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Unexpected Events Activate a Frontal-Basal-Ganglia Inhibitory Network: What Is the Role of the Pre-Supplementary Motor Area?

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Review of Sebastian et al.

We often encounter unexpected events in the environment and must decide on the most appropriate course of action as we react. For example, if a pitcher throws a curveball after throwing fastballs, the batter must rapidly decide whether to swing (action) or to not swing (inhibition). The theory of Wessel and Aron (2017) concerning unexpected events explains how the batter might make quick adaptations to actions in the face of violated expectations. They proposed that unexpected events lead to the interruption of ongoing cognitive and motor programs by the fronto-basal ganglia network, a network mostly known for facilitating outright action cancellation. Thus, this short-lived interruption of ongoing action and cognition is thought to enable quick attentional reorienting and rapid adaptation of action following all unexpected events (i.e., not just those requiring response inhibition).

Consistent with a common role for the fronto-basal ganglia network in adapting action during both cancellation and surprise, unexpected events and action cancellation elicit common functional signatures such as the frontocentral P3 event-related potential measured with electroencephalography, suppression of corticospinal excitability measured with transcranial magnetic stimulation, reduction in isometric force, and behavioral slowing (Parmentier, 2008; Elchlepp et al., 2016; Dutra et al., 2018; Novembre et al., 2019). However, these previous studies did not directly investigate the extent of the neuroanatomical networks involved in detecting unexpected events versus outright action cancellation. In addition, much of the work leading to the hypothesis by Wessel and Aron (2017) of unexpected events involved events that were not only infrequent, but also novel. This raises the question of which aspects of unexpectedness prompt inhibition where none is required. In a recent article, Sebastian et al. (2020) used functional magnetic resonance imaging (fMRI) to test the prediction by Wessel and Aron (2017) that the *entire* fronto-basal ganglia network is recruited in response to familiar unexpected events regardless of whether those events require action inhibition.

Sebastian et al. (2020) provide compelling, network-level evidence in support of the framework of Wessel and Aron (2017). While undergoing fMRI scanning, participants in the study completed a cued Go/NoGo task, wherein expectancy was manipulated by cues that indicated whether the upcoming trial was more likely to be a Go or a NoGo trial. The fMRI data were analyzed using Bayesian methods and conjunction analyses, which are particularly well suited to investigate the prediction that unexpected events linked to different response requirements recruit the *same* network. Differences in blood oxygenation level-dependent (BOLD) activity elicited during Unexpected Go and NoGo trials versus Expected Go and NoGo trials revealed common underlying activation in the right inferior frontal cortex (rIFC), pre-supplementary motor area (pre-SMA), striatum, and subthalamic nucleus (STN). A conjunction analysis further indicated that the same regions were recruited during both Unexpected Go and NoGo trials. Notably, these regions included rIFC, pre-SMA, and STN, which compose the main nodes of the fronto-basal ganglia network implicated in outright action cancellation (Aron, 2011). Moreover, motor slowing was evident in lengthened reaction times in Unexpected Go trials compared with Expected Go trials, though no inhibition was required. Sebastian et al. (2020) thereby provide clear evidence that the fronto-basal ganglia network is recruited by unexpected events requiring action and that its recruitment leads to motor

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inhibitory control. In addition, because they control for novelty in their design by using unexpected stimuli that are infrequent but identical each time they occur, they clarify that infrequency alone is sufficient to recruit this inhibitory network.

It is significant that Sebastian et al. (2020) found both rIFC and pre-SMA to be activated by unexpected events because the respective contributions of these regions during outright action cancellation are widely contested. Though many perspectives on this debate have been offered in the literature, we here summarize two prevalent, opposing views. One view proposes that the rIFC acts as a braking mechanism (Aron et al., 2014), actively implementing inhibitory control by way of the monosynaptic hyperdirect pathway from the rIFC to the STN (Chen et al., 2020). Another view argues that the rIFC is likely involved in orienting attention toward stimuli that cue cancellation (in line with its association with frontal attention networks; Corbetta and Shulman, 2002; Hampshire et al., 2010), but that the pre-SMA more likely implements active action cancellation processes (Duann et al., 2009; Sharp et al., 2010). Based on these perspectives, it is not surprising that Sebastian et al. (2020) found rIFC activation in Unexpected conditions. In contrast, the finding of pre-SMA activation outside the context of outright action cancellation (i.e., during Unexpected Go trials) invites a reconsideration of the functional role of this area in inhibitory tasks. Given the rIFC's connections to STN and the links between STN activity and corticospinal inhibition (Aron and Poldrack, 2006; Wessel and Aron, 2017; Chen et al., 2020), the involvement of pre-SMA is likely not required to induce slowing after unexpected events.

What process, then, is the pre-SMA implementing in response to unexpected events? In considering this question, we think an alternative conceptualization of the task of Sebastian et al. (2020) is highly informative. Their task contains a within-block manipulation of Go/NoGo probability. That is, conditions that contain Expected Go and Unexpected NoGo cues create contingencies closely resembling those of classical NoGo paradigms with unexpected NoGo trials. In these conditions, participants expect to make a response and do not expect having to stop one. Following Expected NoGo and Unexpected Go cues, however, inhibition is the norm and responses are rare. Consequently, the conditions have differences in the degree to which they elicit proactive inhibitory control. Generally, proactive control is conceptualized as biasing response speed to allow for inhibition (Chikazoe et al., 2009), and it has been suggested that the pre-SMA is involved in the implementation of these proactive strategies when preparing to stop (Swann et al., 2012). If the pre-SMA is strictly responsible for implementing proactive control strategies, one might predict the Unexpected Go > Expected Go contrast of Sebastian et al. (2020) to reflect *more* proactive control, and thereby more BOLD activation in pre-SMA than in Unexpected NoGo > Expected NoGo. Yet, using Bayesian evidence, Sebastian et al. (2020) find equivalent activation across nearly all fronto-basal ganglia network regions, including pre-SMA, in their conjunction analysis of these two contrasts. Ostensibly, this speaks against a one-dimensional role for pre-SMA in simply implementing control—it is activated by unexpected events, regardless of the degree of proactive control being implemented.

With this additional insight in hand, we propose a new interpretation of the function that the pre-SMA may serve in relation to unexpected stimuli. We suggest that the pre-SMA is involved in context updating, specifically in reweighting action programs and updating task contingencies, following unexpected events. Indeed, one prevalent view of pre-SMA function is that it is involved in linking actions and rules in the task setting (Nachev et al., 2008). Thus, a context-updating role for the pre-SMA could explain how task behavior is adaptively adjusted after unexpected events. We note that this interpretation is not incompatible with a potential role for pre-SMA in establishing proactive control because proactive control could be a specific example of the consequences of context updating. Nevertheless, in this study, it appears that the processes underpinned by BOLD activity in pre-SMA are similarly active after unexpected events, regardless of whether action cancellation is unexpected or expected. Because all conditions in the task of Sebastian et al. (2020) include some possibility of needing to inhibit actions, it remains to be seen whether the pre-SMA also serves a context-updating role in task contexts without any proactive control. If the pre-SMA indeed accomplishes context updating in noninhibitory control tasks, one might expect to see the BOLD signal in pre-SMA decrease across the task as participants gain experience with unexpected stimuli and less context updating is required to update weightings of the task actions and rules associated with them (cf. Barceló, 2020).

In conclusion, this recent study from Sebastian et al. (2020) provides compelling neuroanatomical evidence that unexpected events recruit a fronto-basal ganglia network for inhibitory control regardless of the action mappings with which they are associated. Moreover, such events interrupt action, either by preventing unnecessary actions or slowing correct actions. We eagerly await further investigations exploring how adaptation of action is accomplished following this automatic inhibition, and we propose that the pre-SMA likely plays a critical role in adjusting motor programs and global contingencies. One thing is clear: whether or not a batter ultimately decides to swing, the same underlying circuit enables rapid processing and adjustments to promote the best course of action when we are thrown "curve balls."

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