The Quest for Hemispheric Asymmetries Supporting and Predicting Executive Functioning

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Abstract

This narrative review addresses the neural bases of two executive functions: criterion setting, that is, the capacity to flexibly set up and select task rules and associations between stimuli, responses, and nonresponses, and monitoring, that is, the process of continuously evaluating whether task rules are being applied optimally. There is a documented tendency for criterion setting and monitoring to differentially recruit left and right lateral prefrontal regions and connected networks, respectively, above and beyond the specific task context. This model, known as the ROtman–Baycrest Battery to Investigate Attention model, initially sprung from extensive neuropsychological work led by Don Stuss. In subsequent years, multimodal lines of empirical investigation on both healthy individuals and individuals with brain damage, coming from functional neuroimaging, EEG, neurostimulation, individual difference approaches, and, again, neuropsychology, so to “complete the circle,” corroborated the functional mapping across the two hemispheres as predicted by the model. More recent electrophysiological evidence has further shown that hemispheric differences in intrinsic prefrontal dynamics are able to predict cognitive performance in tasks tapping these domain-general functions. These empirical contributions will be presented together with contrasting evidence, limits, and possible future directions to better fine-tune this model and extend its scope to new fields.

INTRODUCTION

One of the most intriguing mysteries for cognitive neuroscience is why our brain is composed by two structurally almost equivalent hemispheres. Functional hemispheric asymmetries have been demonstrated in various cognitive domains, such as language (Corballis, 2015; Toga & Thompson, 2003), emotional regulation (Reznik & Allen, 2018; Wyczesany, Capotosto, Zappasodi, & Prete, 2018), and exogenous visuospatial orienting of attention (Sai et al., 2020; Corbetta & Shulman, 2002). Hemispheric asymmetries, however, have not been much investigated for executive functions (EFs), a set of high-level cognitive processes that govern lower-level routine operations, for which prefrontally based brain networks are believed to play a chief role (Miller & Cohen, 2001; Norman & Shallice, 1986). As many other multidimensional organizational gradients of pFC along the rostrocaudal (Badre & Nee, 2018; Nee & D’Esposito, 2017; Reynolds, O’Reilly, Cohen, & Braver, 2012; Badre & D’Esposito, 2007; Koechlin & Summerfield, 2007; Sakai & Passingham, 2003; Fuster, 2001) and ventral–dorsal (O’Reilly, 2010; Petrides, 2005) directions have been described, it is conceivable to expect that there might be gradients of organization across the two frontal lobes as well.

There are, indeed, some classical views implying hemispheric asymmetries in EFs. One of them is the hemispheric encoding retrieval asymmetry (HERA) model proposed by Endel Tulving and associates. This model, however, mainly applies to episodic memory tasks using verbal material (Habib, Nyberg, & Tulving, 2003; Tulving, Kapur, Craik, Moscovitch, & Houle, 1994). According to this model, organizing and encoding new verbal material mainly engages left pFC, whereas retrieval is instead associated with right pFC, especially when requiring effortful monitoring and careful evaluation of the retrieved memory content, such as under low confidence and with weak memory traces (Shalllice & Gipolotti, 2018; Hayama & Rugg, 2009; Henson, Rugg, Shalllice, & Dolan, 2000; Nyberg, Cabeza, & Tulving, 1996).

Another model focusing on functional hemispheric asymmetries in EFs is the “break” model (Wessel & Aron, 2017; Aron, Robbins, & Poldrack, 2014), in which the right inferior frontal cortex is implied in stopping inappropriate motor responses through fronto-BG connectivity. However, also this model is mostly limited to a specific task domain, that is, inhibitory control of motor responses.

If one has to think about a more general model of hemispheric asymmetries in EFs, the contribution by Don Stuss and colleagues, known as the ROtman–Baycrest Battery to Investigate Attention (ROBBIA) model, is what usually comes to mind first (Stuss, Shallice, Alexander, & Picton, 1995). In contrast with the classical view of a unitary central supervisory system with a seat in the frontal lobes, mostly motivated by an initial paucity of empirical investigation (Baddeley, 1998; Norman & Shallice, 1986), the first formulation of the ROBBIA model hypothesized five specific
control processes related to different pFC subregions: energization, task-setting, monitoring, inhibition, and if-then logic (Stuss et al., 1995).

Motivated by findings derived from extensive neuropsychological studies on patients with brain damage, however, the ROBBIA model evolved over the years in an empirically based revised version with respect to what was initially proposed by the authors in their seminal 1995 work (Stuss, 2011; Shallice, Stuss, Picton, Alexander, & Gillingham, 2008a; Picton et al., 2007; Stuss & Alexander, 2007; Stuss et al., 2005; see also Vallesi, 2012; Kaller, Rahm, Spreer, Weiller, & Unterrainer, 2011; Goel & Grafman, 2000). Of the five originally hypothesized processes, the three surviving ones were task-setting, monitoring, and energization.

Task-setting is the capacity to set up and select the rules to perform a task, which was mostly attributed to left lateral pFC (e.g., Alexander, Stuss, & Gillingham, 2009; Shallice et al., 2008a; Alexander, Stuss, Shallice, Picton, & Gillingham, 2005). Monitoring is the ability to evaluate whether task criteria are being applied correctly, which was hypothesized as a typical right lateral prefrontal process (e.g., Vallesi, Mussoni, et al., 2007; Reverberi, Lavaroni, Gigli, Skrap, & Shallice, 2005; Stuss et al., 2005). Energization is a complementary process boosting other operations that lack or lose activation either because they are too novel or complex or because fatigue or boredom emerges over time. Energization was located in superior medial prefrontal regions, including (pre-)SMA and ACC (Alexander et al., 2005; Stuss et al., 2005; Stuss, Binns, Murphy, & Alexander, 2002; Paus, 2001). In this refined version of the ROBBIA model, inhibition was no longer considered as a standalone process, as inhibitory processes can be explained by a mixture of energization, task-setting, and monitoring (Stuss & Alexander, 2007; cf. Friedman & Miyake, 2017). In addition, the if-then logic was dropped and incorporated in task-setting (Stuss, 2011).

Our EF laboratory was born almost by a sort of sprouting from the initial collaborative work with the ROBBIA group (e.g., Vallesi, McIntosh, Alexander, & Stuss, 2009; Vallesi, Picton, & Tulving, 2009; Vallesi, McIntosh, Alexander, & Stuss, 2009; Vallesi, McIntosh, Alexander, & Stuss, 2009; Vallesi, McIntosh, Alexander, & Stuss, 2009; Vallesi, Stuss, McIntosh, Alexander, & Picton, 2009; Vallesi, Stuss, McIntosh, Alexander, & Picton, 2009). We have been working for more than a decade on patients with brain damage in an effort to refine it further and expand its explanatory power also to healthy individuals. Our work originated from extensive work on patients with brain damage, in an effort to refine it further and expand its explanatory power also to healthy individuals. Our work (Vallesi, 2012) started from further reflection on the semantic, anatomical, and temporal characteristics of criterion setting and monitoring, the two key EFs according to the ROBBIA model (Stuss & Alexander, 2007).

I will hereby use the term “criterion setting” instead of task-setting, as the former may be applied more readily to wider contexts. Criterion setting can be semantically defined as a process useful to set up new associations. These associations could occur not only between stimuli and responses as well as stimuli and nonresponses but also between stimuli and other stimuli, such as when forming novel cognitive associations during episodic memory encoding (cf. HERA model by Tulving et al., 1994). In addition, this construct encompasses the flexible selection of already established task rules, criteria, and representations, while also tuning down other potentially competing, but task-inappropriate, representations, as the flip side of the coin. Anatomically, criterion setting involves left-lateralized areas of the inferior and middle prefrontal gyrus (e.g., Stuss & Alexander, 2007). Time-wise, it is a phasic process, akin to the construct of “refreshing” that is, briefly bringing an item into the focus of attention, which is proposed to be left lateralized in pFC (Raye, Johnson, Mitchell, Greene, & Johnson, 2007). However, criterion setting may also be proactive when the task structure allows to investigate this time-related feature, such as when the task can be divided into blocks and early blocks; when the task rules are initially acquired or can be compared with later blocks (e.g., Vallesi, McIntosh, Alexander, et al., 2009; Shallice, Stuss, Picton, Alexander, & Gillingham, 2008b; Alexander et al., 2005); when the task requires a dynamic setup of task rules, for instance, in task-switching (e.g., Tarantino, Mazzonetto, & Vallesi, 2016; Shallice et al., 2008a); or when a preparatory cue phase is separate from a subsequent task execution phase (e.g., Vallesi, McIntosh, Crescentini, & Stuss, 2012).

Monitoring is an umbrella term that comprises reality check and evaluative processes, including checking whether rules are being applied correctly and carefully assessing environmental and internal contingencies and probabilities when useful to optimize behavior. Anatomically, this process should mostly rely on right lateral prefrontal regions (e.g., Stuss & Alexander, 2007; Vallesi, Shallice, & Walsh, 2007; Stuss et al., 2005). Temporally, it is a continuous, tonic type of process akin to sustained attention and vigilance. However, monitoring could also entail a reactive component depending on the task structure.

The criterion setting/monitoring model has been fruitful in inspiring and generating new science, although there are some caveats that need to be mentioned before reviewing some recent findings. First, this is clearly not an all-or-none model, as it is difficult to find clear-cut dissociations in richly connected regions such as prefrontal ones (Duncan, 2010), also considering that even more posterior and computationally simpler regions show graded and dynamic asymmetries rather than all-or-none hemispheric division of labor (Behrmann & Plaut, 2015). Second, it is an incomplete model of executive functioning, as many other processes could be hypothesized with different distributions and gradient directions in pFC (e.g., Badre & Nee, 2018; Pessoa, 2015; Koechlin & Summerfield, 2007; Petrides, 2005). Third, we should not forget that prefrontal areas are not a monolithic structure and are very much involved in cohesive, distributed networks, including fronto-posterior (Assem, Glasser, Van Essen, & Duncan, 2020; Corbetta & Shulman, 2002) and fronto-striatal (Hanakawa, Goldfine, & Hallett, 2017; Alexander, DeLong,
right-lateralized brain activations (Kelley et al., 1998; whereas working with visuospatial material drives more content preferentially activates the left ventrolateral pFC, of executive functioning. More generally, processing verbal & Fellows, 2014), suggesting a material-specific account of executive functioning. More generally, processing verbal content preferentially activates the left ventrolateral pFC, whereas working with visuospatial material drives more right-lateralized brain activations (Kelley et al., 1998; & Strick, 1986) circuits. In particular, in the last decade or so, several neuroimaging studies have identified the fronto-parietal network as a cohesive cognitive control network, including parts of the lateral prefrontal and posterior parietal cortices (e.g., Dosenbach, Fair, Cohen, Schlaggar, & Petersen, 2008), which flexibly changes its connectivity with other networks according to the task goals (Cole et al., 2013; Zanto & Gazzaley, 2013).

In what follows, I shall review multimodal evidence, mainly coming from neuroimaging, electrophysiology, and neuropsychology, which corroborates the ROBBIA model in both healthy and pathological conditions. I will then conclude this selective review by briefly comparing the ROBBIA model with other models and depicting some future directions.

STUDIES ON LEFT LATERALIZATION OF CRITERION SETTING

Some of the typical EF tasks reported to activate left lateral pFC include verbal episodic memory encoding (e.g., Sidhu et al., 2013; Kim et al., 2009; Otten, Henson, & Rugg, 2002; Henson, Rugg, Shallice, Josephs, & Dolan, 1999; Shallice et al., 1994; Tulving et al., 1994), color–word Stroop task (e.g., MacDonald, Cohen, Stenger, & Carter, 2000; Perret, 1974; see Xu, Xu, & Yang, 2016; Derrfuss, Brass, Neumann, & von Cramon, 2005, for meta-analyses), semantic and phonemic fluency tasks (e.g., Baldo, Schwartz, Wilkins, & Dronkers, 2006; Schlösser et al., 1998; Stuss et al., 1998; Perret, 1974; see Wagner, Sebastian, Lieb, Tütscher, & Tadić, 2014, for a meta-analysis), and verbal random number generation (Knoch, Brugger, & Regard, 2005; Jahanshahi, Dirnberger, Fuller, & Frith, 2000; Jahanshahi et al., 1998). All these tasks can be characterized as particularly demanding in terms of verbal processing. Thus, it is unclear whether the left lateralization found for criterion-setting tasks simply depends on their high verbal demands, given the well-known left hemispheric lateralization of most language functions (e.g., Corballis, 2015; Raja Beharelle et al., 2010), or it generalizes to include also nonverbal domains.

Consistent with the domain-specific asymmetry hypothesis, although suppressing prepotent but task-irrelevant operations tends to be left-lateralized when the classical verbal Stroop task is used (MacDonald et al., 2000), a role of the right pFC has been observed when suppressing nonverbal distracting stimuli in a flanker task (Hazeltine, Poldrack, & Gabrieli, 2000). Moreover, damage to the left VLPFC leads to increased interference costs in the color–word Stroop task but not in the spatial flanker task, whereas damage to the right homologous region leads to the opposite dissociation (Geddes, Tsuchida, Ashley, Swick, & Fellows, 2014), suggesting a material-specific account of executive functioning. More generally, processing verbal content preferentially activates the left ventrolateral pFC, whereas working with visuospatial material drives more right-lateralized brain activations (Kelley et al., 1998; & Strick, 1986). During the cue phase preceding the actual implementation of the perceptual and decision-making-related processes, there was a significant recruitment of left middle frontal gyrus (and right cerebellum). This pFC region was
specifically involved when it was required to switch toward an accurate decision strategy in the current trial after a hasty decision-making requirement in the previous trial (speed-to-accuracy switch). These results were interpreted by attributing a criterion-setting role to the left lateral pFC, extending previous findings to the flexible regulation of speed-accuracy strategies in perceptual decision-making. The left prefrontal activation positively correlated with subsequent accuracy in the color estimation task when switching from speed to accuracy strategies; moreover, it also positively correlated with distance between response criteria (parameter “a” of a diffusion model; Voss & Voss, 2007). These findings suggest a role of left dorsolateral pFC (DLPFC) in flexibly adopting stricter decision criteria, in a context with minimal verbal demands.

Given the relatively low number of participants (N = 12) and the use of a correlational neuroimaging method (fMRI) in this study, we tried to replicate these results with an approach that would allow drawing firmer causal inferences. Therefore, in a follow-up neuropsychological study (Campanella, Skrap, & Vallesi, 2016), we showed that patients with surgical excision of left prefrontal tumors, when compared to patients with right prefrontal tumors and controls, adopted a response criterion (as shown by means of the diffusion model) that was too permissive when they had to change response strategy from quick to accurate.

Together, these two studies (Campanella et al., 2016; Vallesi et al., 2012) show that flexibly selecting stricter response criteria (causally) involves left lateral pFC. Time-wise, this process is proactive (cue-related in the fMRI study) and phasic (as it occurred with a trial-by-trial switching manipulation). These studies, however, used a single task version requiring perceptual decision-making.

The subsequent step was to gather more convincing evidence by means of studies manipulating different domains within the same group of participants and session. Individual EF tasks, indeed, show low correlations because of task impurity even when tapping the same construct (Miyake et al., 2000; Burgess, 1997). Because EFs by definition control other operations, EF tasks inescapably rely on cognitive processes not directly measured by those tasks per se. It is therefore plausible that nonexecutive cognitive demands explain a fair amount of performance variability in individual executive tasks. Therefore, multiple measures of the same construct are necessary to obtain an estimate of the underlying EF, above and beyond the task specific.

We used this approach in several of our studies (e.g., Ambrosini, Arbula, Rossiato, Pacella, & Vallesi, 2019; Tarantino, Mazzonetto, Formica, Causin, & Vallesi, 2017; Capizzi, Ambrosini, Arbula, Mazzonetto, & Vallesi, 2016a; Babcock & Vallesi, 2015; Capizzi, Fehér, Penolazzi, & Vallesi, 2015; Vallesi, Arbula, Capizzi, Causin, & D’Avella, 2015). In some cases (e.g., Furlan, Babcock, & Vallesi, 2018; Capizzi et al., 2016a; Capizzi, Ambrosini, Arbula, Mazzonetto, & Vallesi, 2016b), we kept task material constant and only changed the nature of the task that participants had to perform on this material (and consequently the required EF).

As already mentioned, left-lateralized criterion setting involves strategically organizing the available material for subsequent use, such as in episodic memory encoding (Buckner et al., 1999). In this sense, criterion setting may also be required during inductive reasoning, the process of discovering/building up a general rule or pattern based on specific instances belonging to that rule. Left lateral pFC is involved in inductive reasoning, as demonstrated by evidence coming from split-brain patients (Gazzaniga & Smylie, 1984), patients with cortical lesions (Reverberi et al., 2005), and healthy individuals (Jia et al., 2011; Specht, Lie, Shah, & Fink, 2009; Yang, Liang, Lu, Li, & Zhong, 2009; Goel & Dolan, 2000; Goel, Gold, Kapur, & Houle, 1997). Typically, though, inductive reasoning studies use verbal material. Thus, these studies are less informative when addressing the effect of domain on localizations of inductive reasoning processes, because both domain-based and process-based distinctions predict left lateralization in those cases. Some studies showed a left frontal involvement in spatial inductive reasoning (Crescentini et al., 2011; Reverberi et al., 2005) but did not directly compare spatial with verbal inductive reasoning.

In an fMRI study (Babcock & Vallesi, 2015), we investigated whether the processes engaged during inductive reasoning interact with task domain in the brain. Importantly, inductive reasoning was manipulated in both verbal and spatial domains within participants. The task was organized in short periods during which stimuli were continuously shown (i.e., epochs). In particular, in each epoch, participants saw random letters consecutively presented in random spatial positions. In the verbal epochs, they had to decide which semantic category the words that serially emerged in the context of initially random letters belonged to (e.g., f-i-n-g-e-r; s-h-o-u-l-d-e-r… = body parts), whereas in the spatial domain, they had to decide which spatial pattern emerged from randomly presented letter positions (e.g., a spiral, a straight line). The fMRI results showed activations in bilateral ventrolateral pFC and posterior cerebellum for spatial rule search and only left (more extensive) ventrolateral pFC activations for verbal rule search, when these inductive reasoning epochs were compared to working memory control epochs within each task domain. Importantly, the two domains recruited a common region of left ventrolateral pFC, as shown by a conjunction analysis.

A follow-up multivoxel pattern analysis on a subsample of the same data (N = 13; Furlan et al., 2018) showed that domain was decodable well above chance, as shown by permutation-based statistical testing, in the left ventrolateral pFC, reaching an above-chance classification accuracy of >67.3% in the left lateral orbital gyrus and not in right homologous regions or other more posterior regions. A replication analysis with the same participants tested 2 years later basically confirmed these findings, although the individual multivoxel representations of task domains
changed, suggesting that these representations are not stable but adaptably mapped in the left ventrolateral pFC “on demand” (Furlan et al., 2018). More generally, these results are compatible with a previous neuropsychological study (Langdon & Warrington, 2000), where impairments on spatial reasoning were reported in patients with left hemisphere lesions as well as in patients with right hemisphere lesions, but only patients with left brain damage were impaired on verbal reasoning tasks (also see Duncan & Owen, 2000).

In another fMRI study (Vallesi et al., 2015), we investigated criterion setting in the context of verbal and spatial task-switching. As in our previous fMRI study (Babcock & Vallesi, 2015), we again kept physical stimuli the same, and participants’ performance was matched between domains. Participants were presented with written words. In “verbal” blocks, participants had to switch between two grammatical rules (i.e., judging either the gender or proper/common name status of each word), whereas in “spatial” blocks, they had to judge the words according to either their roll (clockwise vs. anticlockwise) or pitch (upward vs. downward) rotation. Task-switching blocks, when compared with single task blocks, showed a left-lateralized involvement of fronto-parietal regions in the context of verbal rules. A more bilateral pattern, especially in pFC, was instead observed for switching between spatial rules. A conjunction analysis confirmed that the common regions involved in task-switching were localized both in left inferior prefrontal and parietal cortices and in bilateral supplementary motor cortex.

However, the domain factor also played a critical role in driving lateralized brain activity, although in different subregions. This was demonstrated by means of a statistical lateralization map approach (Liégeois et al., 2002), which allows a direct statistical comparison between the level of activation of each voxel in one hemisphere and its homologue voxel in the opposite hemisphere, after normalizing the brain activity to a symmetric template and applying smoothing. This analysis revealed that hemispheric asymmetries in the frontal lobes (more ventrally than in the conjunction analysis results) were more biased toward the left side for the verbal domain than for the spatial one and vice versa, demonstrating that prefrontal hemispheric asymmetries may also be modulated by the more specific nature of the tasks to be performed during task-switching, although at locations different from process-based asymmetries.

Another ERP study on a similar task-switching paradigm requiring switching within either verbal or spatial rules (Capizzi et al., 2016a) showed domain-general electrophysiological markers of task-switching. In particular, switch trials in both domains, when compared to repeat task trials, were associated with an early (265–310 msec) larger positivity developing over left parieto-occipital channels and with a later (350–450 msec) negativity more pronounced over medial left fronto-central sites. The involvement of left-lateralized prefrontal generators in this task-switching study was further confirmed by ERP source analysis. However, distinct brain mechanisms for each type of domain during the preparatory cue–target interval in task-switching can also be observed when between-domain switching is required (Capizzi et al., 2015; Minnissi, Marzi, & Nobre, 2005).

Overall, these studies (Capizzi et al., 2016a; Babcock & Vallesi, 2015; Vallesi et al., 2015) showed that criterion setting, both when one has to search a rule (inductive reasoning) and when one has to flexibly select it (task-switching), is left lateralized in frontal or fronto-parietal regions (also see Kim, Cilles, Johnson, & Gold, 2012), although right prefrontal activity is additionally observed for tasks with visuospatial demands (Babcock & Vallesi, 2015; Vallesi et al., 2015).

We also found that structural connectivity in anterior portions of the corpus callosum, which connects the two pFCs, correlates with performance in two nonverbal task-switching contexts (Vallesi, Mastrorilli, Causin, D’Avella, & Bertoldo, 2016). In particular, a conjunction analysis showed that higher fractional anisotropy and lower mean diffusivity in the genu predict lower mixing costs with both color–shape and spatial versions of the task-switching paradigm, but not with the mixing costs for grammatical task-switching. The latter result could be because of the strong left hemispheric specialization for language functions (e.g., Herve, Zago, Petit, Mazoyer, & Tzourio-Mazoyer, 2013) and suggests that the importance of interhemispheric connectivity underlying EF depends on the task context.

**FLIP SIDE OF THE COIN: CRITERION SETTING AS INTERFERENCE CONTROL**

The neuroimaging results we obtained with inductive reasoning and task-switching paradigms (Babcock & Vallesi, 2015; Vallesi et al., 2015) are compatible with the metaphor used to describe the role of the left lateral pFC in verbal episodic memory encoding, as “sculpting” the response space (Fletcher et al., 2000). A contribution of the left lateral pFC has been indeed reported especially when a specific association between different items (mostly words, but also response types) has to be selected and encoded among other competing associations that are consequently tuned down and sent to the background (Fletcher et al., 2000; Thompson-Schill, D’Esposito, & Kan, 1999; Thompson-Schill, D’Esposito, Aguirre, & Farah, 1997). Event-related fMRI (e.g., Fletcher, Stephenson, Carpenter, Donovan, & Bullmore, 2003; Wagner, Koutstaal, & Schacter, 1999) and ERP source analysis (Kim et al., 2009) evidence has also shown that left pFC activation at encoding is linked with subsequent retrieval success.

Another task that more directly requires the selection of nonroutine operations over more automatized ones is also associated with left prefrontal activations is the classical verbal Stroop task (Derrfuss et al., 2005). An fMRI study of ours (Floden, Vallesi, & Stuss, 2011) showed that, across participants, greater activation of the left DLPFC is related
to a reduced behavioral Stroop interference (whereas ACC activations showed an opposite correlation), particularly in blocks in which the specific Stroop condition (e.g., baseline word reading, color naming, or Stroop interference trials) was not exogenously cued in advance, which maximally taxed criterion setting.

The Stroop task, however, strongly relies on verbal processing, which could be a confounding factor in explaining left lateralization. Therefore, to overcome this limitation, in another EEG study, we focused on a spatial version of the Stroop task (Tafuro, Ambrosini, Puccioni, & Vallesi, 2019), considering that some previous studies using Stroop-like spatial tasks have shown predominantly right prefrontal activations (e.g., Hazeltine et al., 2000). Although both younger and older adults were tested, I will only focus on the results concerning younger adults here. In this case, we hypothesized that (left prefrontally based) processes involved in Stroop interference resolution, an important aspect of criterion setting, could be tracked by the modulation of different frequency bands. A greater event-related increase in early theta (and lower alpha) frequencies was found in bilateral dorsomedial and DLPFC estimated brain sources for the incongruent condition than for the congruent one. This theta increase was positively correlated with the behavioral Stroop effect. In the light of this correlation, the theta increase was interpreted as an electrophysiological marker of cognitive control requirements (Cavanagh & Frank, 2014; Cohen, 2014; Sauseng, Griesmayr, Freunberger, & Klimesch, 2010). We also found stronger beta (19–24 Hz) suppression in a relatively early time window (400–600 msec) for incongruent conditions than for congruent ones. This beta modulation was associated, through source reconstruction analyses, with posterior portions of the left middle and superior frontal gyri. This beta-band effect was interpreted as a cognitive marker of interference control implementation (Spitzer & Haegens, 2017; Antzoulatos & Miller, 2016), through a mechanism involving the amplification of task-relevant representations (Banich, 2009; Egner & Hirsch, 2005) or the selection of task-relevant rules (Zhao et al., 2015; Wang, Li, Zheng, Wang, & Liu, 2014; Stuss, 2011; Derrfuss et al., 2005).

As previously proposed within the episodic memory field, the left pFC is thought to set the response criteria (i.e., “sculpts the response space”) by combining suppression of the inappropriate response criteria, on the one side, and selection of the appropriate ones, on the other (Fletcher et al., 2000; Frith, 2000). A critical question that emerged was whether setting the criteria for avoiding inappropriate responses, without the complementary demand to set the criteria to execute an overt response, is a sufficient condition to observe activation in the left pFC. To test this, we adapted a task design used to study criterion setting in frontal patients (Alexander, Stuss, Picton, Shallice, & Gillingham, 2007) to a go/no-go task (Vallesi, McIntosh, Alexander, et al., 2009). In that case, task-setting was required independently of the selection and preparation of an alternative motor response. The critical event was a low-frequency (25%) Stroop-like no-go letter (e.g., “red X” or “blue O”) given by the complementary combinations of color and identity with respect to that defining more frequent (50%) go stimuli (e.g., “red O” or “blue X”). Less demanding no-go trials (i.e., colored numbers) were also included as a control condition (25%). The results showed that the selection of nonroutine operations activates left inferior pFC even when no explicit response is required, especially in early stages (first vs. second run; Vallesi, McIntosh, Alexander, et al., 2009). The involvement of left pFC in early stages of task execution is demonstrated also in other tasks, including for instance, the already-described episodic memory encoding (Fletcher et al., 2000) and continuous motor performance in a spatial compatibility task (Alexander et al., 2005). Functional connectivity analysis showed that the left ventrolateral pFC was part of a more distributed network, spanning frontal, parietal, and temporal regions, which underpins learning task criteria for not responding to the conflicting no-go condition (Vallesi, McIntosh, Alexander, et al., 2009; Derrfuss et al., 2005). Right prefrontal activity has been additionally reported when visuospatial demands/materials are embedded in typical criterion-setting tasks (e.g., Babcock & Vallesi, 2015), cognitive association formation (Kim et al., 2009; Fletcher et al., 1998), flexible selection of rules or response strategies (Campanella et al., 2016; Vallesi et al., 2012, 2015; Kim et al., 2012), and resolution of interference (Tafuro et al., 2019; Floden et al., 2011; Vallesi, McIntosh, Alexander, et al., 2009; Derrfuss et al., 2005). Right prefrontal activity has been additionally reported when visuospatial demands/materials are embedded in typical criterion-setting tasks (e.g., Babcock & Vallesi, 2015; Vallesi et al., 2015; Kelley et al., 1998). Figure 1A summarizes the prefrontal activations found in five fMRI studies on criterion setting by the author’s group. Notwithstanding a clear tendency for these studies to activate left prefrontal areas, it is however clear that the precise location within the left lateral pFC varies according to the specific experimental contrast (Figure 1A) and future research should address this anatomical variability.

**STUDIES ON RIGHT-LATERALIZED MONITORING PROCESSES**

Neuropsychological evidence from the ROBBIA model (Stuss et al., 2005) showed that the performance on a simple RT task such as the foreperiod (FP) paradigm could be specifically affected by lesions in different prefrontal regions. In this paradigm, the preparatory interval before a target stimulus (the so-called FP) is manipulated either block-wise or on a trial-by-trial basis. Normally, performance varies substantially according to how the preparatory interval is manipulated. Thus, RTs are usually shorter for longer FPs than for shorter ones in the variable FP paradigm. This effect cannot be attributed to the fact that there is simply more time available to prepare a response...
in the long FP, as the opposite pattern (shorter RTs for shorter FPs) is observed when the FP is kept constant in a block of trials. According to a classical model (Niemi & Näätänen, 1981) and a more recent dual-process one (Vallesi, Lozano, & Correa, 2013; Vallesi & Shallice, 2007), this effect is rather because of a process of continuously monitoring that the stimulus has not occurred yet, and so enabling the individual to exploit the increase in the conditional probability of its occurrence (hazard function) during a trial in the variable FP paradigm.

Because this classical variable FP effect is eliminated by lesions in the right lateral pFC (Stuss et al., 2005), this deviant behavioral pattern was interpreted as a marker of a deficit in a right-lateralized monitoring process. Multimodal evidence coming from focal lesions (Arbula et al., 2017; Triviño, Correa, Arnedo, & Lupiñáñez, 2010; Vallesi, Mussoni, et al., 2007; Stuss et al., 2005); brain stimulation (Vallesi, Shallice, et al., 2007); and neuroimaging (Coull, Cotti, & Vidal, 2016; Vallesi, McIntosh, Shallice, et al., 2009) confirmed that monitoring conditional probabilities in the temporal domain requires right lateral prefrontal regions. We also showed a dissociation with another (probably lower level) behavioral phenomenon observed with the variable FP paradigm, that is, sequential FP effects (i.e., longer RTs when the preceding FP is longer than the current one) that are not modulated by lesions (Vallesi, Mussoni, et al., 2007) or by inhibitory TMS (Vallesi, Shallice, et al., 2007) on the right lateral pFC and do not correlate with fMRI activation on the same region (Vallesi, McIntosh, Shallice, et al., 2009).

More recent findings of an fMRI study using Bayesian modeling showed that the bilateral inferior pFC, along with other nodes of fronto-parietal networks, responds to both violation of expectations (i.e., surprise) and updating of prior beliefs during a modified FP task (Visalli, Capizzi, Ambrosini, Mazzonetto, & Vallesi, 2019). This suggests that the relation of the lateral pFC to the hazard function might deal more with the detection and resolution of expectancy violation than with tracking the passage of time. It could be speculated that, through connections with dorsal ACC, this region could implement top–down control for immediate (surprise) or future (updating) actions (Cocchi, Zalesky, Fornito, & Mattingley, 2013; Dosenbach et al., 2008). Of note, however, the study by Visalli and colleagues (2019) differed from former ones using the FP paradigm (Coull et al., 2016; Vallesi, McIntosh, Shallice, et al., 2009; Vallesi & Crescentini, Neuroimage, 2011; Vallesi et al., Cortex, 2015; Vallesi et al., Human Brain Mapping, 2012; Vallesi et al., Neuroimage, 2009; Vallesi et al., Neuroimage, 2011; Vallesi et al., Journal of Cognitive Neuroscience, 2009; Vallesi et al., Neuroimage, 2011; Vallesi et al., Human Brain Mapping, 2012; Vallesi et al., Journal of Cognitive Neuroscience, 2009; Vallesi et al., Neuroimage, 2009; Vallesi et al., Human Brain Mapping, 2012; Vallesi et al., Journal of Cognitive Neuroscience, 2009).
Vallesi, Mussoni, et al., 2007), because the analyses were target-locked instead of warning-locked. This implies that these findings could not speak in favor or against the (monitoring) role of the right pFC in the hazard function that develops during the time interval between warning and target stimuli (i.e., the FP). Future FP studies based on Bayesian modeling should possibly focus on this portion of the task.

To extend the investigation of the monitoring role of the right lateral pFC, in another fMRI study (Vallesi & Crescentini, 2011), we asked participants to track the trajectory of an ideal car moving within a roundabout and to identify when the car would crash into the guard rail. Trajectories were manipulated to show different degrees of regularity and predictability. The fMRI results showed that the inferior/middle frontal gyri and inferior parietal lobule in the right hemisphere were maximally activated and functionally connected when monitoring regular predictable trajectories as compared with random or misleading (i.e., zigzag) unpredictable trajectories. These findings demonstrate that this frontline-parietal network is recruited for monitoring regular events that can meaningfully inform expectancy, while it disregards environmental contingencies that are not prognostic about future events.

Results showing right pFC involvement in monitoring within a single task version could however be because of the specific features of that task (e.g., material, domain) rather than of the putative process involved (i.e., monitoring). More convincing are those studies that demonstrate a right pFC involvement when monitoring is required for different types of content or context within a single experimental session. For instance, an fMRI study on long-term memory retrieval showed the same level of activation in the right DLPFC, independently of whether postretrieval evaluation was applied to semantic or episodic information (Hayama & Rugg, 2009). It is particularly intriguing that the two tasks employed, which strongly rely on typically left-lateralized processing of verbal material, were associated with right-lateralized activations in postretrieval monitoring. Similarly, right dorsolateral and ventrolateral prefrontal activations are specifically observed when syllabic and semantic decision-making has to be applied on acoustically degraded versus intact speech stimuli, that is, when the task requires careful monitoring of deteriorated verbal material kept in working memory (Sharp, Scott, & Wise, 2004).

In another EEG-fMRI coregistration study (Tarantino et al., 2017), participants were required to continuously monitor sequences of either faces (associated with right-lateralized processing) or tools (left-lateralized) to detect particular targets, while performing another ongoing task. In control blocks, they were asked to perform the ongoing task only. The contrast between monitoring and control blocks showed the sustained involvement of bilateral fronto-parietal regions, irrespective of the task domain. ERPs showed a positivity specific for monitoring trials, which was common to both tasks and was used as an additional regressor for the fMRI analysis. In the face task, this analysis revealed that this component relies on right-lateralized areas, including inferior parietal and middle frontal areas. In the tool task, however, no above-threshold fronto-parietal areas correlated with the trial-by-trial ERP activity. The lack of evidence for the tool task makes the conclusions concerning the right lateralization of interdomain monitoring less compelling, although it could be because of many reasons, including insufficient power.

Another fMRI study (Fleck, Daselaar, Dobbins, & Cabeza, 2006) showed an involvement of the right DLPFC in low-confidence decisions, regardless of whether these decisions concerned verbal memory retrieval or color perception. Interestingly, low-confidence decisions are those in which the internal or external weak evidence available needs to be supposedly monitored further to optimize task compliance. In addition, ACC, among other regions, showed similar confidence-related activations. Importantly, ACC activity was predicted by both RT and confidence parameters, suggesting also a role of task difficulty in this case, whereas right DLPFC activity was predicted by confidence only in mixed-effect regression and not by RTs, against a pure task-difficulty account of its involvement.

In an additional ERP study, we employed monitoring demands while administering ongoing decision-making tasks in different domains (Capizzi et al., 2016b). In each monitoring block, monitoring was required either in the spatial domain (i.e., looking for a particular spatial orientation of a target word) or in the nonspatial one (i.e., looking for a specific letter in the target word). Monitoring requirements, when compared to an ongoing RT control task alone, did not interact with the task context (spatial, nonspatial). Monitoring instead generally involved both visuoperceptual mechanisms (enhanced N1 and sustained negativity in posterior sites; see Benn et al., 2014, for related fMRI evidence) and a widespread late positivity, whose cortical generators were identified through source analysis over right-lateralized fronto-parietal regions. Although caution should be used because of the risk of inverse inference and imprecision of ERP source solutions, these findings replicate previous fMRI studies on monitoring showing that the right lateral pFC is maximally activated in time-based monitoring (e.g., Vallesi, McIntosh, Shallice, et al., 2009; Coull, Frith, Büchel, & Nobre, 2000), extending them to provide evidence of the domain-general nature of right-lateralized monitoring in the context of spatial and nonspatial tasks.

Core monitoring mechanisms are typically right-lateralized in pFC, although the precise location of the recruited regions within the right lateral pFC may vary depending on the experimental paradigm (see Figure 1B). Moreover, similarly to what I described for criterion setting, prefrontal hemispheric asymmetries related to monitoring can also be modulated by the task domain. In an fMRI study investigating episodic memory (Johnson et al., 2005; Johnson, Baye, Mitchell, Greene, & Anderson, 2003), for instance, it was found that right pFC regions were associated with old/new decisions while retrieving both verbal and
pictorial materials, but a portion of the left pFC additionally showed old/new-related activity specific to verbal material.

**INTRINSIC HEMISPHERIC ASYMMETRIES INFLUENCE PERFORMANCE ON EFS**

Up to now, functional prefrontal asymmetries were shown in a task-driven fashion. We wondered whether they are also present at rest and, if so, whether they are meaningful. In other words, would intrinsic asymmetric prefrontal activity, if present, be able to account for interindividual differences in EF performance?

In a series of individual difference companion EEG studies (Ambrosini, Capizzi, Arbula, & Vallesi, 2020; Ambrosini & Vallesi, 2016, 2017), we used EEG distributed source imaging to investigate whether functional hemispheric asymmetries at rest could predict EFs. Specifically, we obtained the right–left hemispheric asymmetry score for the log-transformed ratio between relative power in beta and alpha bands (β/α), as a proxy measure of lateralization of intrinsic activity in 75 bilateral cerebral sources. Computing derived EEG measures by combining different bands overcomes the limits of traditional spectral measures focusing on single frequency bands. Measures combining multiple EEG bands have been shown to have high reliability and thus could be used as electrophysiological fingerprints of an individual (Campisi & La Rocca, 2014; La Rocca, Campisi, & Scarano, 2014; Näpflin, Wildi, & Sarnthein, 2007). In particular, a spectral shift from alpha to beta has been previously used as an operationalization of resting-state brain dynamics associated with spontaneous fronto-parietal network activity linked to increased attentional investment (Laufs et al., 2006). By using this electrophysiological activation measure, we found that the laterality score has a predictive functional meaning especially in mid-DLPCF reconstructed brain source. In this portion of the DLPCF, indeed, the laterality score predicts performance with a good level of process-related specificity, compatibly with the ROBBIA-derived model, and generalizes across multiple task contexts and domains.

For example, we found that intrinsic left-lateralized β/α activity over the mid-DLPCF (and pre-SMA) predicted smaller Stroop effects in both verbal and spatial domains. The domain generality was demonstrated by an intersection analysis showing that, in the mid-DLPCF ROI, the two Pearson correlations between the β/α lateralization index and each (spatial and verbal) Stroop effect were both significant (Ambrosini & Vallesi, 2017). On the other hand, intrinsic right-lateralized β/α activity over this mid-DLPCF predicted better performance in monitoring target events in temporal, spatial, and letter-detection tasks (Ambrosini et al., 2020).

Finally, a third related study is worth mentioning here (Ambrosini & Vallesi, 2016). It focused on the performance in three different task-switching paradigms after resting-state EEG recording, that is, the classical color–shape task-switching, and verbal and spatial variants of this paradigm. Compound measures of the target executive processes were obtained by using z-transformed average switching costs (i.e., RT difference between switch and repeat conditions in task-switching blocks) and mixing costs (i.e., RT difference between repeat trials in task-switching and in single task blocks) in these three task-switching paradigms. In particular, switching and mixing costs were used as (inverse) efficiency measures for phasic and sustained cognitive control processes, akin to criterion setting and monitoring, respectively, which have already been reported to be linked to prefrontal asymmetries (Braver, Reynolds, & Donaldson, 2003) and to rely on independent underlying latent variables (Smith, Banich, & Friedman, 2019). The only region that survived false discovery rate correction in the interaction analysis with significantly opposite correlations between the EEG-based lateralization index and the two behavioral compound measures of switching and mixing costs was again the mid-DLPCF. In particular, rightward asymmetrical activity (β/α ratio) in this generator predicted smaller mixing costs, whereas leftward asymmetrical activity predicted smaller switching costs, compatibly with a role of these lateralized activities in monitoring and criterion setting. These results are compatible with those from other groups. For instance, lower switch costs have been linked with intrinsic fMRI connectivity of a hub in the left pFC region, which was however centered a bit more ventrally, that is, the left inferior frontal junction (Yin, Wang, Pan, Liu, & Chen, 2015). Moreover, left-scalp frontal alpha power reduction during resting state predicted better Wisconsin Card Sorting Test performance (Çiçek & Naçlıçak, 2001). The latter findings were not replicated in another study by Gordon et al. (2018), who however used switch behavioral measures and scalp-related EEG measures different from those used in our study (Ambrosini & Vallesi, 2016).

These studies expanded our understanding of the underlying causes of the interindividual variability in executive functioning. In particular, they showed that a left–right prefrontal hemispheric specialization for criterion setting and monitoring, respectively, not only exists independently of specific task requirements but is also present at rest and it shows predictive power for subsequent EF-related behavior.

**ALTERNATIVE ACCOUNTS OF FUNCTIONAL PREFRONTAL ASYMMETRIES**

There are also alternative accounts of the role of the two lateral pFCs in executive functioning. According to Goel’s model (Goel, 2015, 2019), for instance, the right pFC complements the left pFC “interpreter” (Thompson-Schill et al., 1997; Gazzaniga, 1995) by maintaining and even inflating uncertainty, allowing for the exploration of nonstandard solutions and more flexible planning. This account would predict a positive correlation of right pFC activations with RTs during decision-making, because
enhancing uncertainty should delay the decision time, but such a correlation has not always been observed when explicitly tested (Fleck et al., 2006). In our view, the role of the right pFC is to continuously check contingencies under uncertain contexts to optimize behavior. The fact that left frontal patients seem to explore too many possibilities when planning (Goel, 2015) could be also accounted for by an exaggerated continuous monitoring effort by the right lateral pFC (because of lack of inhibition from the homologous side) than to enhancing uncertainty. We agree on the fact that right frontal involvement is more prominent in uncertain, low-confidence conditions; explaining why this happens is where our view differs from Goel’s (2015) position.

Another already mentioned influential model proposes that the right inferior frontal cortex is involved in top-down suppression of motor responses when relevant environmental or internal signals have been captured. Activation of the right inferior frontal cortex is typically observed in paradigms requiring response inhibition (Nakata et al., 2008; Aron, Robbins, & Poldrack, 2004; Rubia, Smith, Brammer, & Taylor, 2003), and virtual and real lesions in this region impair response inhibition (Molenberghs et al., 2009; Chambers et al., 2006; Aron, Fletcher, Bullmore, Sahakian, & Robbins, 2003; but see Swick, Ashley, & Turkmen, 2008, for evidence of inhibitory deficits after left pFC damage).

Classically used inhibitory paradigms, such as go/no-go and stop-signal tasks, however, also require other related cognitive processes, including response selection, sustained attention, working memory, and monitoring (Cistad & Boulinguez, 2013; Chambers, Garavan, & Bellgrove, 2009; Mostofsky & Simmonds, 2008). Through various approaches, including experimental psychology, fMRI, EEG, and computational models, it has been demonstrated that inhibition does not require dedicated control mechanisms beyond context-monitoring ones, and that these mechanisms are the same irrespective of whether infrequent stimuli are associated with a request to stop or rather to initiate a response (Hampshire, 2015; Erika-Florence, Leech, & Hampshire, 2014; Chatham et al., 2012; Dodds, Morein-Zamir, & Robbins, 2011; Walthier, Friederich, Stippich, Weisbrod, & Kaiser, 2011; Sharp et al., 2010).

Finally, functionally multipotent fronto-parietal regions sustaining several cognitive abilities have been described (Assem et al., 2020; Duncan & Owen, 2000). Some of these studies point to a left lateralization of some of these general purpose nodes. For instance, a PET study showed that the left lateral pFC was commonly activated during tasks conceived to tax various EFs, including updating, shifting, and inhibition (Collette et al., 2005). We also recently found that damage to the left inferior frontal junction produced the most severe cognitive deficits across multiple neuropsychological tests, a result that survived even after removing verbal tests from the analyses (Arbula et al., 2020). Trying to conciliate these findings with those describing a process-specific role of these and other pFC subregions, as reviewed here for the ROBBIA model, should be an important target of future research.

TOWARD A SYNTHESIS

Given all the accumulated evidence reviewed above, we used a confirmatory factor analysis to “close the loop,” as Don Stuss used to say, by formally testing multiple theoretical models on how the two investigated executive processes might interact with the task domain (Ambrosini et al., 2019). Previous factor analysis works on EF were usually uninformative regarding how the models corroborated through factor analysis might be implemented in the brain. Moreover, previous studies did not systematically and explicitly take into account the involved task domains or material when assessing the EF latent structure. Controlling for task domain seems critical, also in the light of evidence showing that interindividual variability for each domain may significantly affect performance in EF tasks (Naber, Vedder, Brown, & Nieuwenhuis, 2016; Deary, Penke, & Johnson, 2010). In our study (Ambrosini et al., 2019), we tackled these issues by examining whether the ROBBIA model, which is based on the functional hemispheric differences in lateral pFC (Vallesi, 2012; Stuss, 2011; Stuss & Alexander, 2007), holds true above and beyond domain-specific subdivisions.

To this aim, we administered a battery of computerized tasks assessing criterion setting and monitoring to a sample of 157 healthy young adults. Switch costs, Stroop costs, and an attentional shift index in dichotic listening were used as measures of criterion setting, whereas mixing costs, target monitoring costs, and RTs on variable (long) FPs were included as measures of monitoring. Notably, we used materials and/or task versions that required cognitive component operations known to be lateralized, such as verbal (left-lateralized), visuospatial, and implicit temporal (right-lateralized) processes. Therefore, the task domains were orthogonal to the required EFs. By doing this, we were able to test a process-based, domain-independent model of organization of EFs, in which performance is explained by two latent variables representing the criterion setting and monitoring constructs. In addition, we directly contrasted this process-based model with a purely domain-based model, in which performance is explained by two latent variables representing left- and right-lateralized low-level cognitive processes involved in the tasks we used, and also with a process-based but domain-dependent model, in which performance is explained by the interaction between the two lateralized EFs and the two lateralized task domains.

Confirmatory factor analysis showed that performance variance could be explained according to a process-based model (criterion setting vs. monitoring), which provided a much better fit to the observed data as compared to a purely domain-based model or an interaction model. Moreover, there was also evidence that criterion setting and monitoring are distinct, unrelated executive processes,
as a further factor analysis revealed that performance variance is also well explained when no commonality is shared between these two latent factors.

Of note, this factor analysis solution was obtained despite that tasks classically seen as tapping cognitive inhibition (i.e., verbal and spatial Stroop) were treated together with task-switching paradigms, under the assumption that they also involve criterion setting and not an independent inhibitory module. Consistent with our findings, lesions to the left VLPFC cause deficits in both Stroop and task-switching (Tsuchida & Fellows, 2013). Common left-lateralized fronto-parietal activations underlying Stroop and task-switching performance are also partially corroborated by fMRI evidence (Nee, Wagner, & Jonides, 2007; Derrfuss et al., 2005; Derrfuss, Brass, & von Cramon, 2004) and neural network modeling (Herd et al., 2014). It is however worth testing whether other types of inhibition, including the motor inhibition required in the stop-signal paradigm, show a higher degree of independence from the criterion-setting construct (cf. Chatham et al., 2012).

Finally, it is also useful to relate our factor analysis results with the highly influential model of EFs by Miyake and colleagues (Friedman & Miyake, 2017; Miyake et al., 2000), which was also based on factor analysis. Unlike our model, the set of factors reported in their updated unity and diversity model does not directly originate from brain-related evidence. On their model, there is a common EF factor, which captures variance across all EF tasks, including inhibition-related tasks, and two more specific latent factors, that originate from the residual correlations among updating and shifting tasks, respectively, after removing the correlations because of the common factor (Friedman & Miyake, 2017). Our criterion-setting factor could partially correspond to their shifting factor, although there are also some important differences. For instance, although both models deny a special status to inhibition, we included Stroop performance in criterion setting, whereas they included it in their common factor. The monitoring factor seems instead more semantically related to their updating, as their behavioral tasks used to characterize updating require continuous evaluation of critical events, although their updating requires an additional working memory component. Regarding the common factor, however, we tested a unitary model in which both criterion-setting and monitoring measures were explained by a common latent variable, but this model was significantly worse than the criterion-setting/monitoring model and did not fit the data satisfactorily. Notwithstanding these considerations, a complete evaluation of commonalities and differences between these two models (Ambrosini et al., 2019; Friedman & Miyake, 2017) would require the use of a common set of tasks in a future study.

The distinction between left prefrontally mediated criterion setting and right prefrontally mediated monitoring was also recently causally corroborated in a neuropsychological study with patients with brain tumor (Arbula et al., 2017), who were administered with three easy versions of a go/no-go task: letter discrimination, position discrimination, and an FP task. Although the FP paradigm is not formally a go/no-go task, the warning signal could be interpreted as a sort of no-go stimulus that requires motor inhibition to avoid pretarget anticipations (Boulinguez, Jaffard, Granjon, & Benraiss, 2008). Patients were grouped according to their surgical lesion location as left prefrontal, right prefrontal, and nonprefrontal patients. The behavioral deficits observed in prefrontal patients were in agreement with predictions from the ROBBIA model examined here. Regardless of the specific task version, right prefrontal patients showed more omissions to go stimuli with respect to patients with lesions elsewhere in pFC. This pattern was probably because of deficits of monitoring but also of closely related sustained attention and energization, compatibly with a distribution of lesions mostly encompassing inferior lateral and superior medial prefrontal regions (also see Picton et al., 2007). Conversely, left prefrontal patients showed an increased rate of both go omissions and no-go false alarms, suggesting a target discrimination impairment compatible with a loss of task set. These results are in partial agreement with (and extend to different task contexts) those obtained in a previous go/no-go study by the ROBBIA group (Picton et al., 2007), in which lesions to the right ACC were associated with a higher rate of omissions, whereas lesions to left superior medial frontal areas were accompanied by increased false alarms (also see Swick et al., 2008; Stuss et al., 2002).

**FUTURE DIRECTIONS AND CONCLUSIONS**

The ROBBIA model, and in particular the anatomofunctional characterization of criterion-setting and monitoring processes, was supported using multimodal approaches typical of cognitive neuroscience and interindividual difference perspectives. Notwithstanding this progress, it would be desirable to also adopt advanced network analysis approaches to obtain a wider picture on the brain dynamics underpinning these important executive processes.

It would certainly be also useful to test the applicability of this model in other fields. For instance, it would be desirable in future studies to move from semantic definitions of criterion setting and monitoring to more formal computational models of these complementary EFs through a multidisciplinary approach. More generally, Bayesian modeling and similar computational approaches could be used more extensively to develop precise hypotheses about the neural computations underpinning higher-level cognitive functions and generate refined educated guesses, instead of using fuzzy taxonomies of these complex latent variables that guide neuroimaging analyses for functional localization (Cohen et al., 2017).

As another example of a potentially fruitful multidisciplinary extension of the ROBBIA model, in psychiatry, many positive symptoms, such as hallucinations and delusions, could probably be explained by short circuits in the
connectivity between posterior perceptual regions and more anterior, possibly lateralized, regions implementing EFs like monitoring and reality check (e.g., Shine, O’Callaghan, Halliday, & Lewis, 2014; Coltheart, Langdon, & McKay, 2011; Ffytche, 2008; Perneckz et al., 2008; Ashtari et al., 2007; Vignal, Chauvel, & Halgren, 2000) and also criterion setting (Li, Sweeney, & Hu, 2020).

Finally, it was a Don Stuss’ strong desire to use the acquired theoretical knowledge related to the ROBBIA model to design rehabilitation programs for EFs in patients with brain damage (personal communication). Therefore, applying the ROBBIA principles to build up theory-driven behavioral training programs and neuromodulation protocols aimed at rehabilitating or potentiating executive functioning would certainly do great justice to Don’s precious legacy. An example could be a neurorehabilitation program to alleviate deficits on criterion setting or monitoring, which may focus on adaptive tasks tapping these EFs using several types of material to favor generalization of functional recovery to different task contexts. These behavioral interventions could be coupled with repetitive TMS protocols implemented on left and/or right lateral pFC aimed at rebalancing aberrant interhemispheric dynamics, with the hope of restoring appropriate executive functioning, for instance, after a prefrontal tumor or stroke.

In conclusion, the present selective review documents how fruitful the ROBBIA model has been since its first formulation (Stuss et al., 1995) in stimulating empirical investigation that eventually corroborated and extended this brain-inspired cognitive model, by showing how different EFs such as criterion setting and monitoring are repeatedly implemented by recruiting more left and right lateral prefrontal regions.

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