The Global Nature of Motor System Inhibitory Effects in Response Control: Evidence, Mechanisms, and Postprint Debates

Authors: Lihui Wang

Date: 2023-10-09T00:00:00+00:00

Abstract

In research on response control, the long-standing theoretical perspective has maintained that only effectors interfering with the current goal exhibit inhibitory effects. Summarizing recent research findings, during response control processes, inhibitory effects emerge not only in interfering effectors, but also in task-irrelevant effectors and task-required effectors; inhibitory effects related to response control are not confined to tasks involving response conflict, but rather are broadly present in tasks involving response execution, indicating that the entire motor system demonstrates a global nature of inhibition across multiple contexts. The dual-process model proposes that inhibition of different effectors is controlled by distinct brain regions, while the spotlight model suggests that inhibition of different effectors originates from a single system, the latter aligning with the normalization model in computational neuroscience. The global characteristic of inhibitory effects in response control facilitates consideration of cognitive processing from a collaborative and integrative perspective. Simultaneously, current research also exhibits some controversy regarding the conditions under which this global nature of inhibitory effects emerges. Future studies should differentiate among various effectors and, in combination with computational models, elucidate the coordination mechanisms among effectors, effectors

Full Text

Preamble

ChinaXiv Partner Journal *Advances in Psychological Science* 2023, Vol. 31, No. 9, 1665–1675

https://doi.org/10.3724/SP.J.1042.2023.01665

The Global Inhibitory Effect within the Motor System in Response Control: Evidence, Mechanism, and Controversy

WANG Lihui
(Institute of Psychology and Behavioral Science, Shanghai Jiao Tong University; Shanghai Mental Health Center, Shanghai Jiao Tong University School of Medicine, Shanghai 200030, China)

Abstract: Theories of response inhibition have long held that only the response effector that interferes with the current task goal is inhibited during the implementation of response control. However, recent studies have suggested that inhibition occurs not only at the interfering response effector but also at the task-irrelevant and task-required response effectors. Moreover, inhibition occurs not only in response conflict tasks but also in tasks that involve response execution, i.e., global inhibition within the entire motor system. The dual-process model proposes that the inhibitory processes at different effectors are controlled by different brain areas, whereas the spot-light model proposes that they are controlled by a single system. The spot-light model is consistent with the normalization model in computational neuroscience. Global inhibition offers a new perspective for treating cognition as a coordinated and integrated process. Meanwhile, there are differing opinions regarding the condition in which global inhibition can be observed. Future studies should differentiate the response effectors during response control tasks, as well as use computational modeling to elucidate the coordinative mechanisms between multiple effectors and the computational mechanism of the motor cortex. Future studies should also examine the relationship between dysfunctional global inhibition and response control deficits in populations with mental disorders.

Keywords: response control, global inhibition, motor system, cognitive flexibility
Classification Code: B842

Human thought and action exhibit remarkable adaptability and flexibility. As a healthy functioning organism, humans can flexibly adjust perception and motor functions to achieve goals in constantly changing environments. A core manifestation of this flexible environmental adaptation is response inhibition—the ability to suppress inappropriate or task-irrelevant behaviors to ensure effective execution of goal-relevant actions (Logan, 1994). On the one hand, numerous everyday situations involve response inhibition. For example, when driving a car, we must continuously monitor safety information in our surroundings and stop promptly and accurately when encountering a red light or sudden hazards (such as pedestrians jaywalking) to ensure our own and others' safety. On the other hand, many psychiatric and neurological disorders, including Parkinson' s disease, attention deficit hyperactivity disorder (ADHD), obsessive-compulsive disorder, and substance addiction, are characterized by abnormal response inhibition function (Chambers et al., 2009). Therefore, studying response inhibition not only enhances our understanding of how humans adapt to environments through flexible behavior but also improves our knowledge of psychiatric and neurological disorders, holding significant theoretical and clinical importance.

Traditional theories posit that the response required by the current task goal competes with responses or response tendencies that interfere with this goal, and that interference must be suppressed to ensure goal achievement (Logan, 1994; Ridderinkhof, 2002; Wang & Cai, 2010). Research on response inhibition has a long history, with researchers proposing various theoretical models based on different emphases. Early race models based on the Go/NoGo paradigm (Logan, 1994) suggested that response and response inhibition processes are independent and compete with each other in the initial processing stage, with whichever process reaches threshold first determining the final behavioral outcome. Boucher et al.' s (2007) interactive race model proposed that these processes are no longer independent in later stages, with response inhibition suppressing the response as it approaches threshold. The activation-suppression model based on conflict control (Ridderinkhof, 2002) posited that response inhibition involves two stages: first, the activation of an inappropriate response, followed by its suppression. These processes are not independent; the efficiency of the latter influences the activation strength and time course of the inappropriate response, with substantial individual differences. Aron (2011) noted that early response inhibition models focused on "reactive inhibition" —the passive suppression of already-activated inappropriate responses—and further proposed "proactive inhibition,"which involves advance, active suppression of potential, not-yet-activated inappropriate responses.

Although different theories debate the proactive nature and temporal dynamics of response inhibition, they all agree that only responses interfering with the current task goal need to be suppressed during implementation (Aron, 2011; Salzer et al., 2017). For example, in the classic Go/NoGo paradigm commonly used to study response inhibition, the response to NoGo stimuli is suppressed, and in the Stop-signal task, the response to the stop signal is inhibited. However, increasing evidence suggests that inhibitory effects are not limited to responses interfering with the current task goal but extend to the entire motor system. Moreover, these effects are not exclusive to tasks involving response conflict and response selection but are broadly present in tasks involving general response output and execution. Researchers have thus proposed the concept of "global inhibition" (Duque et al., 2017; Wessel et al., 2013).

This paper systematically reviews recent advances in global inhibition. We first introduce the manifestations of global inhibition, then elaborate on its cognitive and neural mechanisms, followed by a discussion of different perspectives and controversies surrounding this phenomenon, and conclude by summarizing the significance of global inhibition at both cognitive processing and neural computation levels, along with future research directions.

2 Manifestations of Global Inhibition

The core characteristic of global inhibition is suppression of the entire motor system, including not only inhibition of responses that interfere with the current goal but also inhibition of potential responses that are irrelevant to the task, as well as inhibitory processing of the currently required response. To distinguish among these response types, this paper defines three categories of response effectors: (1) *task-required effector*—the effector needed to complete the current task; (2) *interfering effector*—the effector that interferes with or conflicts with task completion (task-required and interfering effectors are collectively termed task-relevant effectors); and (3) *task-irrelevant effector*—the effector unrelated to the current task, which, while task-irrelevant, still belongs to the motor system. Using the Stroop task as an example, if participants are instructed to respond to red stimuli with the left hand and green stimuli with the right hand, when the word "green" is presented in red ink, the left hand is the task-required effector, the right hand is the interfering effector, and all other effectors (e.g., the left foot) are task-irrelevant effectors.

Traditional response inhibition research has focused on two categories: one involves inhibition in Stop-signal and Go/NoGo paradigms, where participants suppress responses from a specific effector when a signal appears (e.g., a stop signal or NoGo stimulus). Although task-required and interfering responses share the same effector in these paradigms, the effector is only considered interfering when response stopping is required. The other category involves response inhibition in conflict control tasks, such as the Stroop paradigm (color-semantic incongruence), Simon paradigm (spatial location-response location incongruence), and Flanker paradigm. In these two types of paradigms, traditional research has defined response inhibition as suppression of the interfering effector, without examining whether other effectors also show inhibitory effects, thus overlooking the global nature of inhibition. Moreover, both task types involve conflict control—Stroop, Flanker, and Simon paradigms involve direct conflict between different effectors, while Stop-signal and Go/NoGo tasks involve conflict between executing and stopping a response, which also falls under conflict control paradigms. However, recent findings indicate that the global nature of inhibitory effects persists even in situations not involving conflict control. Below, we discuss inhibitory effects at different effectors in both conflict control and non-conflict control contexts.

2.1 Response Inhibition in Conflict Control Contexts

The most intuitive way to elicit response inhibition is through conflict control paradigms, and numerous studies using such tasks have demonstrated the global nature of inhibitory effects. Inhibition of task-irrelevant effectors was first observed by Badry et al. (2009). This study used a Stop-signal paradigm requiring manual button presses to specific stimuli; when the stop signal appeared, participants had to withhold their response. Under conditions requiring response inhibition, inhibitory effects were observed not only in the responding hand (the interfering effector) but also in the leg (the task-irrelevant effector), as evidenced by motor-evoked potentials (MEPs) in the leg that were lower than baseline levels measured during resting states without tasks. Another study using a Go/NoGo paradigm requiring manual responses also observed inhibitory effects in the leg (Majid et al., 2012). In this study, the responding hand was the interfering effector and the leg was the task-irrelevant effector, with results showing that MEPs in the leg were lower during successful hand response inhibition compared to resting baseline.

Wessel et al. (2013) required participants to perform a Stop-signal task using eye movements, making saccades to stimulus locations when no stop signal appeared and stopping saccades when a stop signal appeared. Approximately 50 ms before successful saccade inhibition, inhibitory effects appeared in the hand, as MEPs in the hand were lower during correct saccade stopping than during saccade execution or failed stopping. Since this task did not involve hand responses (making the hand a task-irrelevant effector), these results demonstrate that inhibition of the oculomotor system is accompanied by inhibition of the somatomotor system, revealing global inhibitory effects across the motor system (Wessel et al., 2013). Additionally, research has shown that inhibitory effects appear in the hand during speech stopping (Cai et al., 2012), with MEPs in the hand being lower during successful speech inhibition compared to speech execution or failed inhibition, indicating that speech stopping also involves suppression of the hand motor system.

In addition to inhibitory effects at interfering and task-irrelevant effectors, some studies have shown that task-required effectors also exhibit inhibition (Bundt et al., 2016; Klein et al., 2014; Wang et al., 2021). For example, Klein et al. (2014) used a Flanker paradigm requiring participants to respond to the direction of a central arrow among a row of arrows (left hand for leftward arrows, right hand for rightward arrows), where the central arrow direction could be congruent or incongruent with the flanking arrows. Results showed that the task-required effector exhibited inhibitory effects at stimulus onset, with MEPs lower than baseline levels, regardless of whether the flankers were congruent or incongruent. Wang et al. (2021) used a Simon paradigm and found that during resolution of spatial location-response location conflict, both interfering and task-relevant effectors showed inhibitory effects, and these two inhibitory effects were negatively correlated in magnitude. Summarizing these results, although inhibiting the task-required effector seems counterproductive for correct response execution, it may be necessary for resolving response conflict.

2.2 Response Inhibition in Non-Conflict Control Contexts

In experimental situations not involving conflict control, Duque et al. (2010) used a cue-response selection paradigm to examine inhibitory effects during response preparation and selection. In this paradigm, a cue first appeared on the screen informing participants that a response task would follow (Experiment 1). After a delay, a target stimulus appeared on the left or right side of the screen. The cue had no predictive value for target location, and participants had to respond to the target. The experiment included different task contexts: a bilateral response context requiring left-hand responses to left-side stimuli and right-hand responses to right-side stimuli (making one hand the task-required effector and the other the interfering effector), and a unilateral response context requiring responses from different fingers of the same hand (e.g., left little finger for left stimuli and left index finger for right stimuli, or right index finger for left stimuli and right little finger for right stimuli). Results showed that in the bilateral response context, the task-required effector exhibited significant inhibitory effects in the time window closest to target onset following the cue, whereas in the unilateral response context, only the left-hand task-required effector showed significant inhibition, with the right-hand effect not reaching significance. After target onset, in the bilateral context when the left hand was the responding hand, the corresponding interfering effector (right index finger) showed significant inhibitory effects.

In another experiment (Experiment 2), cues were still presented, but the target was an arrow at the center of the screen, and participants were instructed to ignore the arrow direction and respond using only one hand (e.g., only the left index finger). Results showed that in the time window closest to target onset following the cue, both the task-required effector (left index finger) and the task-irrelevant effector (right index finger) exhibited significant inhibitory effects, though inhibition did not reach significance in another task-irrelevant effector (right little finger) that was neurally more distant from the task-required effector (Duque et al., 2010). Based on these varying degrees of inhibition, the authors suggested that the function of global inhibition is to resolve response competition. Although the second task only required left index finger responses, arrows pointing rightward activated stronger response tendencies in the right index finger than in the right little finger, creating greater response competition that required stronger inhibition to ensure correct responding.

A subsequent study further examined the global nature of inhibitory effects in non-conflict control contexts and observed inhibitory effects across task-required, interfering, and task-irrelevant effectors (Greenhouse et al., 2015). Compared to Duque et al. (2010), Greenhouse et al. (2015) added an experiment without cue presentation and a condition that required no response. Results showed that whether in single-hand or dual-hand response experiments, both task-required and task-irrelevant effectors exhibited inhibitory effects. Moreover, inhibition occurred regardless of whether cues were presented, though it appeared earlier when cues were available. However, no inhibitory effects were observed when no response was required. Based on these findings, the authors proposed that the functional role of global inhibition is to serve general response output and execution—whenever the current context requires a response, inhibitory effects appear, making inhibitory processing part of response preparation and output.

While the above evidence indicates inhibitory effects across multiple effectors, distinctions must be made. For interfering and task-irrelevant effectors, inhibitory effects include both reduced neural signals (e.g., motor-evoked potentials) and blocked response output (e.g., correctly stopping the interfering and task-irrelevant effectors). However, for task-required effectors, inhibitory effects generally refer to reduced neural signals without blocked response output, with the inhibition serving to control the timing of the effector' s response execution.

3 Cognitive and Neural Mechanisms of Global Inhibition

Behavioral measures typically only reflect the efficiency of inhibition implementation and cannot reveal inhibitory effects across different effectors, necessitating physiological or neural measures to provide evidence for global inhibition. The most commonly used technique for measuring inhibitory effects is motor-evoked potentials (MEPs). This method uses transcranial magnetic stimulation (TMS) to stimulate a specific region of the primary motor cortex while simultaneously recording electromyography (EMG) from the contralateral effector. The EMG signal measured in this way is called a motor-evoked potential, reflecting neural excitability along the response output pathway from the motor cortex (central nervous system) to the spinal cord (peripheral nervous system) (Bestmann & Duque, 2016; Bestmann & Krakauer, 2015). MEPs measured during task-free resting states serve as an individual' s baseline potential level; when MEPs measured during task performance are significantly lower than baseline, the task is considered to involve inhibitory effects. Numerous studies have used this index to observe inhibitory effects in task-required effectors (Duque et al., 2012; Klein et al., 2014), interfering effectors (van Campen et al., 2014; van den Wildenberg et al., 2010), and task-irrelevant effectors (Majid et al., 2012; Wessel et al., 2013). This technique offers several advantages: First, MEPs can be measured at different time points before and after response execution or inhibition, better revealing the temporal dynamics of inhibitory effects (Freeman & Aron, 2016; van Campen et al., 2014). Second, it can reflect molecular-level neural activity, such as inhibitory neurotransmitter GABA activity detected through paired-pulse TMS (Coxon et al., 2006). When the interval between two TMS pulses is 2–3 ms, the second pulse activates low-threshold GABA neurons in the primary motor cortex, producing intracortical inhibition (Fisher et al., 2002).

Although global inhibition is broader than traditional views of response inhibition, both share similar cognitive-level influencing factors, including attention, top-down control, reward, and motivation (Botvinick & Braver, 2015; Klein et al., 2014; Wang, Braver et al., 2019). Existing studies have manipulated these factors (e.g., high vs. low reward, degree of top-down attentional involvement) while simultaneously observing how neural signals from different effectors change as supporting evidence. These neural signals include surface EMG from effectors, EEG and blood oxygen level-dependent signals from the primary motor cortex, and MEP signals. Reward, as an easily manipulable experimental variable, is frequently used to study response inhibition (Freeman & Aron, 2016; Freeman et al., 2014; Wang, Chang et al., 2019). In addition to these influencing factors, a special factor affecting global inhibition is event abruptness—some researchers argue that global inhibition is more likely to be observed in situations where inhibitory control is suddenly required or where inhibition occurs rapidly (Majid et al., 2012; Wessel & Aron, 2017).

Two theories currently explain global inhibition: the dual-process model and the spot-light model, both supported by neural evidence. The dual-process model posits two independent inhibitory mechanisms: one responsible for inhibiting activation of the task-required effector to prevent premature response threshold crossing before the appropriate time, ensuring timely execution; the other responsible for resolving competition between the task-required effector and non-task-required effectors, suppressing activation of interfering and task-irrelevant effectors to prevent erroneous responses. In terms of neural mechanisms, the former is controlled by the dorsal premotor cortex, while the latter is controlled by the lateral prefrontal cortex (Duque et al., 2012; Labruna et al., 2014). In a study using repetitive TMS (rTMS) to interfere with activity in specific brain regions, Duque et al. (2012) found that after applying rTMS to the lateral prefrontal cortex, inhibition of interfering effectors was weakened; after applying rTMS to the dorsal premotor cortex, inhibition of task-required effectors was weakened. According to this model, although multiple effectors show inhibitory processing that appears "global" phenomenologically, the inhibition at different effectors actually belongs to different inhibitory processes controlled by different brain regions.

The spot-light model proposes that inhibition of task-relevant and task-irrelevant effectors originates from the same inhibitory system, which enhances the signal-to-noise ratio of the motor system through global inhibition (Greenhouse et al., 2015). In this process, simultaneous activation and inhibition of the motor system create gain modulation, such that the gain of motor system neural signals increases proportionally as background noise decreases (Baca et al., 2008; Chance et al., 2002). An analogy would be a classroom where one student is answering a question and the teacher instructs everyone to be quiet—although all students' voices (including the answering student' s) are reduced, the answering student' s voice becomes more salient. A recent study based on EMG from the responding hand supported the spot-light model. Using a Simon paradigm, Wang et al. (2021) also found that stronger inhibitory effects in interfering effectors were associated with weaker inhibitory effects in task-required effectors and faster conflict resolution.

The main difference between the dual-process and spot-light models lies in whether inhibitory processing across different effectors shares a common source, though they do not substantially disagree about the brain network involved in implementing response inhibition. According to traditional theory, response inhibition primarily involves a network from the prefrontal cortex to the basal ganglia, with key prefrontal regions including the pre-supplementary motor area and right inferior frontal cortex. Numerous systematic review papers have explored this network (Aron et al., 2016; Bari & Robbins, 2013; Wang & Cai, 2010), so this paper will not elaborate further.

The spot-light model is consistent with the normalization model in computational neuroscience (Carandini & Heeger, 2012). According to this model, the output strength of a neuron is achieved through a normalization computation of the activity intensity across the entire neuronal population. One variant of this model is shown in the formula. In this formula, I represents the activity of the neuron of interest (e.g., neural signals corresponding to the task-required effector), I represents the activity of other neurons (e.g., the sum of neural signals corresponding to interfering and task-irrelevant effectors). When the activity of the entire neuronal population decreases (e.g., through inhibition), the denominator becomes smaller ($I + I$ both decrease). Meanwhile, because the task-required effector must cross the motor threshold to produce a response, the activity magnitude of neurons corresponding to the task-required effector is much higher than that of other neurons, causing the denominator to decrease proportionally more than the numerator. In this case, neurons corresponding to the task-relevant effector show stronger activity after normalization (the output value R of I after normalization).

Understanding global inhibition from the perspectives of the spot-light model and normalization computation has important psychological and cognitive neuroscience implications. First, both models consistently reflect that response control is not an isolated cognitive component or neural processing mechanism but rather a coordinated cognitive process. This coordinated processing is particularly evident in tasks involving multiple effectors, manifesting as a trade-off between the degree of inhibition applied to interfering or task-irrelevant effectors and that applied to task-required effectors, showing "neural dynamics" (Wang, Chang et al., 2019; Wang et al., 2021). This has important implications for inhibitory training, providing more comprehensive explanations for existing training studies. For example, Go/NoGo training for response inhibition has been found to not only improve inhibition accuracy in NoGo conditions but also significantly speed up responses in Go conditions (Benikos et al., 2013), indicating that inhibitory training enhances not only stopping efficiency but also motor output efficiency. Additionally, this coordinated interaction helps consider the "costs and benefits" of inhibitory training—for instance, what impact does inhibitory training of one effector have on other effectors? How can we balance the different effects training has on multiple effectors? This allows for the design of better, more targeted training tasks based on task goals.

Another important implication is that it reflects common neural computational characteristics across different cognitive processes. From a neural computation perspective, global inhibition involves computational processes across multiple neural populations corresponding to different effectors, rather than simply inhibiting the neural population corresponding to task-irrelevant effectors. This normalization computation pattern of overall neural activity is not unique to the motor system but is also evident in visual attention (Denison et al., 2021), olfactory processing (Zhu et al., 2013), multisensory integration (Ohshiro et al., 2017), value representation and decision-making (Louie et al., 2013), and other cognitive functions. In visual attention, for instance, selective attention to certain information involves not just suppressing neural activity corresponding to distracting information but normalizing computation across the entire visual receptive field (Reynolds & Heeger, 2009). In value representation and decision-making, neural activity in the brain's value representation system for a particular option is not simply a function of that option' s value but is normalized relative to the values of multiple alternative options, with decisions based on normalized rather than absolute values (Louie et al., 2013). Multiple empirical studies have validated the normalization model as an important neural mechanism in visual attention, olfactory processing, multisensory integration, and value representation. However, in response control, there are currently only factor-based experimental results consistent with normalization model predictions; computational modeling-based empirical studies are still lacking. Filling this gap would not only advance research on the neural mechanisms of response control but also demonstrate the fundamentality and universality of the normalization model in neural computation (Reynolds & Heeger, 2009).

4 Controversies Related to Global Inhibition

4.1 Comparison of Different Classification Criteria for Inhibitory Processing

This paper employs two classifications to discuss and illustrate the characteristics of global inhibition: one classifies effectors, and the other classifies whether the cognitive context involves conflict. Notably, these classifications differ markedly from published review papers. For comprehensive coverage of inhibitory effects, Duque et al. (2017) detailed inhibitory processing into standard stopping vs. selective stopping, proactive inhibition vs. reactive inhibition, and preparatory inhibition. Standard vs. selective stopping differs in that the former involves only one effector without requiring effector selection (e.g., classic Stop-signal tasks), whereas the latter requires inhibiting one of two or more effectors. Proactive vs. reactive inhibition differs in that the former can predict whether inhibition will be needed based on experimental context or cues, enabling advance, active inhibition, whereas the latter cannot be predicted. Preparatory inhibition, proposed in contrast to non-preparatory inhibition, centers on cognitive preparation for the effector to be inhibited—for example, preparing to inhibit the right hand when a trial requires left-hand responding.

These classifications are not concerned with whether inhibition is global but aim to comprehensively introduce and summarize inhibitory effects. However, these subcategories lack clear boundaries and logical relationships, with some ambiguous overlaps. For instance, both selective and preparatory inhibition can be proactive or reactive, depending on whether the experimental context provides information to predict upcoming inhibition needs. The authors did not provide explicit, quantifiable classification models for what constitutes proactive selective inhibition. Furthermore, proactive inhibition can be achieved through training; the same experimental context may transition from reactive to proactive inhibition due to repetition of similar trials. These classifications do not reflect the distinction between top-down response inhibition (e.g., proactive and preparatory inhibition) and bottom-up response inhibition (e.g., reactive and non-preparatory inhibition). Additionally, different classification standards serve different purposes. The core of this paper is to discuss the global nature of inhibitory effects, which manifests across multiple effectors and task contexts, hence the classification based on effectors and task contexts. Future research should comprehensively and dialectically consider different classification methods, their different emphases in revealing inhibitory mechanisms, and what theoretical points these different classifications aim to illustrate.

4.2 Is Global Inhibition Independent of Task Context?

One controversy related to global inhibition concerns whether it is broadly involved in various contexts. Duque et al. (2017) argued that global inhibition is conditional and does not appear in selective stopping tasks, which instead show targeted inhibition of the specific effector that needs to be suppressed. For example, when a cue indicating which finger to inhibit is presented before inhibition occurs, no inhibitory effect is observed in leg muscles (task-irrelevant effectors) during the inhibition process (Aron & Verbruggen, 2008). Duque et al. (2017) thus proposed that different inhibitory mechanisms exist: global inhibition is more likely when the task emphasizes speed, whereas selective inhibition is more likely when the task emphasizes control over a specific response. This view treats global and selective inhibition as parallel, non-overlapping categories adopted by different task scenarios.

In contrast, Wessel and Aron (2017) reviewed global inhibition as a universal mechanism of the motor system, merely more observable under certain elicitation conditions, such as those requiring rapid responses. The former view tends to assume different mechanisms underlie different phenomena, whereas the latter considers global inhibition a universal mechanism with varying elicitation strength across experimental contexts. The efficiency of completing selective inhibition may affect the manifestation of global inhibition.

4.3 Comparison of "Holistic" vs. "Local" Theoretical Perspectives

Global inhibition is not merely a phenomenological description but provides a new "holistic" perspective for understanding response control, challenging the traditional "local" view. This holistic perspective can reflect the integrative and coordinated characteristics of the motor system, challenging the "local" and "isolated" perspectives of previous research. From the principle of parsimony, the holistic view offers theoretical economy—a theory with fewer untestable assumptions is more scientific. Under the global inhibition framework, the entire motor system is inhibited, with only differential degrees of inhibition across different motor neuron populations. These degrees can be measured through neural signals without introducing additional new hypothetical variables, representing a "monistic" approach where computational simulation involves different values of a single variable. If we assume global inhibition sometimes exists and sometimes does not, with some effectors being inhibited and others not, and some contexts requiring it while others do not, new assumptions would be needed to explain "which effectors need inhibition, which do not, and which contexts require it," representing a "pluralistic" approach involving multiple variables with multiple values, leading to excessive model degrees of freedom and reduced predictive power.

Compared to "local" theories, "holistic" theories emphasize relationships among components within a system and how these relationships affect the entire system. However, from an applied perspective, designing application systems (such as the aforementioned inhibitory training protocols) requires fully considering mutual influences and constraints among components, increasing design difficulty and complexity.

Nevertheless, whether global inhibition can be observed with existing methods and techniques is conditional, not whether global inhibition itself is conditional. This involves the bottleneck problem of current empirical research relying on p-values for statistical inference (Benjamin et al., 2018). Most current empirical research is based on significance testing with p-values, where "non-observation" of a phenomenon is typically based on null results (i.e., non-significant p-values), which cannot directly support the conclusion that an effect "will not occur" but only that there is "no evidence yet." Therefore, whether global inhibition is broadly involved in various tasks requires not only more empirical evidence but also comprehensive consideration of multiple statistical testing methods, such as Bayesian factor analysis in addition to traditional statistical analysis (Hu et al., 2018). Unlike traditional statistical methods, Bayesian factor analysis does not rely on p-values for statistical inference but quantifies the relative probability of the null hypothesis ("no effect") versus the alternative hypothesis ("effect") being true. A currently followed standard is that if the Bayes factor is greater than 3 (i.e., the probability of the null hypothesis being true is more than three times that of the alternative), there is considered to be some statistical evidence supporting the null hypothesis, allowing the conclusion of "no effect" (Wagenmakers et al., 2018). For example, if traditional statistics yield a non-significant p-value in global inhibition research, we cannot determine whether the null result is due to insufficient statistical power or because the effect truly does not exist. Conducting Bayesian factor analysis might yield BF = 4, leading to the statistical inference that "the probability of the null hypothesis being true is four times that of the alternative," 倾向于得出"这个效应不存在"的结论 rather than "we don' t know whether this effect exists." If BF = 1/4, the inference would be that "the probability of the null hypothesis being true is one-quarter that of the alternative," suggesting insufficient statistical power rather than non-existence of the effect, providing a basis for further verification.

Additionally, in the aforementioned studies that did not observe inhibition in task-irrelevant effectors, this phenomenon may be due to tasks being too simple or participants being over-trained, resulting in weak effects undetectable by traditional measurement methods. For example, Xu et al. (2015) found that selective inhibition could be better accomplished after extensive training, such that inhibiting task-irrelevant effectors no longer incurred additional cognitive costs. This suggests that it is not selective inhibition itself that weakens or eliminates global inhibition, but rather that well-practiced selective inhibition reduces the cognitive cost of inhibiting task-irrelevant effectors. Therefore, the "non-observation" of global inhibition in some studies may reflect insufficient effect magnitude rather than absence of the mechanism.

5 Summary and Outlook

In summary, response control involves not inhibition of a single effector but inhibitory processing of the entire motor system. Moreover, inhibitory effects are not unique to response conflict contexts but are broadly present in situations involving response output and execution. This global and widespread characteristic is important for understanding response output. First, any response output, regardless of whether explicit response conflict exists, requires suppressing task-irrelevant responses or response tendencies from other effectors and controlling the task-required effector to prevent premature responding. Second, from an evolutionary perspective, organisms have a tendency to respond to any external stimulus, and different effectors have differentiated from the same motor system. Humans evolved response inhibition and selective inhibition for current contexts. Therefore, global inhibition at the cognitive level reflects coordinated interactions among components of the motor system, while at the neural level it reflects computational processing efficiency, ensuring efficient response output and execution.

Although global inhibition appears stable across different experimental contexts and multiple effectors, the relationships among inhibitory effects at different effectors remain unclear. As noted, evidence shows that inhibition of one effector (e.g., the right hand) is accompanied by inhibition of another neurally homologous effector (e.g., the right leg), and inhibition of one sub-motor system (e.g., the oculomotor system) is accompanied by inhibition of another sub-motor system (e.g., the somatomotor system). However, the relationships among these inhibitory effects require further investigation. From the perspective of global inhibition, the entire motor system shows inhibitory effects after an inhibitory command is issued, but do the degrees of inhibition differ across subsystems or effectors? One cognitive-level hypothesis is that the stronger the interference an effector causes to the task-required effector, the stronger the inhibition it receives, with interference degree determined by task settings. If a task only requires bimanual button presses and not responses from other effectors, the inhibitory effect on the interfering hand would be stronger than on other effectors. A neural-level hypothesis is that the closer an effector' s neural representation is to that of the task-required effector, the stronger the inhibition it receives, making neural processing more efficient. In real-world situations, cognitive and neural factors likely interact, awaiting future verification.

Existing research on global inhibition has used factor-based experiments, comparing inhibition strength across different levels of an influencing factor (e.g., reward) to reveal global inhibition characteristics. While these factor-based experiments provide qualitative evidence, they cannot specify the precise functional relationships among inhibitory effects at different effectors. Future research should combine highly quantitative computational models to establish these functional relationships. Computational modeling can more accurately reflect how components of the motor system coordinate to improve response efficiency, offer high predictive power for new contexts, and integrate inhibitory effects across processing levels—revealing common patterns across molecular-level GABA activity, cortical-level primary motor cortex activity, and behavioral-level inhibition efficiency based on reaction time and accuracy.

The computational model that best fits current phenomena is the "normalization model." As discussed, the normalization model aligns with the spot-light model and has received support from studies manipulating reward levels (Wang et al., 2021). The normalization model is a classic model in computational neuroscience, not specific to particular cognitive components or experimental contexts (Carandini & Heeger, 2012; Salinas & Sejnowski, 2001), but widely present in visual selective attention (Reynolds & Heeger, 2009), multisensory integration (Ohshiro et al., 2017), and value computation and representation (Louie et al., 2013). Investigating whether the normalization model is the computational mechanism of global inhibition can reveal common computational mechanisms across different cognitive processes.

Response control is closely related to multiple psychological and psychiatric disorders. Behavioral and neural indices of global inhibition can effectively predict symptom severity and relapse rates in these populations, and studying global inhibition characteristics in these groups can enhance overall understanding of motor system processing patterns and efficiency. However, only a few addiction studies have examined global inhibition (Huang et al., 2017; Quoilin et al., 2018; Shen et al., 2019), with no research yet on other disorders such as OCD and ADHD. Future studies should increase research on clinical populations to build more comprehensive, targeted, and predictive models by comparing similarities and differences in inhibitory effects across disorders. Additionally, traditional response inhibition perspectives in designing training tasks have shown poor transfer across task contexts (Enge et al., 2014) and limited intervention effects on disorders (Bowley et al., 2013). The global inhibition perspective offers new insights for training and intervention: first, training task design should consider potential impacts on multiple effectors rather than isolated effects on a single effector; second, tasks reflecting cognitive flexibility and response coordination should be used to improve inhibitory dysfunction in clinical populations rather than focusing solely on response inhibition training for specific stimuli (e.g., addiction cues). Recent studies have found bimanual drumming training effective for intervening in autism and dementia (Cahart et al., 2022; Miyazaki et al., 2020), and current developments in virtual reality technology and digital medicine can provide better conditions and application prospects for developing training protocols that reflect motor system flexibility, enhancing treatment efficacy.

References

Hu, C. P., Kong, X. Z., Wagenmakers, E. -J., Ly, A., & Peng, K. P. (2018). Bayesian factors and their implementation in JASP. *Advances in Psychological Science*, 26(6), 951-965.

Su, B. B., & Zheng, M. H. (2019). Effects of substance-related cues on response inhibition in addicts. *Advances in Psychological Science*, 27(11), 1863–1874.

Wang, Y., & Cai, H. D. (2010). Psychological processing models and neural mechanisms of response inhibition. *Advances in Psychological Science*, 18(2), 220–229.

Zhao, X., Liu, X. T., Zan, X. Y., & Zhou, A. B. (2015). Effects of smoking on response inhibition: Evidence, causes, and controversies. *Advances in Psychological Science*, 23(6), 342–348.

Aron, A. R. (2011). From reactive to proactive and selective control: Developing a richer model for stopping inappropriate responses. *Biological Psychiatry*, 69(12), e55–e68.

Aron, A. R., Herz, D. M., Brown, P., Forstmann, B. U., & Zaghloul, K. (2016). Frontosubthalamic circuits for control of action and cognition. *Journal of Neuroscience*, 36(45), 11489–11495.

Aron, A. R., & Verbruggen, F. (2008). Stop the presses: Dissociating a selective from a global mechanism for stopping. *Psychological Science*, 19(11), 1146–1153.

Baca, S. M., Marin-Burgin, A., Wagenaar, D. A., & Kristan, W. B. Jr. (2008). Widespread inhibition proportional to excitation controls the gain of a leech behavioral circuit. *Neuron*, 57(2), 276–289.

Badry, R., Mima, T., Aso, T., Nakatsuka, M., Abe, M., Fathi, D., ···Fukuyama, H. (2009). Suppression of human cortico-motoneuronal excitability during the stop-signal task. *Clinical Neurophysiology*, 120(9), 1717–1723.

Bari, A., & Robbins, T. W. (2013). Inhibition and impulsivity: Behavioral and neural basis of response control. *Progress in Neurobiology*, 108, 44–79.

Benjamin, D. J., Berger, J. O., Johannesson, M., Nosek, B. A., Wagenmakers, E. -J., Berk, R., ···Johnson, V. E. (2018). Redefine statistical significance. *Nature Human Behavior*, 2(1), 6–10.

Bestmann, S., & Duque, J. (2016). Transcranial magnetic stimulation: Decomposing the processes underlying action preparation. *The Neuroscientist*, 22(4), 392–405.

Bestmann, S., & Krakauer, J. W. (2015). The uses and interpretations of the motor-evoked potential for understanding behaviour. *Experimental Brain Research*, 233(3), 679–689.

Botvinick, M., & Braver, T. (2015). Motivation and cognitive control: From behavior to neural mechanism. *Annual Review of Psychology*, 66, 83–113.

Boucher, L., Palmeri, T. J., Logan, G. D., & Schall, J. D. (2007). Inhibitory control in mind and brain: An interactive race model of countermanding saccades. *Psychological Review*, 114(2), 376-397.

Bowley, C., Faricy, C., Hegarty, B., Johnstone, S. J., Smith, J. L., Kelly, P. J., & Rushby, J. A. (2013). The effects of inhibitory control training on alcohol consumption, implicit alcohol-related cognitions and brain electrical activity. *International Journal of Psychophysiology*, 89(3), 1031–1040.

Braver, T. S. (2012). The variable nature of cognitive control: A dual mechanisms framework. *Trends in Cognitive Sciences*, 16(2), 106–113.

Bundt, C., Abrahamse, E. L., Braem, S., Brass, M., & Notebaert, W. (2016). Reward anticipation modulates primary motor cortex excitability during task preparation. *NeuroImage*, 142, 483–488.

Cahart, M., Amad, A., Draper, S. B., Lowry, R. G., Marino, L., Carey, C., ···Williams, S. C. R. (2022). The effect of learning to drum on behavior and brain function in autistic adolescents. *Proceedings of the National Academy of Sciences of the United States of America*, 119(23), Article e2106244119. https://doi.org/10.1073/pnas.2106244119

Cai, W., Oldenkamp, C. L., & Aron, A. R. (2012). Stopping speech suppresses the task-irrelevant hand. *Brain & Language*, 120(3), 412–415.

Carandini, M., & Heeger, D. J. (2012). Normalization as a canonical neural computation. *Nature Reviews Neuroscience*, 13, 51–62.

Chambers, C. D., Garavan, H., & Bellgrove, M. A. (2009). Insights into the neural basis of response inhibition from cognitive and clinical neuroscience. *Neuroscience & Biobehavioral Reviews*, 33(5), 631–646.

Chance, F. S., Abbott, L. F., & Reyes, A. D. (2002). Gain modulation from background synaptic input. *Neuron*, 35(4), 773–782.

Coxon, J. P., Stinear, C. M., & Byblow, W. D. (2006). Intracortical inhibition during volitional inhibition of prepared action. *Journal of Neurophysiology*, 95(6), 3371–3383.

Denison, R. N., Carrasco, M., & Heeger, D. J. (2021). A dynamic normalization model of temporal attention. *Nature Human Behaviour*, 5(12), 1674–1685.

Duque, J., Greenhouse, I., Labruna, L., & Ivry, R. B. (2017). Physiological markers of motor inhibition during human behavior. *Trends in Neurosciences*, 40(4), 219-236.

Duque, J., Labruna, L., Verset, S., Olivier, E., & Ivry, R. B. (2012). Dissociating the role of prefrontal and premotor cortices in controlling inhibitory mechanisms during motor preparation. *Journal of Neuroscience*, 32(3), 806–816.

Duque, J., Lew, D., Mazzocchio, R., Olivier, E., & Ivry, R. B. (2010). Evidence for two concurrent inhibitory mechanisms during response preparation. *Journal of Neuroscience*, 30(10), 3793-3802.

Enge, S., Behnke, A., Fleischhauer, M., Kuttler, L., Kliegel, M., & Strobel, A. (2014). No evidence for true training and transfer effects after inhibitory control training in young healthy adults. *Journal of Experimental Psychology: Learning, Memory, & Cognition*, 40(4), 987-1001.

Fisher, R. J., Nakamura, Y., Bestmann, S., Rothwell, J. C., & Bostock, H. (2002). Two phases of intracortical inhibition revealed by transcranial magnetic threshold tracking. *Experimental Brain Research*, 143(2), 240-248.

Freeman, S. M., & Aron, A. R. (2016). Withholding a reward-driven action: Studies of the rise and fall of motor activation and the effect of cognitive depletion. *Journal of Cognitive Neuroscience*, 28(2), 237-251.

Freeman, S. M., Razhas, I., & Aron, A. R. (2014). Top-down response suppression mitigates action tendencies triggered by a motivating stimulus. *Current Biology*, 24(2), 212-216.

Greenhouse, I., Sias, A., Labruna, L., & Ivry, R. B. (2015). Nonspecific inhibition of the motor system during response preparation. *Journal of Neuroscience*, 35(30), 10675-10684.

Huang, X., Chen, Y. Y., Shen, Y., Cao, X., Li, A., Liu, Q., ···Yuan, T. F. (2017). Methamphetamine abuse impairs motor cortical plasticity and function. *Molecular Psychiatry*, 22(9), 1274-1281.

Klein, P. A., Petitjean, C., Olivier, E., & Duque, J. (2014). Top-down suppression of incompatible motor activations during response selection under conflict. *NeuroImage*, 86, 138-149.

Labruna, L., Lebon, F., Duque, J., Klein, P. A., Cazares, C., & Ivry, R. B. (2014). Generic inhibition of the selected movement and constrained inhibition of nonselected movements during response preparation. *Journal of Cognitive Neuroscience*, 26(2), 269-278.

Logan, G. D. (1994). On the ability to inhibit thought and action: A users' guide to the stop signal paradigm. In D. Dagenbach & T. H. Carr (Eds.), *Inhibitory processes in attention, memory, & language* (pp. 189-239). San Diego: Academic Press.

Louie, K., Khaw, M. W., & Glimcher, P. W. (2013). Normalization is a general neural mechanism for context-dependent decision making. *Proceedings of the National Academy of Sciences of the United States of America*, 110(15), 6139-6144.

Majid, D. S. A., Cai, W., George, J. S., Verbruggen, F., & Aron, A. R. (2012). Transcranial magnetic stimulation reveals dissociable mechanisms for global versus selective corticomotor suppression underlying the stopping of action. *Cerebral Cortex*, 22(2), 363-371.

Miyazaki, A., Okuyama, T., Mori, H., Sato, K., Ichiki, M., & Nouchi, R. (2020). Drum communication program intervention in older adults with cognitive impairment and dementia at nursing home: Preliminary evidence from pilot randomized controlled trial. *Frontiers in Aging Neuroscience*, 12, Article 142. https://doi.org/10.3389/fnagi.2020.00142

Ohshiro, T., Angelaki, D. E., & DeAngelis, G. C. (2017). A neural signature of divisive normalization at the level of multisensory integration in primate cortex. *Neuron*, 95(2), 399-411.

Quoilin, C., Wilhelm, E., Maurage, P., de Timary, P., & Duque, J. (2018). Deficient inhibition in alcohol-dependence: Let' s consider the role of the motor system! *Neuropsychopharmacology*, 43(9), 1851-1858.

Reynolds, J. H., & Heeger, D. J. (2009). The normalization model of attention. *Neuron*, 61(2), 168-185.

Ridderinkhof, K. R. (2002). Activation and suppression in conflict tasks: Empirical clarification through distributional analyses. In W. Prinz & B. Hommel (Eds.), *Mechanisms in perception and action* (pp. 494-519). Oxford: Oxford University Press.

Salinas, E., & Sejnowski, T. J. (2001). Gain modulation in the central nervous system: Where behavior, neurophysiology, and computation meet. *The Neuroscientist*, 7(5), 430-440.

Salzer, Y., de Hollander, G., & Forstmann, B. U. (2017). Sensory neural pathways revisited to unravel the temporal dynamics of the Simon effect: A model-based cognitive neuroscience approach. *Neuroscience & Biobehavioral Reviews*, 77, 48-57.

Shen, Y., Cao, X., Shan, C., Dai, W., & Yuan, T. F. (2017). Heroin addiction impairs human cortical plasticity. *Biological Psychiatry*, 81(7), e49-e50.

van Campen, A. D., Keuken, M. C., van den Wildenberg, W. P. M., & Ridderinkhof, K. R. (2014). TMS over M1 reveals expression and selective suppression of conflicting action impulses. *Journal of Cognitive Neuroscience*, 26(1), 1-15.

van den Wildenberg, W. P. M., Burle, B., Vidal, F., van der Molen, M. W., Ridderinkhof, K. R., & Hasbroucq, T. (2010). Mechanisms and dynamics of cortical motor inhibition in the stop-signal paradigm: A TMS study. *Journal of Cognitive Neuroscience*, 22(2), 225-239.

Wagenmakers, E., Love, J., Marsmann, M., Jamil, T., Ly, A., Verhagen, J., ···Morey, R. D. (2018). Bayesian inference for psychology. Part II: Example applications with JASP. *Psychonomic Bulletin & Review*, 25(1), 58-76.

Wang, L., Chang, W., Krebs, R. M., Boehler, C. N., Theeuwes, J., & Zhou, X. (2019). Neural dynamics of reward-induced response activation and inhibition. *Cerebral Cortex*, 29(9), 3961-3976.

Wang, L., Luo, X., Yuan, T. F., & Zhou, X. (2021). Reward facilitates response conflict resolution via global motor inhibition: Electromyography evidence. *Psychophysiology*, 58(10), e13896. https://doi.org/10.1111/psyp.13896

Wang, Y., Braver, T. S., Yin, S., Hu, X., Wang, X., & Chen, A. (2019). Reward improves response inhibition by enhancing attentional capture. *Social Cognitive & Affective Neuroscience*, 14(1), 35-45.

Wessel, J. R., & Aron, A. R. (2017). On the globality of motor suppression: Unexpected events and their influence on behavior and cognition. *Neuron*, 93(2), 259-280.

Wessel, J. R., Reynoso, H. S., & Aron, A. R. (2013). Saccade suppression exerts global effects on the motor system. *Journal of Neurophysiology*, 110(4), 883-890.

Xu, J., Westrick, Z., & Ivry, R. B. (2015). Selective inhibition of a multicomponent response can be achieved without cost. *Journal of Neurophysiology*, 113(2), 455-464.

Zhu, P., Frank, T., & Friedrich, R. W. (2013). Equalization of odor representations by a network of electrically coupled inhibitory interneurons. *Nature Neuroscience*, 16(11), 1678-1686.

Note: Figure translations are in progress. See original paper for figures.