# The Brain's brake: Inhibitory mechanisms in cognition and action

Paolo Bartolomeo, Giuseppe Di Pellegrino, Leonardo Chelazzi

## To cite this version:

Paolo Bartolomeo, Giuseppe Di Pellegrino, Leonardo Chelazzi. The Brain's brake: Inhibitory mechanisms in cognition and action. Cortex, 2022, 157, pp.323-326. 10.1016/j.cortex.2022.10.009 . hal-03865455

HAL Id: hal-03865455
https://hal.sorbonne-universite.fr/hal-03865455

Submitted on 22 Nov 2022

The Brain’s Brake: Inhibitory Mechanisms in Cognition and Action

Paolo Bartolomeo, Giuseppe di Pellegrino, Leonardo Chelazzi

PII: S0010-9452(22)00294-5

DOI: https://doi.org/10.1016/j.cortex.2022.10.009

Reference: CORTEX 3586

To appear in: *Cortex*

Received Date: 13 October 2022

Revised Date: 22 October 2022

Accepted Date: 23 October 2022

Please cite this article as: Bartolomeo P, di Pellegrino G, Chelazzi L, The Brain’s Brake: Inhibitory Mechanisms in Cognition and Action, *CORTEX*, https://doi.org/10.1016/j.cortex.2022.10.009.

# The Brain's Brake: Inhibitory Mechanisms in Cognition and Action

Paolo Bartolomeo[1], Giuseppe di Pellegrino[2], Leonardo Chelazzi[3]

1. Sorbonne Université, Institut du Cerveau - Paris Brain Institute - ICM, Inserm, CNRS, AP-HP, Hôpital de la Pitié-Salpêtrière, F-75013 Paris, France , Email : paolo.bartolomeo@icm-institute.org

2. Centre for Studies and Research in Cognitive Neuroscience, Department of Psychology, University of Bologna, 47521 Cesena – FC, Italy Email: g.dipellegrino@unibo.it

3. Dipartimento di Neuroscienze, Biomedicina e Movimento, Sezione di Fisiologia e Psicologia, Università di Verona, Strada Le Grazie, 8, 37134 Verona, Italy Email: leonardo.chelazzi@univr.it

Recent years have witnessed an increasing interest into putative brain mechanisms for exerting inhibitory control onto a variety of processes and representations, including in the domain of action initiation, attention, emotion and memory. In June 2019, a session of the International Neuropsychological Symposium held in Vietri, Italy, was dedicated to these issues. This Special Issue mainly contains contributions to this session, with some additional material. The contributions present abundant behavioral, modeling, neural and clinical evidence about the various dedicated inhibitory systems of the brain. The distinct role of these systems is to inhibit certain processes or representations, depending on the given circumstances (and whose function likely depends as much on inhibitory neurons as it does on excitatory ones). In other words, the brain must sometimes rely on these systems to (rapidly and actively) inhibit – or stop – unwanted motor responses, undesirable thoughts and memories, or the attentional deployment to distracting stimuli. The scope of this Special Issue is to provide an up-to-date landscape of such mechanisms. The growing body of research in this domain has not only provided exciting new empirical findings by means of different techniques and model systems but has also stimulated hot debates at the theoretical level.

### *Inhibition: from neurons to networks*

With inhibitory processes, we are not only referring to the obvious notion that the brain tissue contains inhibitory as well as excitatory neurons; nevertheless, these basic phenomena remain foundational aspects of cognitive functioning. Lourenço, Koukouli, and Bacci (2020) provide an updated account of the complex patterns of balance between excitatory and inhibitory activity in the neocortex, from the dendro-somatic axis of single neurons to canonical cortical circuits, and conclude by providing perspectives on the role of inhibitory circuits in brain disorders. Using a novel co-registration of mouse-trajectories and EEG, Tafuro, Vallesi, and Ambrosini (2020) identify ERP components of movement inhibition and adjustment in a spatial Stroop task, thus shedding light on the close relationship between motor and cognitive control. In a TMS study, Cardellicchio, Dolfini, Fadiga, and D'Ausilio (2020) investigate motor inhibitory processes during a joint action task (i.e., reaching and opening a screw cap bottle held by a confederate). Their findings reveal the critical role played by corticospinal inhibitory mechanisms to achieve spatial and temporal action coordination between interacting agents. Doekemeijer, Verbruggen and Boehler (2021) examine how reward affects response inhibition in a stop-signal task, one of the hallmark tasks to study responses inhibition. Their findings show that reward reduces ‘trigger failures”, i.e., the rate of unsuccessful stop trials, possibly by enhancing attentional processes and invigorating specific attention-related brain areas.

Hoofs et al. (2021) look at the neural underpinnings of response inhibition in the context of motivation and cognitive control interaction. Specifically, their fMRI results focus on the anterior cingulate cortex (ACC), a frontal area that has been implicated in cognitive control and response selection, especially in the context of conflict and value-based decision making.

Neocortical regions interact with subcortical structures to implement inhibitory control. Among the basal ganglia, the subthalamic nucleus is a crucial structure to inhibit unwanted movements. Its “brake” function, however, also extends to the cognitive domain of action selection, as well as to other cognitive domains, including visuo-spatial attention and emotional-motivational control. Van Wijk, Alkemade and Forstmann (2020) present an in-depth analysis of anatomical and functional aspects of the subthalamic nucleus and its associated circuitry, particularly the “hyperdirect” connection from the prefrontal cortex, which could initiate the “stop” process. Van Wijk et al. conclude that the classical tripartite subdivision into sensorimotor, cognitive, and limbic subregions is inadequate, because there is considerable cross-talk between the putative subdivisions. They conclude that regional specialization does exist in the subthalamic nucleus, but without sharply defined borders.

### *Inhibition in attention networks*

In a quest to assess the existence of supramodal mechanisms of attention, Spagna et al. (2020) compared participants’ performance on unimodal vs. crossmodal attentional tasks tapping on executive control resources. Using a clever experimental manipulation and a between-subject design they observed comparable interaction effects in the two tasks. Specifically, whether the interference effect produced by the dual task was caused by visual (i.e., unimodal) or crossmodal (visual and auditory) stimuli, the processing of the first task always interfered with the processing of the second task. This interference effect was observed on the response time pattern, and only under strict time constraints (i.e., the two tasks were separated only by 100ms), while the extent of the effect was significantly smaller when enough time was left between the two tasks (above 1,000ms). These results were in line with the authors’ hypothesis that the same pool of attentional resources was deployed in both tasks.

### *Learning to inhibit distractors in visual search*

Distractor suppression is perhaps the most typical “inhibitory” phenomenon in the domain of selective attention. Can we learn to suppress distractors, in order to reduce their interference with the task at hand? We can indeed optimize distractor suppression, for example when color singleton distractors appear with high, predictable frequency. Won et al. (2020) used fMRI to investigate the neural bases of this learning process, and found that the learned attenuation of distractor interference was related to decreased activations in retinotopic visual cortex. Furthermore, high-frequency distractors led to decreased parietal activity as compared with low-frequency distractors, likely because of lesser attention capture with high-frequency distractors than with low-frequency distractors. Won et al concluded that learning to suppress distractors attenuates distractor-related activity in visual cortex, leading to less competition for attentional priority in frontoparietal networks.

Does this implication of early visual cortex in learned distractor suppression mean that this form of statistical learning might take place also when attention is minimal or absent? Duncan and Theeuwes (2020) found behavioral evidence consistent with this hypothesis. In a training phase, they presented color singletons in high-probability or low-probability locations, but asked participants just to report the global configuration of the display (a global circle or a global diamond shape). Only in a subsequent test phase were participants required to search for a shape singleton (diamonds among circles or circles among diamonds), while ignoring the color singleton. Response times to the targets exhibited a suppression effect (albeit a small and short-timed one), consistent with the contingencies of the previous, global task. Thus, participants could learn statistical regularities even without explicitly paying attention to targets and distractors.

In addition to decreased attentional capture, learned distractor suppression may also attenuate distractor interference by increasing the speed of attention disengagement from the distractor. Can we learn to disengage our gaze faster from frequently occurring distractors? Sauter et al. (2021) used oculomotor analysis to answer positively to this question. Specifically, they show that statistical learning of likely distractor locations decreased the latency of saccades away from the distractor. Sauter et al concluded that there are both pre- and post-selection mechanisms of distractor suppression: respectively, prevention of attention capture and faster attention disengagement. The rapid-disengagement effect might depend on two possibly interacting mechanisms: faster "reject" decisions resulting from a bias in distractor identification, and pro-active suppression of the residual priority signal.

Bonetti, Valsecchi and Turatto (2020) also addressed the issue of distractor suppression by studying the dynamics of eye movements, but they focused on microsaccades during fixation. They asked whether habituation to peripheral distractors (less oculomotor capture after repeated presentations) occurred at the saccadic programming stage, or at the saccade execution stage. Bonetti et al leveraged on the short-lasting, phasic inhibition of microsaccades induced by reflexive saccades. They reasoned that, if habituation of reflexive saccades occurs at the saccade programming stage, then also the occurrence of microsaccades should decrease. If, instead, habituation occurs at the stage of saccade execution, then it should not influence the frequency of microsaccades. The last possibility turned out to be true: microsaccade frequency did not change with habituation. Thus, saccadic programming does not seem to be influenced by habituation to distractors, consistent with studies in monkeys, indicating that saccade adaptation takes place downstream from the superior colliculus.

Lega et al. (2020) explored the causal role of key regions of the ventral attention network, namely the temporoparietal junction (TPJ) and the middle frontal gyrus (MFG) of the right hemisphere, in attentional capture and context-dependent distractor suppression mechanisms. The authors found that in neither site did TMS produce measurable effects in the overall ability to suppress salient-yet irrelevant distractors. However, they provided clear-cut evidence for a direct role of right TPJ in modulating the influence of inter-trial contingencies on distractor filtering mechanisms. In typical conditions, the deleterious impact of a salient distractor in the current trial is mitigated when a distractor is also present in the immediately preceding trial and, conversely, it is magnified following a distractor-absent trial. The authors demonstrated that, under stimulation of the right TPJ, the distractor cost on the current trial was further magnified in the latter condition and robustly minimized in the former condition. Lega et al. concluded that this pattern of results is well accounted for in terms of enhancement of rapid updating mechanisms of an internal model based on evidence gathered through recent events, thus making the system especially susceptible to the last episode of attentional processing. The specific claim made by the authors is that the right TPJ is a crucial hub for the updating of the predictive model that dynamically regulates proactive distractor-filtering mechanisms. Lega et al.'s results fit nicely within an emerging and vivacious area of research concerning the neural bases of distractor filtering, and provide novel evidence on the neural underpinnings of their modulation by recent trial history.

### *Clinical implications*

Deficits of inhibitory processes are prominent in some neurological conditions. Migliaccio et al. (2020) review inhibition deficits in neurodegenerative dementias through behavioral, cognitive, neuroanatomical and neurophysiological studies. In an innovative way, Migliaccio et al. discuss impulsivity and compulsivity behaviors within the spectrum of inhibition deficits. They highlight the current interests and limits of tests and questionnaires available to assess behavioral and cognitive inhibition in clinical practice and in clinical research. Their review contains a compendium of (1) different manifestations of disinhibition across several neurodegenerative diseases, (2) recent findings about structural, metabolic, functional, neurophysiological and neuropathological correlates of inhibition impairments, with emphasis on brain networks supporting such behaviors. Migliaccio et al. conclude by outlining the latest pharmacological treatment options available to treat disinhibition in neurological patients.

### *Perspectives for future research*

The articles collected in this special issue provide an extensive and reasonably complete overview of the rich landscape of present research on inhibitory processes in cognitive, affective, and motor processing. The reader may note that many issues remain unsettled. Among these, at least two deserve mention here, as important candidates for future research efforts. First, it is being disputed whether the brain systems for inhibitory control are supramodal in nature, i.e., are engaged to exert inhibitory control regardless of the critical process or representation, for instance in the domain of perception, action initiation, memory or thought, or whether separate sub-systems exist to take care of inhibition within each sub-domain of brain function. Second, the very nature of the putative inhibitory system is still under debate. According to some, the exquisite role of the system is indeed to inhibit processes or representations; whereas for others inhibitory control is just one facet of cognitive control in general, with no need for a specialized, distinct inhibitory module or network. We hope that the present studies will contribute to set the terms of the debate for these and other open issues in the domain of inhibition, and we wish to warmly thank the authors and the reviewers that allowed us to collect them in this special issue.

## REFERENCES

Bonetti, F., Valsecchi, M., & Turatto, M. (2020). Microsaccades inhibition triggered by a repetitive visual distractor is not subject to habituation: Implications for the programming of reflexive saccades. *Cortex*, *131*, 251–264. https://doi.org/10.1016/j.cortex.2020.07.013

Cardellicchio, P., Dolfini, E., Fadiga, L., & D'Ausilio, A. (2020). Parallel fast and slow motor inhibition processes in Joint Action coordination. *Cortex*, *133*, 346–357. https://doi.org/10.1016/j.cortex.2020.09.029

Doekemeijer, R. A., Verbruggen, F., & Boehler, C. N. (2021). Face the (trigger) failure: Trigger failures strongly drive the effect of reward on response inhibition. *Cortex*, *139*, 166–177. https://doi.org/10.1016/j.cortex.2021.02.025

Duncan, D., & Theeuwes, J. (2020). Statistical learning in the absence of explicit top-down attention. *Cortex*, *131*, 54–65. https://doi.org/10.1016/j.cortex.2020.07.006

Giarrocco, F., Bardella, G., Giamundo, M., Fabbrini, F., Brunamonti, E., Pani, P., & Ferraina, S. (2021). Neuronal dynamics of signal selective motor plan cancellation in the macaque dorsal premotor cortex. *Cortex*, *135*, 326–340. https://doi.org/10.1016/j.cortex.2020.09.032

Hoofs, V., Park, H. R. P., Vermeylen, L., Boehler, C. N., & Krebs, R. M. (2021). Neural underpinnings of valence-action interactions triggered by cues and targets in a rewarded approach/avoidance task. *Cortex*, *141*, 240–261. https://doi.org/10.1016/j.cortex.2021.04.013

Lega, C., Santandrea, E., Ferrante, O., Serpe, R., Dolci, C., Baldini, E., Cattaneo, L., & Chelazzi, L. (2020). Modulating the influence of recent trial history on attentional capture via transcranial magnetic stimulation (TMS) of right TPJ. *Cortex*, *133*, 149–160. https://doi.org/10.1016/j.cortex.2020.09.009

Lourenço, J., Koukouli, F., & Bacci, A. (2020). Synaptic inhibition in the neocortex: Orchestration and computation through canonical circuits and variations on the theme. *Cortex*, *132*, 258–280. https://doi.org/10.1016/j.cortex.2020.08.015

Migliaccio, R., Tanguy, D., Bouzigues, A., Sezer, I., Dubois, B., Le Ber, I., Batrancourt, B., Godefroy, V., & Levy, R. (2020). Cognitive and behavioural inhibition deficits in neurodegenerative dementias. *Cortex*, *131*, 265–283. https://doi.org/10.1016/j.cortex.2020.08.001

Prutean, N., Martín-Arévalo, E., Leiva, A., Jiménez, L., Vallesi, A., & Lupiáñez, J. (2021). The causal role of DLPFC top-down control on the acquisition and the automatic expression of implicit learning: State of the art. *Cortex*, *141*, 293–310. https://doi.org/10.1016/j.cortex.2021.04.012

Sauter, M., Hanning, N. M., Liesefeld, H. R., & Müller, H. J. (2021). Post-capture processes contribute to statistical learning of distractor locations in visual search. *Cortex*, *135*, 108–126. https://doi.org/10.1016/j.cortex.2020.11.016

Spagna, A., Wu, T., Kim, K., & Fan, J. (2020). Supramodal executive control of attention: Evidence from unimodal and crossmodal dual conflict effects. *Cortex*, *133*, 266–276. https://doi.org/10.1016/j.cortex.2020.09.018

Tafuro, A., Vallesi, A., & Ambrosini, E. (2020). Cognitive brakes in interference resolution: A mouse-tracking and EEG co-registration study. *Cortex*, *133*, 188–200. https://doi.org/10.1016/j.cortex.2020.09.024

van Moorselaar, D., Daneshtalab, N., & Slagter, H. A. (2021). Neural mechanisms underlying distractor inhibition on the basis of feature and/or spatial expectations. *Cortex*, *137*, 232–250. https://doi.org/10.1016/j.cortex.2021.01.010

van Wijk, B. C. M., Alkemade, A., & Forstmann, B. U. (2020). Functional segregation and integration within the human subthalamic nucleus from a micro- and meso-level perspective. *Cortex*, *131*, 103–113. https://doi.org/10.1016/j.cortex.2020.07.004

Won, B.-Y., Forloines, M., Zhou, Z., & Geng, J. J. (2020). Changes in visual cortical processing attenuate singleton distraction during visual search. *Cortex*, *132*, 309–321. https://doi.org/10.1016/j.cortex.2020.08.025