 'braking' actions to avoid impulsive responding ('proactive control' in BOX 1). Chemogenetic silencing of dmPFC–striatal neurons in rodents supports this view[77]. Neural recordings from the rodent globus pallidus externa (GPe), downstream of the striatum, during a stopping task are also consistent with such a role[78]. When proactive control was exerted, the trajectory of population-level activity in the GPe, reflecting collective dynamics of many neurons over time, began further away from the trajectory followed during normal movement initiation[78].

Alternatively, the striatum has been suggested to be important when preparing to stop via a more selective mechanism than the global one recruited during reactive stopping[74] ('selective stopping' in BOX 1). Cell type-specific recording experiments in rodents have shown that direct and indirect projections from the striatum are both more active during movement than during immobility[79,80], the co-activation fitting with the idea that the indirect pathway acts on different basal ganglia outputs to selectively suppress actions that compete with the desired one[81].

The precise role of the striatum in simple action-stopping remains unclear, but could be resolved using high temporal resolution neurophysiological recordings from the striatum and downstream GPe (that is, the indirect pathway) to clarify the conditions under which there is a functional activation of the striatopallidal pathway.

Motor cortex and spinal motor neurons. The last cortical region where stopping commands presumably intervene to prevent movement is the primary motor cortex (M1).

TMS over M1 showed that corticospinal excitability is suppressed via a withdrawal of drive to, or an active physiological inhibition (GABAergic) of, agonist-muscle M1 within approximately 140 ms after a stop signal[17,82]. As noted already, this motor system suppression is detectable in task-irrelevant muscles[66,83], and may be mediated by the STN[64].

The timing of the motor system suppression fits with changes in neural activity in primate premotor cortex and M1 (REFS[84,85]). Human studies have shown that changes in motor cortical excitability (and presumably output) during stopping are transmitted very quickly to the muscles[15,31,86]. Successful stopping of manual responses, in which a participant initiates a response but cancels it before it runs to completion, is often associated with a sharp decline in muscle activity within approximately 160 ms after the stop signal[15,31,86], and approximately 20 ms after the global motor system suppression[15]. It remains unclear whether stop commands are always transmitted via M1 or can also target the spinal cord directly.

A different perspective on the basal ganglia. Recently, a variation of the 'classic' action-stopping model was proposed[87], with a key difference in how the stop process is implemented by the basal ganglia. The classic model proposes that the STN implements the stop via the GPi and substantia nigra par reticulata (GPi/SNr) (FIGS 1,2). The new model, motivated by recordings from rodent basal ganglia[88,89], instead proposes that the STN–GPi/SNr pathway serves as a 'pause' to delay actions and that a subsequent, pallidostriatal-mediated 'stop' process cancels them[87]. This suggestion is supported by observations that STN activity peaks too soon (within about 15 ms), is too transient and is not specific enough to stopping trials to fully explain action-stopping in rodents[88]. In a follow-up study, a specific population of pallidal cells called 'arkypallidal cells' were identified, defined by the fact that they solely innervate the striatum[89]. Arkypallidal cells fired after STN neurons and selectively in response to stop signals, rather than to both go and stop signals. The timing of their activity was consistent with precipitating the sudden decline in striatal 'go' activity. Together, these findings provide further evidence of the role of the basal ganglia in action-stopping and specifically implicate an arkypallidostriatal pathway.

Conflict resolution
In the motor domain, the process of resolving competition between competing action plans.

Go–no-go task
A paradigm where the participant is required to perform speeded responses to a go cue and to withhold a response following a no-go cue.

Global motor system suppression
Suppression of motor system excitability detected in task-irrelevant muscle representations when stopping with another effector. Relies on transcranial magnetic stimulation and electromyography methods.

Premanifest Huntington disease
The presymptomatic phase of the disease in an individual carrying the genetic mutation causing it.

Agonist muscle
The muscles that, when activated, are primarily responsible for causing movement about a joint.

The above 'pause-then-cancel' model could unify differing accounts of STN and striatal involvement in stopping, and is consistent with the idea of the STN acting to delay actions in situations of response conflict[54,55,90] or surprise[53,91,92] (see Unexpected events). The fast but brief pause may buy time for deliberation on what (or what not) to do. This could allow actions deemed inappropriate to be cancelled selectively, and actions deemed appropriate to resume after only a short delay[87].

However, the pause-then-cancel model of action-stopping is less complete than the classic model. For example, we do not know which brain regions drive the rodent arkypallidal cells during stopping[87] and, to date, there are no comparable data from arkypallidal cells in humans or non-human primates. Furthermore, human and non-human primate data concerning the temporal flow of activity across brain regions (FIG. 2) are inconsistent with a pause-then-cancel model. First, activity in the PFC[15,27,31,36,50] and the STN[63,65,70] on stop trials occurs substantially later than the STN response in rodents[88,89]. Second, the interval between STN activity and the first behavioural sign of stopping (that is, cancellation of muscle activity) seems very short in humans and non-human primates, unlike in rodents, leaving little room to incorporate a pause. Presently, the classic action-stopping model best explains the human and non-human primate data, and therefore we focus on this model hereafter.

Beyond the stop signal task

Most studies have examined the stopping of simple, discrete actions, such as button presses, within the context of stop signal tasks (level 1 in TABLE 1). However, action-stopping is probably relevant to various human activities, from speaking to walking. Little is known about how action control emerges in these diverse settings, but we suppose that it could sometimes engage the action-stopping network. We now review studies that have begun to examine the stopping of more naturalistic actions, although often still within the context of stereotyped laboratory experiments (levels 1 and 2 in TABLE 1).

Speech. Effective verbal communication relies on fine motor control, including the ability to interrupt speech at any time. Speech is an interesting case because whereas the rIFC has been implicated in the stopping of manual and saccadic actions, the homologous lIFC (also known as Broca's area) has been strongly implicated in the programming of speech[93,94]. Speech production also requires timely control across facial, throat, tongue and respiratory muscles. Control can be directed to any or all of them to influence what sounds are made.

The fact that stopping latencies for speech (for example, when producing a syllable) and manual responses correlate with one another across participants indirectly points to a common neural mechanism[95]. Successful stopping of speech activates the rIFC and the pre-SMA[95], and is associated with similar PFC beta-band activity[96] and STN beta-band activity[97] as stopping manual responses. Moreover, stopping speech produces a global suppression of the motor system[83] that correlates with elevated STN beta-band activity[64]. Possible causal evidence for the involvement of the stopping network has been provided in the form of cessation of speech and manual actions during intraoperative stimulation of the pre-SMA and the rIFC and the lIFC[98–100]. Although stimulation of the IFC in either hemisphere can disrupt speech, it might do so for different reasons: depending on the mode of stimulation and task requirements,

Table 1 | **Degrees of real-world applicability in stopping experiments**

Level	Stopping context	Environment	Action
1	Stop signal task (for example, involving explicit stop cues, such as an arrow turning red)	Highly controlled laboratory setting Repeated trials Stopping can be somewhat anticipated	Simple (for example, involving a single joint or minimal coordination) Contrived (for example, a key press) Discrete Cued
2	Variants of stopping tasks (for example, with stop cues that are more naturalistic, such as an obstacle in the participant's path)	Highly controlled laboratory setting Repeated trials Stopping can be somewhat anticipated	Complex (for example, multijoint or multilimb, or complex coordination) Somewhat naturalistic (for example, speaking or stepping) Discrete Cued
3	Virtual reality or simulated (for example, with stop cues that are again more natural, such as a virtual car braking suddenly in front of the participant while 'driving')	Less constrained laboratory setting Less repetitious trials or events Stopping cannot be easily anticipated	Complex Naturalistic (for example, walking, driving or semi-structured conversation) Discrete or continuous Self-paced
4	Real-world (for example, with stop cues that are entirely natural, resulting from changes in the environment around the participant)	Unconstrained, real-world setting Non-repetitive, truly novel trials and events Stopping is entirely unpredictable	Complex Naturalistic Discrete or continuous Self-paced

Gait
The normal pattern of limb movements underpinning locomotion.

rIFC stimulation could activate the stopping network ('stop'), whereas lIFC stimulation could disrupt the programming of speech ('go').

Stopping of speech and stopping of manual actions seem to rely on similar neural substrates, although further work could be done to demonstrate that this holds true for production of words and sentences, not just of letters or syllables, and for natural communicative contexts.

Gait and balance. Successful gait and balance depend on effective coordination between limb and trunk muscles. The stopping of gait is interesting because it does not entail a complete cessation of all leg or postural muscle activity, but instead often requires a corrective response, such as stepping to maintain balance or to avoid an obstacle. In other words, it often requires switching to another action (BOX 1), rather than simply cancelling the current one, and therefore poses new challenges to the study of action-stopping (such as knowing when and whether a stop occurs during a seemingly continuous action).

Gait and postural control are achieved via the integration of descending outputs from multiple brain systems (including the cortex and the mesencephalic locomotor region) at the level of the spinal cord[101]. Cortico–basal ganglia circuits are thought to have an important role in gait control, particularly when challenging environments demand greater voluntary control[101]. An open question is whether, for example, stopping to avoid unexpected obstacles while walking relies on similar PFC–basal ganglia circuits as those recruited during manual stopping (perhaps with the inclusion of outputs from the STN and GPi/SNr directly to the mesencephalic locomotor region[101]).

The involvement of the basal ganglia in gait is well established. Recent animal experiments involving cell-specific and circuit-specific optogenetic stimulation and calcium imaging have confirmed that activity in the striatum[102], SNr[103], STN and GPe regulates locomotion[104]. In addition, individuals with Parkinson disease often experience problems with gait[105] (see Freezing of gait), and recent local field potential recordings from the STN of such individuals have implicated this region in the regulation of stepping[106]. Future work could directly examine whether the STN is implicated in the stopping of gait.

Several studies now point to the recruitment of global stopping or brake-like mechanisms when gait or balance is disturbed. In one study, participants made voluntary steps to visually presented targets on the floor[107]. In 25% of trials, shortly after participants had initiated a step, a 'jump' of the target to a different location required them to step to the new target instead. The initial reaction to the target jump was a brief reduction in the body's forward acceleration. This 'braking' effect occurred within about 250 ms after the target jump, similar to the SSRT of manual responses, and regardless of whether doing so was helpful (that is, regardless of whether the target jump required a decrease or an increase in step length). Similar non-specific braking effects have been observed in leg muscle activity[108], and would presumably be present in postural (trunk) muscles too, as these are thought to generate the initial momentum of the body when stepping[107]. Another study noted a global motor system suppression when participants attempted to prevent a corrective step after a postural perturbation[109]. The same group found that participants with a shorter manual SSRT showed a greater reduction of leg muscle activity when stopping a corrective step[110], implying that action-stopping measured in simple laboratory tasks is a generalizable capability. Last, recent research in rodents using optogenetics and calcium imaging implicated a dmPFC–STN pathway as being important for visually directed stopping of locomotion[111].

Together, these initial studies suggest potential for overlap in the neural systems for stopping manual actions and gait or postural actions.

Automatic bodily functions. Breathing and blinking are typically 'automatic' actions that can temporarily be brought under voluntary control (for example, when holding breath under water). The suppression of blinking[112,113], coughing[114,115], breathing[116] and the impulse to remove oneself from a noxious stimulus[117] all activate nodes of the stopping network, including the pre-SMA, rIFC, striatum and pallidum. Notably, the pre-SMA and striatum are also more active during deliberately slow, paced breathing[118], which could be interpreted as evidence for a 'braking' role of these regions in the control of breathing.

An open question with these studies is whether the brain activations reflect an actively suppressive mechanism or another process related to the discomfort, difficulty or attentional demands associated with the task. Some evidence corroborates the motor suppression account. First, the 'urge' to act seems to grow with continued suppression[113,115], implicating an inhibitory mechanism in preventing expression of the action. Second, we recently showed that suppressive processes, in the form of GABAergic inhibition and beta-band oscillations, were present in the sensorimotor cortex while suppressing an action that would relieve pain[119]. Third, despite a lack of causal evidence in humans, slowing and complete cessation of breathing have been found following stimulation of the lateral PFC in primates[120].

A notable absentee in the fMRI literature on control of automatic bodily functions is the STN, perhaps because experiment set-ups have not been well suited to monitor activity in such a small structure[57]. One might also ask why an STN-mediated system for reactive stopping would be recruited when there is no external signal calling for an immediate stop. This is pertinent because some have proposed a distinction between externally and internally triggered stopping[117,121]. However, in many cases, the distinction may be blurred, because individuals might use internal sensations, such as a tickly throat, as a proxy external signal to trigger stopping. Furthermore, neuroimaging indicates that both forms of stopping recruit a largely overlapping network of prefrontal structures[117,121].

Overall, neuroimaging data seem to highlight a potential overlap in the control of manual actions and automatic bodily functions, but various caveats and a lack of causal evidence prompt further study.

Kohnstamm phenomenon
A long-lasting (10–60-s) involuntary muscle contraction that develops after a sustained, voluntary isometric contraction: after pushing your arm against a wall for a long period, you experience your arm rising.

Antagonist muscles
The muscles that, when activated, oppose the movement caused by the agonist muscles about a joint.

Tonic control. Stopping tasks focus on the control of brief 'urges' or 'drives' to act but, as we have just seen, some can persist and grow over time. These range from benign urges to scratch an itch, to pathological ones associated with motor tics or compulsive skin-picking[122]. How do we deal with protracted urges? Some urges wax and wane, so one possibility is that action-stopping is applied briefly and repeatedly to stop them whenever they cross some threshold. For constant urges, however, the stopping mechanism could be used tonically for periods of seconds or more. Indeed, the aforementioned work on suppressing pain-relieving actions suggested that the motor inhibitory processes persisted for several seconds[119].

A clear example of tonic inhibitory control over actions comes from a study of the Kohnstamm phenomenon[123]. The Kohnstamm phenomenon involves brain regions implicated in voluntary control, including M1 (REFS[124,125]), and although it feels involuntary[126], it can be brought under voluntary control without recruiting antagonist muscles[124,126]. This implies that a stop process is recruited to suppress ongoing motor output. The mechanisms of such control remain unexplored. However, attempts to stop one arm from rising following the induction of Kohnstamm movements in both arms sometimes results in a brief interruption of both limbs, suggesting that a global stopping mechanism (that is, with a somatotopically broad focus) akin to that in the stop signal task is initially recruited[126].

Studying the neurophysiological correlates of Kohnstamm suppression could reveal the mechanisms underlying tonic control of involuntary actions in health and disease (see Tics).

Unexpected events. Unexpected events result from changes in our environment (such as a door slamming) or our own actions (for example, mispronouncing a word). They have a surprising quality that interrupts ongoing action and thought. A recent theory suggested that unexpected-event-induced interruptions recruit a network similar to that recruited by outright action-stopping[9]. For example, an earlier study showed that unexpected sounds elicited a global motor system suppression at around 150 ms (similar to stop signals; FIG. 2) and slowed motor responding[127].

Recent studies have built on this idea. One showed that unexpected sounds presented after a 'no go' signal not only increased stopping success, pointing to an overlapping process, but were also associated with enhanced activity of the action-stopping network, as indexed by EEG and TMS-induced EMG signals[128]. Meanwhile, unexpected events in a rodent study disrupted licking, just as optogenetic activation of the STN did[53]. Importantly, optogenetic inactivation of the STN blunted this effect of unexpected events, providing strong evidence for a causal role of the STN in surprise-induced interruptions.

So far, a picture is emerging whereby motor interruptions prompted by unexpected events recruit a system analogous to that used in voluntarily stopping actions, albeit by pausing rather than stopping outright. This suggests that the system may be recruited automatically or voluntarily to partially or fully interrupt actions, although this idea awaits further verification. The emerging picture also indirectly speaks to a long-running debate about the specificity of rIFC activation[19,35,129,130]. Previous neuroimaging showed that infrequent cues that do not require stopping still recruited the rIFC, questioning whether rIFC activation in stopping tasks reflected a stop process[131]. In light of the literature on unexpected events, it is plausible that those infrequent cues recruited motor inhibitory processes triggered by an rIFC–STN pathway, which would explain the slowing of responses.

From laboratory to real world

Despite being preliminary in most cases, the evidence presented so far suggests that the scope of the action-stopping model could extend beyond the standard task. Yet those examples still rely on contrived experimental paradigms where the same stopping demands are encountered repeatedly. Examining real-world stopping was recently made possible by technological advances in wearable MEG devices[132] and near-infrared spectroscopy[133]. In addition, new devices being used in individuals being monitored or treated for various disorders can provide stable, long-term intracranial neural recordings and controlled brain stimulation, and have been integrated with wireless scalp EEG devices and gaze or motion tracking devices for concurrent neurophysiological and behavioural evaluation during free movement[134].

A challenge as we move towards real-world scenarios is knowing in any given moment whether behavioural stopping has occurred. It might be tempting to rely on indirect markers, such as right prefrontal beta-band activity. However, this runs the risk of reverse inference[135]; that is, assuming that similar neural correlates observed in one context (such as walking) reflect the same mental processes identified in another (such as the stop signal task). One way to minimize this risk would be to adopt a programmatic approach (FIG. 3). For example, following on from the aforementioned gait and stepping studies (level 2 in TABLE 1 and FIG. 3), one could progress to evaluating stopping and its neural correlates during unconstrained gait in a virtual reality setting, where naturalistic events in the visual scene might cause someone to stop (level 3 in FIG. 3). The question then is whether those moments rely on the same neural substrates as stopping in the simpler laboratory tasks. If so, event-related brain stimulation could be used to disrupt prefrontal or basal ganglia processing and provide causal evidence for their involvement, for example by having an individual receive stimulation around the time of a door closing in front of them. This virtual world investigation would then provide motivation for fully real-world studies of gait as people walk around their neighbourhoods (level 4 in FIG. 3).

A similar approach could be used to study driving, beginning with simple manual stop signal tasks (level 1) and progressing to reaching-and-grasping tasks (level 2). One could then envisage individuals with wearable MEG devices or scalp EEG devices or patients with intracranial EEG devices sitting in driving simulators with gaze

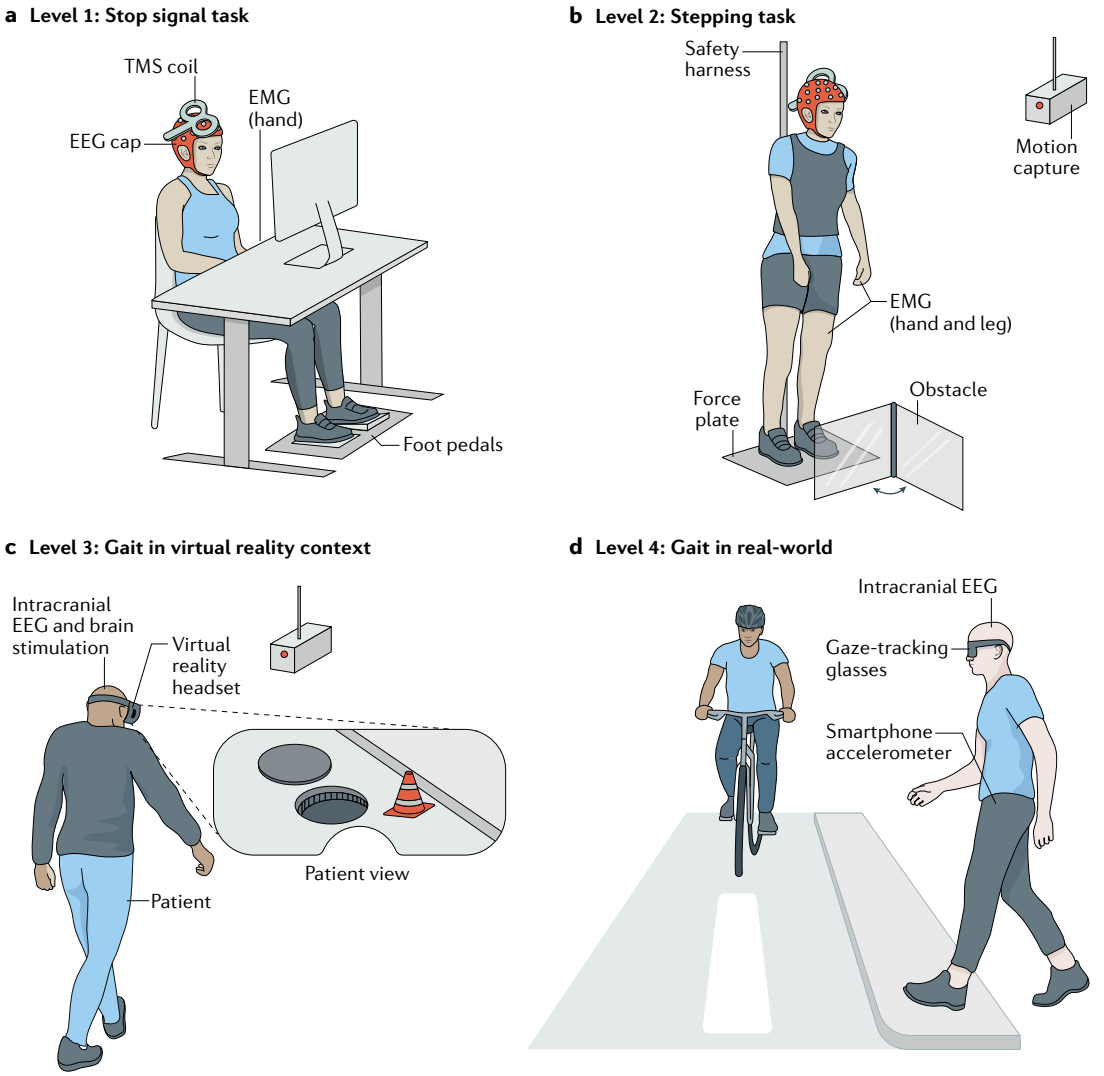

Fig. 3 | **From the laboratory to the real-world: gait. a** | A research programme might begin by studying stopping in the laboratory with the stop signal task (level 1 in TABLE 1), using the primary effectors involved in the high-level behaviour of interest — in this case, the legs. Neurophysiological techniques can be used to look for the neural correlates of stopping, such as beta-band activity in the right prefrontal cortex measured using electroencephalography (EEG) and global motor system suppression measured using transcranial magnetic stimulation (TMS) and electromyography (EMG; here, on the task-unrelated hand muscle). **b** | One could then progress to more complex and naturalistic actions, but still within a highly constrained laboratory setting (level 2 in TABLE 1). In this example, the participant is instructed to perform simple stepping actions. On some trials, an obstacle suddenly appears, requiring the participant to prevent the step. Here, EEG and TMS could be used alongside EMG, force plates and motion-capture imaging, which provide behavioural readouts of action-stopping. **c** | The next step might involve free-moving and naturalistic gait while individuals explore virtual environments. Use of wearable EEG devices, in this case an intracranial device implanted in a patient for recording and stimulating the brain, could be combined with motion tracking[134] (level 3 in TABLE 1). Numerous situations could conceivably involve action-stopping: an open manhole, another person crossing one's path or a door closing. Sudden body or limb decelerations time-locked to the events in the visual scene would provide indices of behavioural stopping, such as the latency of stopping, and would provide a time window in which to look for neural correlates of stopping. **d** | Finally, one might approach real-world studies, as people explore their normal environments. Here, use of wearable EEG devices in patients could be combined with gaze tracking[134] and smartphone-based accelerometry[176] to examine similar instances in which the stopping network might be recruited (level 4 in TABLE 1).

tracking and measurements of steering, acceleration and braking enabling the quantification of behaviour (level 3). Here, seeing a car in your blind spot as you begin changing lanes might cause you to interrupt the planned turning of the steering wheel. Similar events could then be studied in real cars with use of wearable EEG devices combined with gaze and motion tracking (level 4).

Even with this programmatic approach, there remains an important issue that may affect the extension of the stopping literature to the real world. Although the standard stop signal task purports to measure reactive stopping, it still involves some anticipatory slowing of responses on trials where no stop signal is presented — response times are longer than in a choice reaction time

task[136] and increase with the likelihood of needing to stop[137]. Yet, how common is anticipatory slowing in the real world? When driving, you might anticipate having to reduce pressure on the accelerator as you approach traffic lights; however, the need to stop or brake cannot always be predicted. Although unexpected-event paradigms have been developed as a response to this criticism, the events are still encountered many times in a study. An alternative might be to study one-off events[138], but these are not amenable to studying the neural correlates of behaviour, which are unreliable at the single-trial level. It may also be difficult to dissociate direct sensory effects on behavioural interruption (for example, see REF.[139]), akin to a 'startle', from recruitment of the stopping network. A challenge, therefore, is to understand whether, and to what extent, the mechanisms of stopping differ when the need to do so is anticipatable versus completely unexpected.

Movement disorders

We now turn to whether variation in the functioning of the action-stopping network underlies clinical problems. Dysfunctional PFC–basal ganglia networks have been proposed to contribute to the symptoms experienced by patients with movement and psychiatric disorders[11,12,122]. Although these issues have been reviewed extensively[11,12,122], the focus has been either on psychiatric symptoms (such as impulsivity) where the theoretical and empirical link between real-world behaviour and action-stopping is often poorly defined or weak[140] or on various motor symptoms that do not all fit within the action-stopping framework. Here we focus specifically on movement disorder symptoms that have a more direct conceptual link with action-stopping.

Stuttering. Stuttering is characterized by periods of silence, sound prolongations and sound or syllable repetitions. Although there is no single cause thought to underlie stuttering, these symptoms might sometimes reflect an aberrant stopping mechanism. Such a mechanism could prematurely interrupt an ongoing motor programme or inhibit successive motor programmes that relate to the next syllable[141].

The fact that stopping of manual responses is impaired in people who stutter[142–144] suggests there may be a dysfunction in the action-stopping network at a higher level in the brain than the motor output. Recent meta-analysis of fMRI studies has confirmed an earlier suggestion[145] of a right-lateralized hyperactivity, including in the right pre-SMA and rIFC, during speech in people who stutter compared with those who do not, and in dysfluent versus fluent speech[146]. Stuttering severity was also recently shown to correlate with structural connectivity in the right frontal aslant tract between the hyperactive pre-SMA–SMA and the rIFC[141]. Although this right-hemisphere hyperactivity could be explained in several ways — for example, as a compensatory adaptation to the left hemisphere-induced dysfluency[147,148] — it could indeed reflect an aberrant action-stopping system. Future studies combining detailed psychophysical evaluations of dysfluent speech (for example, characterizing the precise timing of speech interruptions) with examination of the neural correlates of stopping using high temporal resolution methods could clarify the putative role of the stopping network in stuttering. One prediction is that periods of stuttering are accompanied by a global motor system suppression and elevated beta-band power in the right PFC. Another prediction is that disruption of the hyperactive rIFC or pre-SMA with TMS during dysfluent speech might temporarily restore fluent speech.

Tics. Tics are sudden, involuntary movements or vocalizations that are contextually inappropriate. Tic generation is thought to be due to activation of a dysfunctional corticostriatal pathway[149,150]. This results in the release of stereotyped movements that would normally be prevented by tonic inhibitory output from the GPi/SNr. Tics therefore seem more a problem with action-initiation than action-stopping per se. Accordingly, a meta-analysis showed that the stopping of voluntary actions in people with tics, at least those without co-morbid disorders such as attention deficit hyperactivity disorder, is comparable to that in people without tics[151].

Although tics may not arise from a problem with action-stopping, stopping may be relevant for how tics are controlled. Indeed, a defining characteristic of tics is that they can often be temporarily suppressed by volition[152]. Moreover, new research shows that the ability to suppress tics early in childhood is negatively correlated with tic severity in the future[153]. Understanding tic suppression is therefore clinically relevant[154].

The notion of 'suppressing' a tic might only be a metaphor; however, it could also actually reflect an action-stopping mechanism that prevents aberrant motor drive[155]. This fits with the observation that suppressing a tic does not usually abolish the urge to tic[156]. Evaluating whether tic suppression does actually recruit an action-stopping system requires neuroscience studies. Although imaging has implicated some regions of the PFC (including the rIFC, lIFC, pre-SMA and dorsolateral PFC), along with the striatum and the pallidum, in tic suppression[112,157,158], activation of these regions is not specific enough to a particular process to be sure. Causal brain stimulation studies may therefore be useful here.

A notable TMS study showed global motor system suppression during bouts of sustained, voluntary tic suppression compared with when participants were allowed to make tics freely[155]. This result is compatible with action-stopping, although it has also been shown that when patients voluntarily suppress tics, they can perform simple motor tasks with other effectors[159]. Overall, there is a hint that action-stopping is relevant in control of tics, but it is not definitive, and there are open questions about how global or selective the action-stopping mechanism used to control them might be.

Freezing of gait. Parkinson disease is characterized by various motor symptoms, including absent or slowed movements, tremor, rigidity and gait disturbances. Although many of these can potentially be broadly attributed to excitation–inhibition imbalance in basal ganglia circuits[122], the mechanisms underlying the motor symptoms are likely to be manifold. One instance where

the stopping network may be applicable is in the freezing of gait — a temporary and involuntary slowing or stopping[105]. The triggers include turning, approaching narrow passages, distraction and cognitive load or stress[160]. A recent theory proposes that all these triggers engender a form of conflict (sensory–motor, affective or cognitive)[161]. Normally, conflict, such as that between response options, is proposed to trigger hyperdirect inputs from the PFC to the STN to 'apply the brakes' and aid in conflict resolution. However, in Parkinson disease, dysfunction of this pathway is proposed to lead to freezing.

Preliminary evidence supports this idea. An EEG study with participants with Parkinson disease found that, compared with normal walking, freezing episodes were associated with elevated theta-band activity over frontocentral electrodes[162], a common signature of response conflict[37]. Another showed that (frontocentral) cortico–STN coupling in the theta band or the alpha band was reduced during freezing[163], consistent with dysfunction of the hyperdirect pathway. An innovative fMRI study using a virtual reality stepping paradigm, with visual cues designed to induce freezing, provided complementary evidence: freezing-like behaviour, in the form of prolonged stepping latencies when approaching doorways, was associated with impaired pre-SMA–STN connectivity[164].

Box 2 | **Neural bases of action-stopping: open questions and controversies**

A body of literature supports the idea of a prefrontal cortex–basal ganglia–thalamocortical network being crucial for action-stopping. Yet this support is not without challenge, and there remain a number of open questions about the precise anatomy, physiology and function of the network.

- Is action-stopping a unitary process enacted solely via the hyperdirect pathway, or does it entail a hyperdirect pathway-mediated 'pause' followed by a striatally mediated 'stop'?
- Are the global effects of reactive stopping on the motor system attributable to the subthalamic nucleus (STN), and does this reflect an anatomical system with truly broad STN-to-pallidum connectivity?
- Recent computational modelling suggests that a failure to stop can occur because the process was triggered too late or else because it was not triggered at all ('trigger failures')[14]. This implies that behavioural stopping can be dissociated into different processes — the trigger for control, and the actual brake — and is relevant to the ongoing debate about different functions of different prefrontal brain regions during stopping[19,35,129,130]. Does this distinction map onto the right inferior frontal junction for attentional capture and triggering of the control process, and the pars opercularis for the control?
- Is there a mechanistic link between beta-band oscillations in the stopping network and action-stopping, or are these oscillations epiphenomenal? Although evidence is accumulating to support a possible role for beta-band oscillations in action-stopping[15,31,50,64,119], some work has questioned its functional relevance[36,51].
- Does prefrontal beta-band activity locate predominantly to the right inferior frontal cortex or the pre-supplementary motor area? Electrocorticography has implicated both regions[27]. However, most electroencephalography and magnetoencephalography studies have emphasized the importance of the right prefrontal cortex[15,31,32,34], with only few neurophysiological studies focusing on the medial prefrontal cortex[50,51].
- How does right prefrontal beta-band activity stand up against other neurophysiological correlates of stopping? The P300 event-related potential detected over frontocentral electrodes has been proposed as a sensitive marker of the stop process[185,186]. However, questions have been raised about whether its onset latency (typically >225 ms) is too long for it to contribute to stopping[15] and whether it is specific enough to stopping[15,187]. This contrasts with right prefrontal beta-band activity, which increases specifically on stop trials and occurs before the cancellation of muscle activity[15,31,32].

A recent review of many neurophysiological studies suggested that there are dissociable PFC–basal ganglia networks for processing conflict (that is, serving to pause action by raising the threshold of evidence needed for a decision) versus for action-stopping, and that these are characterized by low-frequency oscillations and beta-band activity, respectively[37]. The aforementioned studies on freezing of gait pointed to low-frequency oscillations, consistent with freezing of gait being attributable to disruptions in conflict processing. However, a recent study found increases in both STN low-frequency and beta-band oscillatory power during freezing behaviour[165]. Thus, it seems possible that the conflict system initially slows gait and the stopping system suspends it entirely during freezing episodes.

Experimental paradigms that use virtual reality to prompt different responses could be used to test these ideas and to test whether freezing is associated with other neurophysiological correlates of stopping network activity, such as the global motor system suppression[166].

Conclusions

Research in different species over the past few years supports key claims of the originally described action-stopping model, and goes further. The rIFC (especially the ventral pars opercularis) is crucial for stopping, and is functionally and structurally connected to the ventral STN, apparently by a hyperdirect pathway; activity of the rIFC precedes that in the STN, and the putative signature of STN function is global motor system suppression that precedes the cancellation of muscle activity, which in turn precedes the SSRT. Although several open questions about this model remain (BOX 2), we feel the neural basis is well-enough established to turn now to the important question of ecological validity.

Here we have considered behaviours at increasing levels of real-worldness. First, we summarized laboratory research on speech, gait, tonic control, automatic bodily functions and unexpected events. In each case, there are various levels of evidence showing that similar brain regions are activated, or neurophysiological signatures are elicited. However, given the problem of reverse inference, future work should seek causal evidence that these regions are important for stopping in each context. Second, we considered possible studies, beyond the laboratory, that could take advantage of technical advances in the recording and perturbation of neural activity in freely moving participants. These studies would put the generalizability of the action-stopping network to a serious test: asking whether the recruitment of a PFC–STN hyperdirect pathway really does occur outside repetitive trials of simple, discrete and prescribed actions.

We highlighted specific instances where the stopping network could be involved in the generation of, or compensation for, motor symptoms of movement disorders. Current evidence is strongest for the freezing of gait in Parkinson disease, in which neuroimaging indicates the importance of pre-SMA–STN function, although there remains a good case for further exploring the role of the stopping network in stuttering and tic

Box 3 | **Questions about the wider applicability of the action-stopping network**

The putative action-stopping network was developed on the basis of neuroscience studies performed in the laboratory using simple, often manual, stopping tasks and is assumed to generalize broadly to other actions and behavioural contexts. The questions here may guide research aimed at testing this assumption.

- Is the reactive stopping network recruited to stop naturalistic actions such as walking or speaking, and can we demonstrate this in real-world settings (such as when having a conversation)?
- Does the behaviourally selective stopping of complex, multicomponent actions (such as stopping throwing a ball while continuing to run) involve a selective or global mechanism? How does one toggle the switch between selective and global stopping?
- How is the stop process of dynamic, inertial movements coordinated across agonist and antagonist muscles about a joint to allow concomitant suppression and activation that presumably act to brake limb motion?[188]
- Is the stopping network recruited to exert tonic control over persistent movement 'urges' or 'drives', or is it recruited phasically and repeatedly whenever such drives or urges reach some critical threshold?
- Does the voluntary suppression of motor tics rely on the suppression of motor output via the action-stopping network?
- Does stuttering reflect the inappropriate recruitment of the stopping network that interrupts speech, or a compensatory response to aid in the regulation of already dysfluent speech?
- Does freezing of gait reflect the inappropriate recruitment of the stopping network triggered by internally or externally triggered conflict?

control (BOX 3). Although we have not explored the role of the action-stopping network in psychiatric disorders in this Review, some recent results point to the engagement of a stopping system in preventing unwanted thought intrusions[167,168]. This suggests a common process for stopping action and thought, consistent with a long-standing model[3,169]. The potential extension of the action-stopping network to blocking long-term memory retrieval[169], current working memory[91] and, more generally, in thought control is intriguing and would benefit from more study. It has high relevance for understanding intrusive thinking[170], particularly in clinical disorders.

We focused on the rapid action-stopping network. There are, however, other modes of inhibitory control that may engage slightly different pathways (BOX 1). Fully discussing those other modes with regard to naturalistic behaviour is beyond the scope of this Review; our aim was to focus on the simple action-stopping mode as the best-developed case. We see hints that this action-stopping network is engaged in myriad other contexts, however.

A final point about ecological validity concerns the relation between SSRT and other behavioural metrics. SSRT, like many measures of executive function[140], relates only weakly to self-reported measures of real-world self-control[140]. How can we reconcile this with the proposal that the rapid action-stopping system might underpin many moments of everyday life? We suggest that the speed of stopping may not be as important as whether and when stopping is triggered. Indeed, recent work using a new mathematical model of behaviour during the stop signal task estimated the frequency of failures to trigger the stop process, and found this to be better correlated with measures of behavioural impulsivity (such as delay aversion) than SSRT[171]. However, when real-world stopping demands speed (for example, for fast corrections of gait or balance), we would expect to see a closer relationship between behavioural stopping latency or success and SSRT[110].

The simple stop signal paradigm was launched by Logan and Cowan in 1984 (REF.[5]) on the basis that it was a model for the stopping of action and thought. Nearly 40 years later, with considerable information about the brain regions, circuits and neurophysiological signatures of action-stopping, the time has come to assess whether the action-stopping model is mostly an artefact of the laboratory setting or a core function of everyday life.

Published online: 29 July 2021

1. Diamond, A. Executive functions. *Annu. Rev. Psychol.* **64**, 135–168 (2013).
2. Miyake, A. et al. The unity and diversity of executive functions and their contributions to complex "frontal lobe" tasks: a latent variable analysis. *Cognit. Psychol.* https://doi.org/10.1006/cogp.1999.0734 (2000).
3. Guo, Y., Schmitz, T. W., Mur, M., Ferreira, C. S. & Anderson, M. C. A supramodal role of the basal ganglia in memory and motor inhibition: meta-analytic evidence. *Neuropsychologia* **108**, 117–134 (2018).
4. Verbruggen, F. et al. A consensus guide to capturing the ability to inhibit actions and impulsive behaviors in the stop-signal task. *eLife* **8**, e46323 (2019).
5. Logan, G. D. & Cowan, W. B. On the ability to inhibit thought and action: a theory of an act of control. *Psychol. Rev.* **91**, 295–327 (1984).
6. Sebastian, A. et al. Disentangling common and specific neural subprocesses of response inhibition. *NeuroImage* https://doi.org/10.1016/j.neuroimage.2012.09.020 (2013).
7. Sebastian, A. et al. Differential effects of age on subcomponents of response inhibition. *Neurobiol. Aging* https://doi.org/10.1016/j.neurobiolaging.2013.03.013 (2013).
8. Raud, L., Westerhausen, R., Dooley, N. & Huster, R. J. Differences in unity: the go/no-go and stop signal tasks rely on different mechanisms. *NeuroImage* **210**, 116582 (2020).
9. Wessel, J. R. & Aron, A. R. On the globality of motor suppression: unexpected events and their influence on behavior and cognition. *Neuron* **93**, 259–280 (2017).
10. Aron, A. R. From reactive to proactive and selective control: developing a richer model for stopping inappropriate responses. *Biol. Psychiatry* **69**, e55–e68 (2011).
An earlier influential review of the literature on different modes of action control and their putative neural bases.
11. Chambers, C. D., Garavan, H. & Bellgrove, M. A. Insights into the neural basis of response inhibition from cognitive and clinical neuroscience. *Neurosci. Biobehav. Rev.* **33**, 631–646 (2009).
12. Bari, A. & Robbins, T. W. Inhibition and impulsivity: behavioral and neural basis of response control. *Prog. Neurobiol.* **108**, 44–79 (2013).
13. Bissett, P. G., Jones, H. M., Poldrack, R. A. & Logan, G. D. Severe violations of independence in response inhibition tasks. *Sci. Adv.* **7**, eabf4355 (2021).
14. Matzke, D., Love, J. & Heathcote, A. A Bayesian approach for estimating the probability of trigger failures in the stop-signal paradigm. *Behav. Res. Methods* **49**, 267–281 (2017).
15. Jana, S., Hannah, R., Muralidharan, V. & Aron, A. R. Temporal cascade of frontal, motor and muscle processes underlying human action-stopping. *eLife* **9**, e50371 (2020).
A multimodal neurophysiological study providing motivation for the temporal 'flow' model of processing throughout the stopping network in humans.
16. Smittenaar, P., Guitart-Masip, M., Lutti, A. & Dolan, R. J. Preparing for selective inhibition within frontostriatal loops. *J. Neurosci.* **33**, 18087–18097 (2013).
17. Wildenberg, W. P. M., van den, Burle, B., Vidal, F., Molen, M. W. van der & Ridderinkhof, K. R. Mechanisms and dynamics of cortical motor inhibition in the stop-signal paradigm: a TMS study. *J. Cogn. Neurosci.* **22**, 225–239 (2009).
18. Aron, A. R., Behrens, T. E., Smith, S., Frank, M. J. & Poldrack, R. A. Triangulating a cognitive control network using diffusion-weighted magnetic resonance imaging (MRI) and functional MRI. *J. Neurosci.* **27**, 3743–3752 (2007).
19. Aron, A. R., Robbins, T. W. & Poldrack, R. A. Inhibition and the right inferior frontal cortex: One decade on. *Trends Cognit. Sci.* **18**, 177–185 (2014).
20. Aron, A. R. & Poldrack, R. A. Cortical and subcortical contributions to stop signal response inhibition: role of the subthalamic nucleus. *J. Neurosci.* **26**, 2424–2433 (2006).
21. Konishi, S., Nakajima, K., Uchida, I., Sekihara, K. & Miyashita, Y. No-go dominant brain activity in human inferior prefrontal cortex revealed by functional magnetic resonance imaging. *Eur. J. Neurosci.* https://doi.org/10.1046/j.1460-9568.1998.00167.x (1998).
22. Konishi, S. et al. Common inhibitory mechanism in human inferior prefrontal cortex revealed by event-related functional MRI. *Brain* https://doi.org/10.1093/brain/122.5.981 (1999).
23. Garavan, H., Ross, T. J. & Stein, E. A. Right hemispheric dominance of inhibitory control: An event-related functional MRI study. *Proc. Natl Acad. Sci. USA* **96**, 8301–8306 (1999).
24. Aron, A. R., Fletcher, P. C., Bullmore, E. T., Sahakian, B. J. & Robbins, T. W. Stop-signal inhibition disrupted by damage to right inferior frontal gyrus in humans. *Nat. Neurosci.* **6**, 115–116 (2003).
A classic study of patients with brain lesions showing that the rIFC is crucial for action-stopping.

25. Chambers, C. D. et al. Executive "brake failure" following deactivation of human frontal lobe. *J. Cognit. Neurosci.* **18**, 444–455 (2006).
26. Verbruggen, F., Aron, A. R., Stevens, M. A. & Chambers, C. D. Theta burst stimulation dissociates attention and action updating in human inferior frontal cortex. *Proc. Natl Acad. Sci. USA* **107**, 13966–13971 (2010).
27. Swann, N. C. et al. Roles for the pre-supplementary motor area and the right inferior frontal gyrus in stopping action: electrophysiological responses and functional and structural connectivity. *NeuroImage* **59**, 2860–2870 (2012).
28. Madsen, K. S. et al. Response inhibition is associated with white matter microstructure in children. *Neuropsychologia* **48**, 854–862 (2010).
29. Bartoli, E., Aron, A. R. & Tandon, N. Topography and timing of activity in right inferior frontal cortex and anterior insula for stopping movement. *Hum. Brain Mapp.* **39**, 189–203 (2018).
30. Suda, A. et al. Functional organization for response inhibition in the right inferior frontal cortex of individual human brains. *Cereb. Cortex* **30**, 6325–6335 (2020).
31. Hannah, R., Muralidharan, V., Sundby, K. K. & Aron, A. R. Temporally-precise disruption of prefrontal cortex informed by the timing of beta bursts impairs human action-stopping. *NeuroImage* https://doi.org/10.1016/j.neuroimage.2020.117222 (2020).
32. Sundby, K. K., Jana, S. & Aron, A. R. Double blind disruption of right inferior frontal cortex with TMS reduces right frontal beta power for action-stopping. *J. Neurophysiol.* https://doi.org/10.1152/jn.00459.2020 (2020).
33. Swann, N. et al. Intracranial EEG reveals a time- and frequency-specific role for the right inferior frontal gyrus and primary motor cortex in stopping initiated responses. *J. Neurosci.* **29**, 12675–12685 (2009).
34. Schaum, M. et al. Right inferior frontal gyrus implements motor inhibitory control via beta-band oscillations in humans. *eLife* **10**, 1–28 (2021).
35. Swick, D. & Chatham, C. H. Ten years of inhibition revisited. *Front. Hum. Neurosci.* **8**, 115–116 (2014).
36. Chen, W. et al. Prefrontal-subthalamic hyperdirect pathway modulates movement inhibition in humans. *Neuron* **106**, 579–588.e3 (2020).
A study in individuals with Parkinson disease supporting the existence of a functional connection between the rIFC and the STN that is relevant to stopping.
37. Aron, A. R., Herz, D. M., Brown, P., Forstmann, B. U. & Zaghloul, K. Frontosubthalamic circuits for control of action and cognition. *J. Neurosci.* **36**, 11489–11495 (2016).
38. Rae, C. L., Hughes, L. E., Weaver, C., Anderson, M. C. & Rowe, J. B. Selection and stopping in voluntary action: a meta-analysis and combined fMRI study. *NeuroImage* **86**, 381–391 (2014).
39. Watanabe, T. et al. Effects of rTMS of pre-supplementary motor area on fronto basal ganglia network activity during stop-signal task. *J. Neurosci.* **35**, 4813–4823 (2015).
40. Floden, D. & Stuss, D. T. Inhibitory control is slowed in patients with right superior medial frontal damage. *J. Cognit. Neurosci.* **18**, 1843–1849 (2006).
41. Roberts, R. E. & Husain, M. A dissociation between stopping and switching actions following a lesion of the pre-supplementary motor area. *Cortex* **63**, 184–195 (2015).
42. Kohl, S. et al. Cortical paired associative stimulation influences response inhibition: cortico-cortical and cortico-subcortical networks. *Biol. Psychiatry* **85**, 355–363 (2019).
43. Cai, W., George, J. S., Verbruggen, F., Chambers, C. D. & Aron, A. R. The role of the right presupplementary motor area in stopping action: two studies with event-related transcranial magnetic stimulation. *J. Neurophysiol.* **108**, 380–389 (2012).
44. Nachev, P., Kennard, C. & Husain, M. Functional role of the supplementary and pre-supplementary motor areas. *Nat. Rev. Neurosci.* **9**, 856–869 (2008).
45. Thiebaut de Schotten, M., Dell'Acqua, F., Valabregue, R. & Catani, M. Monkey to human comparative anatomy of the frontal lobe association tracts. *Cortex* **48**, 82–96 (2012).
46. Rae, C. L., Hughes, L. E., Anderson, M. C. & Rowe, J. B. The prefrontal cortex achieves inhibitory control by facilitating subcortical motor pathway connectivity. *J. Neurosci.* **35**, 786–794 (2015).
47. Inase, M., Tokuno, H., Nambu, A., Akazawa, T. & Takada, M. Corticostriatal and corticosubthalamic input zones from the presupplementary motor area in the macaque monkey: comparison with the input zones from the supplementary motor area. *Brain Res.* **833**, 191–201 (1999).
48. Isoda, M. & Hikosaka, O. Role for subthalamic nucleus neurons in switching from automatic to controlled eye movement. *J. Neurosci.* **28**, 7209–7218 (2008).
49. Allen, C., Singh, K. D., Verbruggen, F. & Chambers, C. D. Evidence for parallel activation of the pre-supplementary motor area and inferior frontal cortex during response inhibition: a combined MEG and TMS study. *R. Soc. Open Sci.* **5**, 171369 (2018).
50. Wessel, J. R. β-Bursts reveal the trial-to-trial dynamics of movement initiation and cancellation. *J. Neurosci.* **40**, 411–423 (2020).
51. Errington, S. P., Woodman, G. F. & Schall, J. D. Dissociation of medial frontal β-bursts and executive control. *J. Neurosci.* **40**, 9272–9282 (2020).
52. Li, B., Nguyen, T. P., Ma, C. & Dan, Y. Inhibition of impulsive action by projection-defined prefrontal pyramidal neurons. *Proc. Natl Acad. Sci. USA* **117**, 202000523 (2020).
A rodent optogenetic study confirming the importance of a dmPFC–STN pathway for action control.
53. Fife, K. H. et al. Causal role for the subthalamic nucleus in interrupting behavior. *eLife* **6**, e27689 (2017).
54. Cavanagh, J. F. et al. Subthalamic nucleus stimulation reverses mediofrontal influence over decision threshold. *Nat. Neurosci.* **14**, 1462–1467 (2011).
55. Herz, D. M. et al. Mechanisms underlying decision-making as revealed by deep-brain stimulation in patients with Parkinson's disease. *Curr. Biol.* **28**, 1169–1178.e6 (2018).
56. Wiecki, T. V. & Frank, M. J. A computational model of inhibitory control in frontal cortex and basal ganglia. *Psychol. Rev.* **120**, 329–355 (2013).
57. de Hollander, G., Keuken, M. C., van der Zwaag, W., Forstmann, B. U. & Trampel, R. Comparing functional MRI protocols for small, iron-rich basal ganglia nuclei such as the subthalamic nucleus at 7 T and 3 T. *Hum. Brain Mapp.* **38**, 3226–3248 (2017).
58. Swann, N. et al. Deep brain stimulation of the subthalamic nucleus alters the cortical profile of response inhibition in the beta frequency band: a scalp EEG study in Parkinson's disease. *J. Neurosci.* **31**, 5721–5729 (2011).
59. Ray, N. J. et al. The role of the subthalamic nucleus in response inhibition: evidence from deep brain stimulation for Parkinson's disease. *Neuropsychologia* **47**, 2828–2834 (2009).
60. Mirabella, G. et al. Deep brain stimulation of subthalamic nuclei affects arm response inhibition in Parkinson's patients. *Cereb. Cortex* **22**, 1124–1132 (2012).
61. van den Wildenberg, W. P. M. et al. Stimulation of the subthalamic region facilitates the selection and inhibition of motor responses in Parkinson's disease. *J. Cognit. Neurosci.* **18**, 626–636 (2006).
62. Bastin, J. et al. Inhibitory control and error monitoring by human subthalamic neurons. *Transl. Psychiatry* **4**, e439–e439 (2014).
63. Benis, D. et al. Response inhibition rapidly increases single-neuron responses in the subthalamic nucleus of patients with Parkinson's disease. *Cortex* **84**, 111–123 (2016).
64. Wessel, J. R. et al. Stop-related subthalamic beta activity indexes global motor suppression in Parkinson's disease. *Mov. Disord.* **31**, 1846–1853 (2016).
A study of individuals with Parkinson disease supporting the idea that the global motor system suppression is related to basal ganglia (STN) output.
65. Benis, D. et al. Subthalamic nucleus activity dissociates proactive and reactive inhibition in patients with Parkinson's disease. *NeuroImage* **91**, 273–281 (2014).
66. Badry, R. et al. Suppression of human cortico-motoneuronal excitability during the stop-signal task. *Clin. Neurophysiol.* **120**, 1717–1723 (2009).
67. Hazrati, L. N. & Parent, A. Convergence of subthalamic and striatal efferents at pallidal level in primates: an anterograde double-labeling study with biocytin and PHA-L. *Brain Res.* **569**, 336–340 (1992).
68. Miyachi, S. et al. Somatotopically arranged inputs from putamen and subthalamic nucleus to primary motor cortex. *Neurosci. Res.* **56**, 300–308 (2006).
69. Kelly, R. M. & Strick, P. L. Macro-architecture of basal ganglia loops with the cerebral cortex: Use of rabies virus to reveal multisynaptic circuits. *Prog. Brain Res.* **143**, 447–459 (2004).
70. Pasquereau, B. & Turner, R. S. A selective role for ventromedial subthalamic nucleus in inhibitory control. *eLife* **6**, e31627 (2017).
A non-human primate study supporting the idea that the ventral portion of the STN is specifically involved in action-stopping, consistent with this region receiving inputs from the lateral PFC.
71. Ye, Z. et al. Predicting beneficial effects of atomoxetine and citalopram on response inhibition in Parkinson's disease with clinical and neuroimaging measures. *Hum. Brain Mapp.* **37**, 1026–1037 (2016).
72. Zandbelt, B. B., Bloemendaal, M., Neggers, S. F. W., Kahn, R. S. & Vink, M. Expectations and violations: delineating the neural network of proactive inhibitory control. *Hum. Brain Mapp.* **34**, 2015–2024 (2013).
73. Zandbelt, B. B., Bloemendaal, M., Hoogendam, J. M., Kahn, R. S. & Vink, M. Transcranial magnetic stimulation and functional MRI reveal cortical and subcortical interactions during stop-signal response inhibition. *J. Cogn. Neurosci.* **25**, 157–174 (2013).
74. Majid, D. S. A., Cai, W., Corey-Bloom, J. & Aron, A. R. Proactive selective response suppression is implemented via the basal ganglia. *J. Neurosci.* **33**, 13259–13269 (2013).
75. Rao, J. A. et al. Disruption of response inhibition circuits in prodromal Huntington disease. *Cortex* **58**, 72–85 (2014).
76. Jahfari, S., Stinear, C. M., Claffey, M., Verbruggen, F. & Aron, A. R. Responding with restraint: what are the neurocognitive mechanisms? *J. Cognit. Neurosci.* **22**, 1479–1492 (2010).
77. Terra, H. et al. Prefrontal cortical projection neurons targeting dorsomedial striatum control behavioral inhibition. *Curr. Biol.* **30**, 4188–4200.e5 (2020).
78. Gu, B.-M., Schmidt, R. & Berke, J. D. Globus pallidus dynamics reveal covert strategies for behavioral inhibition. *eLife* **9**, 1–19 (2020).
79. Klaus, A. et al. The spatiotemporal organization of the striatum encodes action space. *Neuron* **95**, 1171–1180.e7 (2017).
80. Jin, X., Tecuapetla, F. & Costa, R. M. Basal ganglia subcircuits distinctively encode the parsing and concatenation of action sequences. *Nat. Neurosci.* **17**, 423–430 (2014).
81. Mink, J. W. The basal ganglia: focused selection and inhibition of competing motor programs. *Prog. Neurobiol.* **50**, 381–425 (1996).
82. Coxon, J. P., Stinear, C. M. & Byblow, W. D. Intracortical inhibition during volitional inhibition of prepared action. *J. Neurophysiol.* **95**, 3371–3383 (2006).
83. Cai, W., Oldenkamp, C. L. & Aron, A. R. Stopping speech suppresses the task-irrelevant hand. *Brain Lang.* **120**, 412–415 (2012).
84. Pani, P. et al. Visual salience of the stop signal affects the neuronal dynamics of controlled inhibition. *Sci. Rep.* **8**, 1–13 (2018).
85. Jerjian, S. J., Sahani, M. & Kraskov, A. Movement initiation and grasp representation in premotor and primary motor cortex mirror neurons. *eLife* **9**, 1–26 (2020).
86. Raud, L. & Huster, R. J. The temporal dynamics of response inhibition and their modulation by cognitive control. *Brain Topogr.* **30**, 486–501 (2017).
87. Schmidt, R. & Berke, J. D. A pause-then-cancel model of stopping: evidence from basal ganglia neurophysiology. *Philos. Trans. R. Soc. B: Biol. Sci.* https://doi.org/10.1098/rstb.2016.0202 (2017).
88. Schmidt, R., Leventhal, D. K., Mallet, N., Chen, F. & Berke, J. D. Canceling actions involves a race between basal ganglia pathways. *Nat. Neurosci.* **16**, 1118–1124 (2013).
89. Mallet, N. et al. Arkypallidal cells send a stop signal to striatum. *Neuron* **89**, 308–316 (2016).
90. Frank, M. J., Samanta, J., Moustafa, A. A. & Sherman, S. J. Hold your horses: impulsivity, deep brain stimulation, and medication in parkinsonism. *Science* **318**, 1309–1312 (2007).
91. Heston, J. et al. Activation of subthalamic nucleus stop circuit disrupts cognitive performance. *eNeuro* https://doi.org/10.1523/ENEURO.0159-20.2020 (2020).
92. Wessel, J. R. et al. Surprise disrupts cognition via a fronto-basal ganglia suppressive mechanism. *Nat. Commun.* **7**, 1–10 (2016).
93. Ardila, A., Bernal, B. & Rosselli, M. How localized are language brain areas? A review of Brodmann areas involvement in oral language. *Arch. Clin. Neuropsychol.* **31**, 112–122 (2016).

94. Stewart, L., Walsh, V., Frith, U. & Rothwell, J. C. TMS produces two dissociable types of speech disruption. *NeuroImage* **13**, 472–478 (2001).
95. Xue, G., Aron, A. R. & Poldrack, R. A. Common neural substrates for inhibition of spoken and manual responses. *Cereb. Cortex* **18**, 1923–1932 (2008).
96. Wagner, J., Wessel, J. R., Ghahremani, A. & Aron, A. R. Establishing a right frontal beta signature for stopping action in scalp EEG: implications for testing inhibitory control in other task contexts. *J. Cognit. Neurosci.* **30**, 107–118 (2018).
97. Ghahremani, A. et al. Stopping and slowing manual and spoken responses: similar oscillatory signatures recorded from the subthalamic nucleus. *Brain Lang.* **176**, 1–10 (2018).
98. Kinoshita, M. et al. Role of fronto-striatal tract and frontal aslant tract in movement and speech: an axonal mapping study. *Brain Struct. Funct.* **220**, 3399–3412 (2015).
99. Lüders, H. et al. Localization of cortical function: new information from extraoperative monitoring of patients with epilepsy. *Epilepsia* **29**, S56–S65 (1988).
100. Filevich, E., Kühn, S. & Haggard, P. Negative motor phenomena in cortical stimulation: Implications for inhibitory control of human action. *Cortex* **48**, 1251–1261 (2012).
101. Takakusaki, K. Functional neuroanatomy for posture and gait control. *J. Mov. Disord.* **10**, 1–17 (2017).
102. Gritton, H. J. et al. Unique contributions of parvalbumin and cholinergic interneurons in organizing striatal networks during movement. *Nat. Neurosci.* **22**, 586–597 (2019).
103. Rizzi, G. & Tan, K. R. Synergistic nigral output pathways shape movement. *Cell Rep.* **27**, 2184–2198.e4 (2019).
104. Pamukcu, A. et al. Parvalbumin$^+$ and Npas1$^+$ pallidal neurons have distinct circuit topology and function. (2020) https://doi.org/10.1523/JNEUROSCI.0361-20.2020.
105. Ebersbach, G., Moreau, C., Gandor, F., Defebvre, L. & Devos, D. Clinical syndromes: parkinsonian gait. *Mov. Disord.* **28**, 1552–1559 (2013).
106. Fischer, P. et al. Alternating modulation of subthalamic nucleus beta oscillations during stepping. *J. Neurosci.* **38**, 5111–5121 (2018).
107. Bancroft, M. J. & Day, B. L. The throw-and-catch model of human gait: evidence from coupling of pre-step postural activity and step location. *Front. Hum. Neurosci.* **10**, 635 (2016).
108. Potocanac, Z., Pijnappels, M., Verschueren, S., van Dieën, J. & Duysens, J. Two-stage muscle activity responses in decisions about leg movement adjustments during trip recovery. *J. Neurophysiol.* **115**, 143–156 (2016).
109. Goode, C., Cole, D. M. & Bolton, D. A. E. Staying upright by shutting down? Evidence for global suppression of the motor system when recovering balance. *Gait Posture* **70**, 260–263 (2019).
An innovative study in humans attempting to study the neural basis of action-stopping in a more naturalistic gait-and-balance context.
110. Rydalch, G., Bell, H. B., Ruddy, K. L. & Bolton, D. A. E. Stop-signal reaction time correlates with a compensatory balance response. *Gait Posture* **71**, 273–278 (2019).
111. Adam, E., Johns, T. & Sur, M. Cortico-subthalamic projections send brief stop signals to halt visually-guided locomotion. https://doi.org/10.1101/2020.02.05.936443 (2020).
112. van der Salm, S. M. A. et al. Distinctive tics suppression network in Gilles de la Tourette syndrome distinguished from suppression of natural urges using multimodal imaging. *NeuroImage Clin.* **20**, 783–792 (2018).
113. Berman, B. D., Horovitz, S. G., Morel, B. & Hallett, M. Neural correlates of blink suppression and the buildup of a natural bodily urge. *NeuroImage* **59**, 1441–1450 (2012).
114. Mazzone, S. B., Cole, L. J., Ando, A., Egan, G. F. & Farrell, M. J. Investigation of the neural control of cough and cough suppression in humans using functional brain imaging. *J. Neurosci.* **31**, 2948–2958 (2011).
115. Ando, A. et al. Neural correlates of cough hypersensitivity in humans: evidence for central sensitisation and dysfunctional inhibitory control. *Thorax* **71**, 323–329 (2016).
116. McKay, L. C., Adams, L., Frackowiak, R. S. J. & Corfield, D. R. A bilateral cortico-bulbar network associated with breath holding in humans, determined by functional magnetic resonance imaging. *NeuroImage* **40**, 1824–1832 (2008).
117. Lynn, M. T., Demanet, J., Krebs, R. M., van Dessel, P. & Brass, M. Voluntary inhibition of pain avoidance behavior: an fMRI study. *Brain Struct. Funct.* **221**, 1309–1320 (2016).
118. Critchley, H. D. et al. Slow breathing and hypoxic challenge: cardiorespiratory consequences and their central neural substrates. (2015) https://doi.org/10.1371/journal.pone.0127082.
119. Sundby, K. K., Wagner, J. & Aron, A. R. The functional role of response suppression during an urge to relieve pain. *J. Cognit. Neurosci.* **31**, 1404–1421 (2018).
120. Smith, W. K. The representation of respiratory movements in the cerebral cortex. *J. Neurophysiol.* **1**, 55–68 (1938).
121. Schel, M. A. et al. Neural correlates of intentional and stimulus-driven inhibition: a comparison. *Front. Hum. Neurosci.* **8**, 27 (2014).
122. Jahanshahi, M. & Rothwell, J. C. Inhibitory dysfunction contributes to some of the motor and non-motor symptoms of movement disorders and psychiatric disorders. *Philos. Trans. R. Soc. B: Biol. Sci.* **372**, 20160198 (2017).
123. de Havas, J., Gomi, H. & Haggard, P. Experimental investigations of control principles of involuntary movement: a comprehensive review of the Kohnstamm phenomenon. *Exp. Brain Res.* **235**, 1953–1997 (2017).
124. Ghosh, A., Rothwell, J. & Haggard, P. Using voluntary motor commands to inhibit involuntary arm movements. *Proc. Biol. Sci.* **281**, 20141139 (2014).
125. Parkinson, A., McDonagh, M. & Vidyasagar, R. Brain activation in an involuntary human action. *Brain Res.* **1304**, 57–65 (2009).
126. de Havas, J., Ghosh, A., Gomi, H. & Haggard, P. Voluntary motor commands reveal awareness and control of involuntary movement. *Cognition* **155**, 155–167 (2016).
127. Wessel, J. R. & Aron, A. R. Unexpected events induce motor slowing via a brain mechanism for action-stopping with global suppressive effects. *J. Neurosci.* **33**, 18481–18491 (2013).
128. Dutra, I. C., Waller, D. A. & Wessel, J. R. Perceptual surprise improves action stopping by nonselectively suppressing motor activity via a neural mechanism for motor inhibition. *J. Neurosci.* **38**, 1482–1492 (2018).
129. Hampshire, A. & Sharp, D. J. Contrasting network and modular perspectives on inhibitory control. *Trends Cognit. Sci.* **19**, 445–452 (2015).
130. Aron, A. R., Robbins, T. W. & Poldrack, R. A. Right inferior frontal cortex: addressing the rebuttals. *Front. Hum. Neurosci.* **8**, 905 (2014).
131. Sharp, D. J. et al. Distinct frontal systems for response inhibition, attentional capture, and error processing. *Proc. Natl Acad. Sci. USA* **107**, 6106–6111 (2010).
132. Boto, E. et al. Moving magnetoencephalography towards real-world applications with a wearable system. *Nature* **555**, 657–661 (2018).
133. Lacerenza, M. et al. Wearable and wireless time-domain near-infrared spectroscopy system for brain and muscle hemodynamic monitoring. *Biomed. Opt. Express* https://doi.org/10.1364/boe.403327 (2020).
134. Topalovic, U. et al. Wireless programmable recording and stimulation of deep brain activity in freely moving humans. *Neuron* **108**, 322–334.e9 (2020).
A demonstration of novel technology for wearable devices for recording and perturbing brain activity, and its integration with other behavioural recording devices.
135. Poldrack, R. A. Can cognitive processes be inferred from neuroimaging data? *Trends Cognit. Sci.* **10**, 59–63 (2006).
136. Verbruggen, F. & Logan, G. D. Proactive adjustments of response strategies in the stop-signal paradigm. *J. Exp. Psychol.* **35**, 835–854 (2009).
137. Lee, W.-T. & Kang, M.-S. Electrophysiological evidence for distinct proactive control mechanisms in a stop-signal task: an individual differences approach. *Front. Psychol.* **11**, 1105 (2020).
138. Horstmann, G. The surprise-attention link: a review. *Ann. N. Y. Acad. Sci.* **1339**, 106–115 (2015).
139. Liang, F. et al. Sensory cortical control of a visually induced arrest behavior via corticotectal projections. *Neuron* **86**, 755–767 (2015).
140. Eisenberg, I. W. et al. Uncovering the structure of self-regulation through data-driven ontology discovery. *Nat. Commun.* **10**, 1–13 (2019).
141. Neef, N. E. et al. Structural connectivity of right frontal hyperactive areas scales with stuttering severity. *Brain* **141**, 191–204 (2018).
A neuroimaging study highlighting the relationship between connectivity in right prefrontal regions of the stopping network and stuttering severity.
142. Eggers, K., de Nil, L. F. & van den Bergh, B. R. H. Inhibitory control in childhood stuttering. *J. Fluen. Disord.* **38**, 1–13 (2013).
143. Markett, S. et al. Impaired motor inhibition in adults who stutter – evidence from speech-free stop-signal reaction time tasks. *Neuropsychologia* **91**, 444–450 (2016).
144. Treleaven, S. B. & Coalson, G. A. Manual response inhibition and quality of life in adults who stutter. *J. Commun. Disord.* **88**, 106053 (2020).
145. Fox, P. T. et al. A PET study of the neural systems of stuttering. *Nature* **382**, 158–162 (1996).
146. Belyk, M., Kraft, S. J. & Brown, S. Stuttering as a trait or state - an ALE meta-analysis of neuroimaging studies. *Eur. J. Neurosci.* **41**, 275–284 (2015).
147. Kell, C. A. et al. How the brain repairs stuttering. *Brain* **132**, 2747–2760 (2009).
148. Preibisch, C. et al. Evidence for compensation for stuttering by the right frontal operculum. *NeuroImage* **20**, 1356–1364 (2003).
149. Mink, J. W. Basal ganglia dysfunction in Tourette's syndrome: a new hypothesis. *Pediatric Neurol.* **25**, 190–198 (2001).
150. Kataoka, Y. et al. Decreased number of parvalbumin and cholinergic interneurons in the striatum of individuals with Tourette syndrome. *J. Comp. Neurol.* **518**, 277–291 (2010).
151. Morand-Beaulieu, S. et al. The puzzling question of inhibitory control in Tourette syndrome: a meta-analysis. *Neurosci. Biobehav. Rev.* **80**, 240–262 (2017).
152. Koller, W. C. & Biary, N. M. Volitional control of involuntary movements. *Mov. Disord.* **4**, 153–156 (1989).
153. Kim, S. et al. Tic suppression in children with recent-onset tics predicts 1-year tic outcome. *J. Child. Neurol.* **34**, 757–764 (2019).
154. Fründt, O., Woods, D. & Ganos, C. Behavioral therapy for Tourette syndrome and chronic tic disorders. *Neurol. Clin. Pract.* **7**, 148–156 (2017).
155. Ganos, C. et al. Motor cortical excitability during voluntary inhibition of involuntary tic movements. *Mov. Disord.* **33**, 1804–1809 (2018).
A study in individuals with tics demonstrating that tonic voluntary suppression of tics is associated with a global motor system suppression akin to that seen when stopping voluntary actions.
156. Brandt, V. C. et al. Temporal relationship between premonitory urges and tics in Gilles de la Tourette syndrome. *Cortex* **77**, 24–37 (2016).
157. Ganos, C. et al. The neural correlates of tic inhibition in Gilles de la Tourette syndrome. *Neuropsychologia* **65**, 297–301 (2014).
158. Peterson, B. S. et al. A functional magnetic resonance imaging study of tic suppression in tourette syndrome. *Arch. Gen. Psychiatry* **55**, 326–333 (1998).
159. Zapparoli, L., Macerollo, A., Joyce, E. M., Martino, D. & Kilner, J. M. Voluntary tic suppression and the normalization of motor cortical beta power in Gilles de la Tourette syndrome: an EEG study. *Eur. J. Neurosci.* https://doi.org/10.1111/ejn.14548 (2019).
160. Ehgoetz Martens, K. A. et al. The functional network signature of heterogeneity in freezing of gait. *Brain* **141**, 1145–1160 (2018).
161. Lewis, S. J. G. & Shine, J. M. The next step: a common neural mechanism for freezing of gait. *Neuroscientist* **22**, 72–82 (2016).
162. Shine, J. M. et al. Abnormal patterns of theta frequency oscillations during the temporal evolution of freezing of gait in Parkinson's disease. *Clin. Neurophysiol.* **125**, 569–576 (2014).
163. Pozzi, N. G. et al. Freezing of gait in Parkinson's disease reflects a sudden derangement of locomotor network dynamics. *Brain* **142**, 2037–2050 (2019).
A study in individuals with Parkinson disease demonstrating that connectivity in a putative PFC–STN hyperdirect pathway is involved in the freezing of gait.
164. Matar, E. et al. Identifying the neural correlates of doorway freezing in Parkinson's disease. *Hum. Brain Mapp.* **40**, 2055–2064 (2019).
165. Chen, C. C. et al. Subthalamic nucleus oscillations correlate with vulnerability to freezing of gait in patients with Parkinson's disease. *Neurobiol. Dis.* **132**, 104605 (2019).
166. Rubinstein, T. C., Giladi, N. & Hausdorff, J. M. The power of cueing to circumvent dopamine deficits: a review of physical therapy treatment of gait disturbances in Parkinson's disease. *Mov. Disord.* **17**, 1148–1160 (2002).

167. Castiglione, A. & Aron, A. R. Unwanted memory intrusions recruit broad motor suppression. *J. Cogn. Neurosci.* https://doi.org/10.1162/jocn_a_01642 (2020).
168. Castiglione, A., Wagner, J., Anderson, M. & Aron, A. R. Preventing a thought from coming to mind elicits increased right frontal beta just as stopping action does. *Cereb. Cortex* **29**, 2160–2172 (2019).
A neurophysiological study showing that stopping an unwanted thought intrusion from coming to mind is associated with a similar prefrontal beta-band signature as stopping an action.
169. Anderson, M. C. & Green, C. Suppressing unwanted memories by executive control. *Nature* **410**, 366–369 (2001).
170. Visser, R. M. et al. Neuropsychological Mechanisms of Intrusive Thinking. In: Kalivas P. W. and Paulus M. P. (eds). Vol. 30, 124–184 (The MIT Press, 2020).
171. Skippen, P. et al. Reliability of triggering inhibitory process is a better predictor of impulsivity than SSRT. *Acta Psychol.* **192**, 104–117 (2019).
172. Klaus, A., Alves da Silva, J. & Costa, R. M. What, if, and when to move: basal ganglia circuits and self-paced action initiation. *Annu. Rev. Neurosci.* **42**, 459–483 (2019).
173. Nambu, A., Tokuno, H. & Takada, M. Functional significance of the cortico-subthalamo-pallidal "hyperdirect" pathway. *Neurosci. Res.* **43**, 111–117 (2002).
174. Osada, T. et al. An essential role of the intraparietal sulcus in response inhibition predicted by parcellation-based network. *J. Neurosci.* **39**, 2509–2521 (2019).
175. Hannah, R. & Jana, S. Disentangling the role of posterior parietal cortex in response inhibition. *J. Neurosci.* **39**, 6814–6816 (2019).
176. Silsupadol, P., Teja, K. & Lugade, V. Reliability and validity of a smartphone-based assessment of gait parameters across walking speed and smartphone locations: body, bag, belt, hand, and pocket. *Gait Posture* **58**, 516–522 (2017).
177. Cai, W., Oldenkamp, C. L. & Aron, A. R. A proactive mechanism for selective suppression of response tendencies. *J. Neurosci.* **31**, 5965–5969 (2011).
178. Majid, D. S. A., Cai, W., George, J. S., Verbruggen, F. & Aron, A. R. Transcranial magnetic stimulation reveals dissociable mechanisms for global versus selective corticomotor suppression underlying the stopping of action. *Cereb. Cortex* **22**, 363–371 (2012).
179. Jahfari, S. et al. How preparation changes the need for top-down control of the basal ganglia when inhibiting premature actions. *J. Neurosci.* **32**, 10870–10878 (2012).
180. Aron, A. R. & Verbruggen, F. Stop the presses: dissociating a selective from a global mechanism for stopping: research article. *Psychol. Sci.* **19**, 1146–1153 (2008).
181. Mars, R. B., Piekema, C., Coles, M. G. H., Hulstijn, W. & Toni, I. On the programming and reprogramming of actions. *Cereb. Cortex* **17**, 2972–2979 (2007).
182. Boecker, M. et al. When response inhibition is followed by response reengagement: an event-related fMRI study. *Hum. Brain Mapp.* **32**, 94–106 (2011).
183. Isoda, M. & Hikosaka, O. Switching from automatic to controlled action by monkey medial frontal cortex. *Nat. Neurosci.* **10**, 240–248 (2007).
184. Neubert, F.-X., Mars, R. B., Buch, E. R., Olivier, E. & Rushworth, M. F. S. Cortical and subcortical interactions during action reprogramming and their related white matter pathways. *Proc. Natl Acad. Sci. USA* **107**, 13240–13245 (2010).
185. Greenhouse, I. & Wessel, J. R. EEG signatures associated with stopping are sensitive to preparation. *Psychophysiology* **50**, 900–908 (2013).
186. Wessel, J. R. & Aron, A. R. It's not too late: The onset of the frontocentral P3 indexes successful response inhibition in the stop-signal paradigm. *Psychophysiology* **52**, 472–480 (2015).
187. Huster, R. J., Messel, M. S., Thunberg, C. & Raud, L. The P300 as marker of inhibitory control – fact or fiction? *Cortex* **132**, 334–348 (2020).
188. Atsma, J., Maij, F., Gu, C., Medendorp, W. P. & Corneil, B. D. Active braking of whole-arm reaching movements provides single-trial neuromuscular measures of movement cancellation. *J. Neurosci.* **38**, 4367–4382 (2018).

Acknowledgements
The authors gratefully acknowledge funding support from the US National Institutes of Health (NS106822 and DA026452) and comments on the manuscript from J. Rothwell.

Author contributions
The authors contributed equally to all aspects of the article.

Competing interests
The authors declare no competing interests.

Peer review information
Nature Reviews Neuroscience thanks D. Bolton, S. Konishi and the other, anonymous, reviewer(s) for their contribution to the peer review of this work.