Research report

Dynamic and strategic aspects of executive processing

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Abstract

Executive cognitive functions have been postulated to include both dynamic behavioral selection and strategic goal-setting or response preparation. To investigate the relation between these aspects of executive processing, we embedded an event-related oddball paradigm within a blocked design. Subjects responded to infrequent targets presented within a series of standard stimuli that required no response; this task alternated with a visually similar nontask condition. Using functional magnetic resonance imaging (fMRI), we found that a set of brain regions including dorsolateral prefrontal cortex (dlPFC), insular cortex, cingular cortex, and the basal ganglia demonstrated transient activation both to target stimuli and to the onset of task blocks. Within the parietal cortex, there was a dissociation such that the supramarginal gyrus exhibited greater activity to the target stimuli than to block onsets, while the converse pattern was observed in the intraparietal sulcus. Sustained positive activity during task blocks was present in the caudate and supplementary motor area, while sustained negative activity was present in the precuneus and medial parietal cortex. We conclude that dlPFC and related brain regions mediate both dynamic and strategic processing, through the preparation and selection of rules for behavior.
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1. Introduction

Executive processes control changes in thought and behavior based on information from the sensory environment. As typically characterized, executive processes are dynamic, meaning that they exert active but transient control over behavior. Neuroimaging studies have demonstrated that many executive processes evoke activity in a network of brain regions [28] that includes dorsolateral prefrontal cortex (dlPFC), related subcortical regions including the basal ganglia and thalamus, and selected temporal and parietal regions [1,2,5,18,25,31]. As we have previously shown, activity within this network increases or decreases based upon short-term stimulus patterns, indicating its sensitivity to moment-to-moment changes in the context for behavioral selection [15]. Converging evidence from patient studies has shown that damage to this network results in impairments to behavioral flexibility across different contexts and stimuli and to anticipation of future events [12,20,22].

Although it is clear that activity in this network is evoked by events that require application of executive control (e.g., that require changes from a prepotent response to an infrequent response), how this activity relates to other more strategic or goal-oriented aspects of executive processing is less clear. One function commonly reported to be mediated by dlPFC is working memory, which is often defined as the active maintenance of stimulus information over a delay interval. Early studies by Jacobsen [16] demonstrated that dlPFC damage impairs monkeys' ability to maintain information over a delay period, a result later confirmed by electrophysiological studies in nonhuman primates [11,29] and neuroimaging studies in humans [6,17,21,36]. Working memory has important strategic consequences for behavior, notably in the insulation of stimulus information and task goals against distraction [3]. Another potentially interesting class

of strategic processes includes the initiation of modes of responding, as frequently studied using task-switching paradigms. Transient dlPFC activity is evoked by switching from one task to another regardless of whether the tasks themselves evoke such activity [8,41]. Furthermore, task switching is impaired with prefrontal damage [30,32].

Based on these latter results, it is possible that studies that measure transient activation could miss important aspects of executive function. Consider the common oddball task, which requires subjects to attend for the presence of infrequent target stimuli that require a different behavioral response than frequent standard stimuli. In most variants of this task, the standard and target stimuli are presented in rapid succession throughout the task blocks, and researchers investigate whether the target events evoke transient electrophysiological or hemodynamic changes. Note that participants in this task remain in the same response state throughout, such that they must continuously attend for the presentation of the target stimuli from the beginning to the end of each experimental run. Thus, it is impossible to determine whether the very performance of the task evokes activity independent of the target events within the task. For example, activity in a given brain region could be influenced by the performance of the task, reflecting processes associated with vigilance, sustained attention, or motor preparation. Alternatively, there could be no increases in activity during task performance except for those associated with the target events themselves. Without variance in the response state within the task, these two possibilities are indistinguishable.

To investigate the relation between dynamic and strategic executive processes, we embedded a standard event-related executive processing task as described above within a blocked design [4,7,9], while measuring changes in blood oxygenation level using functional magnetic resonance imaging (fMRI). Participants detected infrequently presented target shapes within a stream of nontarget shapes. We alternated task blocks where targets were present and responses were required, with visually similar nontask blocks where no targets were present and no responses were required. Our key experimental question was whether the same regions that show transient increases in fMRI activity to the target events would exhibit changes in activity associated with the task blocks, such as sustained

increases in activity throughout a block or transient increases in activity at the onset of the block.

We tested for two forms of strategic, task-related activity: sustained increases in activity during task blocks compared to nontask blocks, and transient increases in activity at block transitions. Of significant interest will be double dissociations between brain regions that are often coactive in executive processing tasks, such as within prefrontal and parietal cortices, if one region is associated with dynamic changes and another with strategic changes.

2. Methods

2.1. Participants

Fourteen healthy volunteers (mean age: 26 ± 8 years; 10 female, 4 male) gave written consent for their participation, as approved by the Institutional Review Board of Duke University Medical Center.

2.2. Experimental design

On each trial, a single object was presented at fixation for 250 ms (see Fig. 1), with stimulus-onset asynchrony fixed at 1500 ms. Three types of objects were presented: blue circles, blue squares, and red triangles. The size and shading of each object varied across trials (mean size of about $4°$), although the base color and shape were kept constant. The stimulus series was divided into alternating task and nontask blocks, each consisting of 16 stimuli (24 s). In task blocks, the blue shapes were presented, and the subjects pressed a button with their right hand when a blue circle appeared (8% of task trials) but made no response when blue squares appeared (92%). The first three stimuli in each block were always nontargets, as was the last stimulus. Targets never occurred on successive trials. Otherwise, the targets were presented randomly within the block. In nontask blocks, all stimuli were red triangles that required no response.

Before the scanner sessions, subjects practiced the task for 30 min in a behavioral testing laboratory. Subjects were instructed to respond as quickly as possible to the circles while maintaining a low error rate, and they were told that no targets would be presented during the nontask periods.
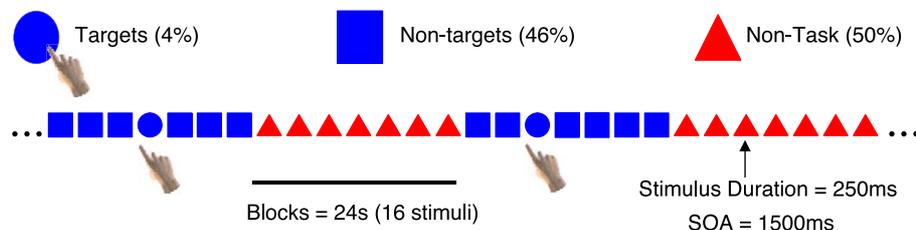

Fig. 1. Schematic of the experimental design. Subjects viewed a series of shapes, each presented for 250 ms with a 1500-ms stimulus-onset asynchrony (SOA). During task blocks, subjects pressed a button at the occurrence of targets (blue circles; 8%) that were infrequently presented within a series of nontargets (blue squares; 92%). During nontask blocks, red triangles were presented that required no response. Each block consisted of 16 stimuli.

Subjects fixated on a cross at the center of the display during the experiment. Stimuli were presented and responses were recorded using CIGAL [45]. Each subject participated in eight 9-min runs, for a total of 88 task/nontask cycles and approximately 110 target events.

2.3. fMRI methods

Functional images were acquired using BOLD contrast T_2^*-weighted spiral echoplanar MRI (TR, 2000 ms; TE, 40 ms; flip angle, 90°; voxel size, 4×4×4 mm) on a 1.5-T GE (Waukesha, WI) scanner. For each subject, 28 axial slices were selected parallel to the line connecting the anterior and posterior commissures. High-resolution 3D SPGR images were acquired to aid in normalization and coregistration.

The experimental analyses used a combination of SPM99 (Wellcome Department of Cognitive Neurology, London) and custom MATLAB (Mathworks) scripts. Functional images were corrected for subject motion and slice timing and were normalized into a standard stereotaxic space for comparison across subjects. Each subject's data were analyzed using a general linear model. Within that model, four regressors were created, reflecting changes associated with the target events, the onset of the task blocks, the onset of the nontask blocks, and sustained activity during the task blocks. The regressors for the target events and block transitions were created by convolving impulses at the onset of each stimulus with a theoretical hemodynamic response (SPM99) at each event of interest. The regressor for task-related sustained activity was created by convolving a theoretical hemodynamic response with a boxcar waveform determined by the task timing. Additional nuisance factors were included in the model to remove scanner drift across runs.

The output of the general linear model for each subject was used as the basis of a second-order random-effects analysis across subjects. The random effects analysis determined the final activation maps and was used to select functional regions of interest. We report regions of activity that passed a significance threshold of α=0.0005, with a minimum cluster size of 2 adjacent active uninterpolated voxels [10,46].

3. Results

Mean response time to targets across subjects was 460 ms, with individual subjects' mean response times ranging from 388 to 750 ms. Responses were very accurate (99.2% correct detection). The false positive rate, reflecting responses to nontarget squares, was 0.3%, and responses were slower on these trials compared to targets (mean response time: 643 ms; $t(11)=2.23$, $p<0.05$). There were no responses during the nontask blocks, indicating that the blocked design adequately separated task and nontask periods.

Detection of an infrequent target elicited activity in a set of regions in prefrontal, parietal, and limbic cortices, along with activity in related subcortical regions (see Table 1). Shown in Fig. 2A are foci of significant activation ($p<0.0005$) in the anterior middle frontal gyrus (MFG;

Table 1
Coordinates of maximal significance values

Region	Target				Sustained				Task onset				Task offset			
	Side	x	y	z	Side	x	y	z	Side	x	y	z	Side	x	y	z
Middle frontal gyrus	R	38	38	34					R	36	42	38				
Anterior/medial cingulate	B	0	4	44					B	0	10	44				
Insula	B	38	6	12					B	40	8	8				
Central sulcus	L	−36	−30	58					L	−38	−28	58				
									L	−45	−46	50				
Putamen	L	−24	6	2					B	−26	−10	12				
Thalamus	B	−16	−34	14					B	0	−24	12				
Cerebellum	R	12	−54	−9												
STS	R	61	−55	21												
SMG	R	61	−42	45												
Lingual/fusiform gyri	R	28	−92	−2					B	−24	−78	−8				
Intraparietal sulcus	R	24	−72	44					B	26	−76	44				
Posterior cingulate /precuneus									B	2	−46	54				
									B	0	−22	42				
Precentral sulcus									R	54	0	32				
Caudate	R	14	−2	20	L	−18	−6	26								
Supplementary motor area					L	−8	−2	64	B	−2	−8	64				
Precuneus/retrosplenial cortex					B	**18**	**−70**	**14**								
Precuneus					R	**8**	**−66**	**65**								
Posterior thalamus					L	**−16**	**−34**	**4**								
Ventromedial prefrontal cortex													L	**−6**	**46**	**0**

Listed are coordinates in MNI space of the centroids of clusters of significant activation. If a cluster was active in more than one condition, the location of the most significant voxel in each condition is indicated. Hemisphere is indicated as left (L), right (R), or bilateral (B). Where separate foci of activation was present bilaterally, the coordinate reflects the hemisphere with more extensive activation. Coordinates in bold typeface indicate significant negative activity.
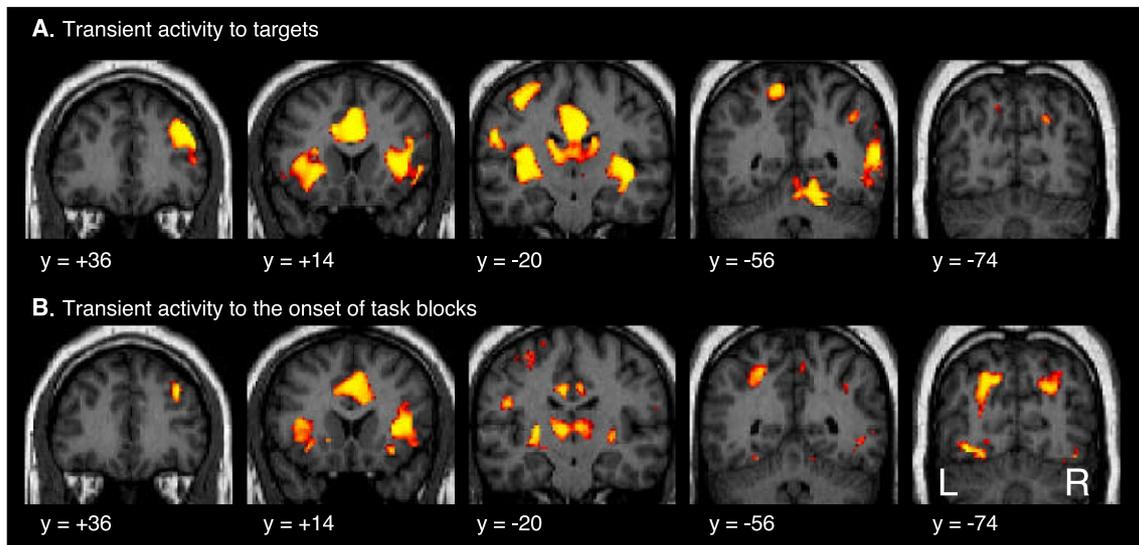
Fig. 2. Transient activity to the detection of targets and the onset of task blocks. We identified brain regions that showed significant transient activity to the targets (A) or to the onset of task blocks (B). Visible in the overlaid color maps are clusters exceeding a significance threshold of $p<0.0005$ with a minimum cluster size of 2 adjacent uninterpolated voxels. Similar brain regions are active in both conditions, including dorsolateral prefrontal cortex, anterior insular cortex, cingulate cortex, motor cortex, the basal ganglia, and the thalamus. The supramarginal gyrus and cerebellum were active to the targets but not to the block onsets, while the intraparietal sulcus was more active to the block onsets than to the targets. The left hemisphere is shown on the left side of these images.

shown on the slice at $y=+36$) and the supramarginal gyrus (SMG; $y=-56$); these activation locations are consistent with those previously reported in nonblocked oddball tasks [18]. Activity in both of these regions was right-lateralized, consistent with previous reports. We also found significant activity in the cingulate gyrus (CNG, bilateral), beginning anteriorly ($y=+14$) and extending posteriorly ($y=-20$) to approximately the coronal plane of the posterior commissure. Significant activity was also found in the anterior and middle insular cortex (INS, bilateral; $y=+14$, -20), the basal ganglia, and thalamus. Finally, we found regions of significant activity spanning the central sulcus in the right hemisphere and within the cerebellum in the left hemisphere. As the subjects responded by pressing a button with their right hand, these foci reflect the contra- and ipsilateral organization, respectively, of these motor-related regions.

We next identified brain regions that evinced transient increases in activity with the onset of the experimental task.

Immediately apparent was the striking correspondence with the previously described target-related activation (see Fig. 2). Block onsets evoked activity in a set of regions similar to that described above, including MFG ($y=+36$), CNG ($y=+14$), INS ($y=+14$), the thalamus ($y=-20$), and the basal ganglia ($y=-20$). Significant activity was also present in the primary motor cortex ($y=-20$), although no suprathreshold activity was found in the cerebellum. We note that this correspondence in motor cortex was present although no responses were required (or made) for the block onsets. Within the parietal cortex, there was a double dissociation between regions active to target events and regions active to task onsets. Whereas activity in the right SMG was present to the target events, no activity in that region was found for the block onsets. Conversely, significant and spatially extensive bilateral activity was found in the bilateral intraparietal sulcus (IPS; $y=-56$, -74) to the block onsets, but only a small focus of activity in the right IPS was found to the targets.
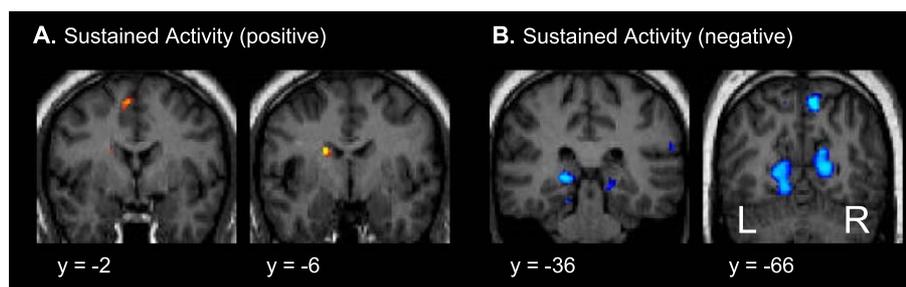

Fig. 3. Sustained activity during task blocks. Shown are regions with significant positive (A) and negative (B) sustained activity during the experimental task, independent of the target events themselves. The overlaid color maps show clusters exceeding a significance threshold of $p<0.0005$ with a minimum cluster size of two adjacent uninterpolated voxels. Foci of increased activity were found in the caudate and supplementary motor area, while foci of decreased activity were found in the precuneus, posterior thalamus, and superior parietal lobule. The left hemisphere is shown on the left side of these images.

None of the regions had significant decreases in activity at task onset, nor were there any regions with significant increases in activity at task offset. One region, along the cingulate sulcus in ventromedial frontal cortex, exhibited a significant transient decrease in activation at task offset (see Table 1).

We additionally investigated whether there was significant sustained activity associated with the task blocks (Fig. 3). By including independent regressors for the targets and task blocks within the same general linear model analysis, we could identify regions with sustained activity that was independent of the timing of target events. Two regions showed significant positive sustained activity (i.e., greater activity in task blocks than nontask blocks): the caudate ($y=-6$) and the supplementary motor area (SMA; $y=-2$) within the medial frontal gyrus. Several posterior regions had significant negative sustained activity (i.e., greater activity in nontask blocks), including the precuneus ($y=-66$) and posterior thalamus ($y=-36$). Note that these regions do not overlap with the areas exhibiting transient activity. To verify that no sustained activity was present in the latter, we examined the time courses of activity in blocks without any target events. Although activity was present at block onset, there was no evidence for significant sustained activity in those regions.

4. Discussion

Our results support the idea that distinct, but partially overlapping, sets of brain regions support dynamic and strategic executive processes. Three results are primary. First, a restricted set of anterior brain regions including dlPFC exhibits increased activity both to target stimuli and to the onset of task blocks, although the former requires a behavioral response while the latter has no such overt response requirements. Second, distinct sets of regions within the parietal cortex exhibit activity to targets and block onsets, reflecting different roles in executive processing. Third, the regions associated with targets do not show significant sustained activity across task blocks. Instead, positive sustained activity was found in regions associated with motor preparation, while negative sustained activity was found in regions associated with monitoring the external world. We next consider the implications of these results for theories of cognitive function.

Previous neuroimaging and lesion studies have demonstrated that dlPFC, CNG, and related regions are associated with the active control of behavior. In general, experimental paradigms that require subjects to inhibit a planned or prepotent behavior and/or select a novel behavior evoke activity in dlPFC, especially in the right hemisphere [5,15,18,25]. This selection process has been described as depending upon contextual novelty [38], as even well-practiced behaviors that are unexpected based upon context will evoke dlPFC activity [14]. Likewise, the

hallmark of dlPFC damage is an impairment in the selection of plans for behavior; such patients are unable to flexibly choose among possible alternatives, preferring well-practiced behaviors regardless of context [22,23,27]. Mesulam [26] has characterized the role of the prefrontal cortex, taken generally, as allowing transcendence of a default mode for behavior. Intact prefrontal cortex allows extension of behavior beyond passive responses to external stimuli, such that one can change behavior flexibly based upon context and can anticipate the consequences of future actions [19].

Our results indicate that a set of brain regions including dlPFC supports two executive processes: selection of responses and changes in response state. These two processes seem prima facie to be distinct and exclusive, in that the former guides action and thus involves interaction with motor systems, while the latter does not. However, some current conceptions of executive function argue that they are not distinct, but instead reflect two forms of the same process. Miller and Cohen [28] have theorized that the prefrontal cortex, in particular, organizes the mappings between goals and the means for achieving them. In many cases, these mappings may be from behaviors to outcomes, as for the generation of responses to targets in the present experiment. But in other cases, the mappings may be from mental states to outcomes, as in the changes from nontask to task blocks. We support this view, and further suggest that no real distinction exists between these two forms of control, as both reflect context-driven changes in the organization of behavior. Regardless of whether a cue indicates the selection of a specific behavior (e.g., press the left button now) or the selection of a specific strategy (e.g., attend to the left hemifield now), the resulting signal that a previous context is no longer valid will evoke transient dlPFC activity.

While there was substantial overlap between regions supporting response selection and changes in response sets, the correspondence between the areas supporting these processes was not complete. We found a clear dissociation within the parietal cortex, such that the right lateral parietal cortex (SMG) exhibited clear activity to the target events but not to the block onsets. However, the bilateral superior parietal cortex (i.e., IPS) was more active to the block onsets than to the targets. Of note is that both parietal regions are often observed to be coactive with dlPFC and CNG, albeit in different experimental paradigms. Activity in SMG has been consistently reported in the oddball task and similar paradigms [5,24,25,43], in agreement with the results from the present study. On the other hand, coactivity of prefrontal regions with IPS has been reported in working memory tasks, such as the common delayed-match-to-sample and delayed response paradigms [17,21,37,39]. Note that this latter activation is typically found both to memoranda and response stimuli (as well as sometimes during the delay interval), despite the very different requirements of those stimuli.

We suggest that these differences reflect a dissociation in control processes within the parietal cortex, such that the superior parietal cortex mediates the establishment of plans for behavior and that the lateral parietal cortex is associated with selection of the appropriate response for a particular stimulus. Recent work using single-cell recordings in primates has demonstrated that neurons in monkey area LIP, which is thought to be a homologue of human IPS, reflect the motivational value associated with different decisions [33,34,40]. Thus, responses that have a higher expected value regardless of their frequency are associated with greater activity in LIP [34], reflecting learned relations among stimuli, responses, and rewards. In contrast, the lateral parietal cortex has been implicated in selection of infrequent responses, as suggested by source localization of the commonly observed P300 potential [44]. The target-related P300 (or P3b) is evoked when a subject responds to an infrequent event, as when pressing a button to a rare target in a string of nontargets. Importantly, the P300 is modulated by the context of preceding events, such that the same stimulus may evoke a large or small potential depending upon whether it differs from the preceding stimuli [42]. Based on these previous results and those from the current study, we hypothesize that the IPS and SMG may support strategic organization of behavior and dynamic selection of behavior, respectively.

Although activity was present in many regions during the task blocks due to the presence of target stimuli, the only regions that had significant positive activity that was independent of the targets were the SMA and caudate. This activity is unsurprising, given that both regions are associated with motor preparation, and as such the sustained activity that we observed is likely to reflect motor readiness during the task block compared to the response-free nontask blocks.

Of more interest is the relative absence of sustained activity in other regions, notably dlPFC. As alluded to above, many studies of working memory, including electrophysiological studies in nonhuman primates [11,16,29] and neuroimaging studies in humans [6,17,21], have demonstrate sustained dlPFC activity when stimuli are maintained in anticipation of a response. Within the current task, there were no differential memory requirements across the blocks, in that subjects had to remember only the task rules and had to maintain those rules throughout. Thus, maintenance processes would not be expected to be greater during task blocks. Similarly, many of the active regions, notably dlPFC and parietal cortex, have been implicated in the control of attention and in sustained attention or vigilance [35]. In the absence of significant sustained activity, we speculate that this prefrontal–parietal network may instead primarily support behavioral control processes, as evident by the large transient responses observed, that may themselves be extended in time within delay intervals. Under this interpretation, sustained activity would reflect reactivation of transient control processes, rather than a separate process that must be invoked during tasks. Additional evidence from designs with longer task blocks and reduced density of target events could clarify whether sustained activation is present, even when no target events occur.

Of increasing methodological value is the use of mixed-design fMRI to understand the relation between transient and sustained activity [4,7,9]. For example, in a mixed-design study of recognition memory, Donaldson et al. [7] found transient activity in prefrontal and basal ganglia regions similar to those from the present study, as well as in temporal and parietal regions associated with the specific memory task, but only a few regions of sustained activity. Here, in addition to the sustained positive activity described above, we also found sustained negative activity in the precuneus and parietal cortex. Such decreases have been reported in many functional neuroimaging studies [13], and have been hypothesized to reflect environmental monitoring processes that are inhibited during goal-directed behaviors. We also extended earlier mixed-design studies by explicitly considering transient activity at block onset and offset, which as demonstrated here, may play an important role in task performance.

In conclusion, we suggest that activity to targets and block-onsets may reflect two related components of a single executive process: the selection and preparation of rules for behavior. The distinction between dynamic and strategic aspects of executive processing, therefore, may be a function of task requirements, rather than of different modes of cognition.

Acknowledgements

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