

Letter

Evidence Supports Specific Braking Function for Inferior PFC

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How are motor responses stopped? One theory is that this is done via a braking circuit in the human brain that includes the right posterior inferior frontal cortex (rIFC) [1], as part of a wider network, of which more below. In a recent Opinion article in this journal, Hampshire and Sharp [2] argued that rIFC and its connection pathways do not support a discrete cognitive function, such as stopping. Instead, for them, rIFC is part of multi-demand cortex (MDC) that underlies many different control processes.

Their argument rests mostly on their own functional magnetic resonance imaging (fMRI) studies [3–5], in which they fail to find any difference in rIFC between stop tasks versus other tasks. We have several concerns with this logic. The proposal that prefrontal cortex (PFC) supports an all-purpose cognitive control function has recurred repeatedly in research. One potential reason for its constant rediscovery is that it is in essence a ‘null hypothesis’ (i.e., it hypothesizes no functional differences in PFC). Thus, our overarching worry is that imprecision in any aspect of design, region of interest, or analysis will produce a nondifference between conditions that supports that view. Indeed, the studies of Hampshire and colleagues are affected by such imprecision.

Region of Interest Definition

In one study, Hampshire and colleagues [4] picked a ‘right IFC’ region of interest (ROI; $x = 42$, $y = 18$, $z = -6$), which is not IFC at all, but very likely anterior

insula. Notably, a recent meta-analysis of response inhibition tasks showed that rIFC is dissociable from right anterior insula ($x = 38$, $y = 20$, $z = -4$) [6]. Another study by Hampshire and colleagues used independent components analysis to show that seven subregions within right frontal-opercular cortex were indistinguishable for four tasks (one was a stop task) [3]. However, none of those loci overlapped with the likely focus of the rIFC braking function. When the locus we suggested (based on meta-analysis) was then examined, no difference was found [5]. However, at that locus, there was not even significant activation for stopping itself. This makes the nondifference between conditions uninformative. More generally, we are puzzled by the independent components approach. These components are spatial clusters because they have different spatiotemporal activity, but what are the activity differences if there are no task differences in the first place?

Task, Behavior, and Design

In one of the aforementioned studies [4], the ‘stopping accuracy’ was approximately 80% (and these data were reused in Study 1 in [5]). Such a high rate, especially absent reaction time data, implies that subjects may not have been stopping at all (but rather choosing not to go). Similarly, in Study 3 of [5], accuracy on no-go trials was also very high (>90%), and reaction time data were again absent. Moreover, these studies used tasks in different scanning blocks rather than in mixed blocks, which introduces problems. For example, in [4], the monitoring and stopping tasks were compared with different baselines, the monitoring task involved working memory absent from the stopping task, and the monitoring task preceded the stopping task during scanning.

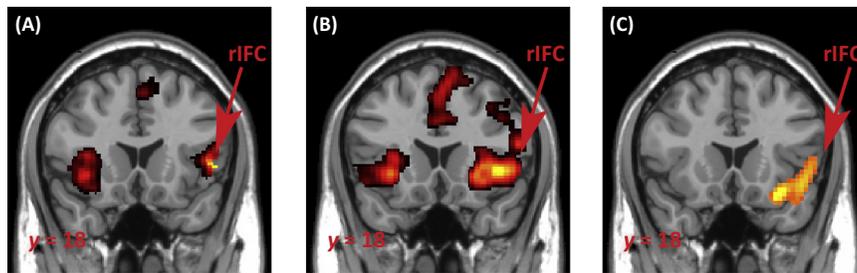
Arrayed against their fMRI studies are several showing positive evidence that there are dissociations for rIFC (Figure 1) [7–9]. Hampshire and Sharp also ignore other

dissociations, including one showing that rIFC lesions affected stopping and not mere infrequent responding [10]. Dissociations should count for more than null findings that can arise from imprecision.

Hampshire and Sharp also ignore evidence from high spatiotemporal electrocortigraphy showing that rIFC is more active for the well-controlled comparison of successful versus failed stop trials; moreover before the time of stopping elapses (see Box 2 in [1]).

Hampshire and Sharp argue that rIFC is merely part of MDC, and this system is uniformly engaged by diverse task demands. This has the serious problem that the area of lateral PFC that MDC is proposed to occupy has shrunk over the years, and its most recent instantiation no longer includes most of IFC; instead, it includes middle frontal gyrus and a narrow premotor strip (that is dissociable from IFC, at least in the left hemisphere) [11].

Hampshire and Sharp's theory about how the brake is implemented is also imprecise. For them, the stop signal produces a ‘...top-down [MDC] potentiation [which] has the secondary effect of influencing competing processes by lateral inhibition, thereby producing a slowing of routine responses’ [2]. How exactly does this occur? Instead, we have provided a specific account [1]. In the case of infrequent stop signals, or salient/surprising (especially behaviorally relevant) events, the need to stop (or interrupt) action is conveyed to rIFC, which is a prefrontal node that has privileged access to the motor system to turn on a brake. (Note that this does not have to be its only ‘dedicated’ role; it could also participate in other networks.) When stopping/interrupting must be rapid, rIFC activates the subthalamic nucleus of the basal ganglia (perhaps via the presupplementary motor area), which inhibits thalamocortical drive, blocking the go response. Unlike Hampshire and Sharp's theory, this account is



Trends in Cognitive Sciences

Figure 1. Examples of Functional Magnetic Resonance Imaging (fMRI) Studies Showing Dissociations in Right Posterior Inferior Frontal Cortex (rIFC) for Stopping Versus Other Requirements Using Well-controlled Comparisons. The contrasts are: (A) The conjunction of ‘successful stop trials in a stop relevant block versus stop trials in a stop irrelevant block’ and ‘unsuccessful stop trials in a stop relevant block versus stop trials in a stop irrelevant block’ [7]; (B) NoGo trials versus infrequent Go trials [8]; and (C) (successful stop trials – Go trials when the stop signal is relevant) versus (responding on stop signal trials – Go when the stop signal is irrelevant) [9]. Data replotted with permission from [7] (A), [8] (B), and [9] (C).

mechanistically and anatomically specific and continues to be tested in different species and at many levels, including timing and connectivity (e.g., [12]).

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