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Motivation and cognitive control in the human prefrontal cortex

Frédérique Kounieher, Sylvain Charron & Etienne Koechlin

The prefrontal cortex (PFC) subserves cognitive control, that is, the ability to select thoughts or actions in relation to internal goals. Little is known, however, about how the PFC combines motivation and the selection processes underlying cognitive control. We used functional magnetic resonance imaging in humans and found that the medial and lateral PFC have a parallel hierarchical organization from posterior to anterior regions for motivating and selecting behaviors, respectively. Moreover, using functional connectivity analyses, we found that functional interactions in this parallel system from medial to lateral PFC regions convey motivational incentives on the basis of rewards/penalties regulating the differential engagement of lateral PFC regions in top-down selection. Our results indicate that motivation is a dissociable function, reveal how the PFC integrates motivation and cognitive control in the service of decision-making, and have major implications for current theories of prefrontal executive function.

The PFC subserves the ability to select and motivate thoughts or actions in relation to internal goals. More specifically, the lateral prefrontal cortex (LPC) is involved in what is usually termed cognitive control¹ by forming a hierarchy of top-down selection processes from posterior to anterior regions for selecting appropriate behaviors^{2–5}. Converging evidence suggests that this hierarchy is functionally organized according to the temporal structure of events involved in action selection, which defines the crucial levels of cognitive control⁴. Thus, posterior LPC regions subserve transient control⁶ by selecting sensorimotor associations for immediate action according to the information conveyed by concomitant contextual signals (a process referred to as contextual control)³. In contrast, middle LPC regions subserve sustained control over behavioral episodes⁶ by adjusting selection in posterior LPC regions according to the information conveyed by temporally remote events (a process referred to as episodic control)³. In addition to this lateral LPC hierarchy of control processes, the medial frontal cortex (MFC) is more specifically involved in motivating behaviors by monitoring motivationally salient events such as errors, conflict situations, rewards and penalties^{7–9}. Little is known, however, about how motivation and cognitive control are integrated together: that is, how the MFC and LPC interact in the service of optimal decision-making.

To clarify this issue, we hypothesized that motivational processes in the MFC energize the cascade of top-down control processes in the LPC through lateral interactions between MFC and LPC regions^{10–12}. Thus, consistent with the pattern of anatomical connections linking MFC and LPC regions^{13–15}, we reasoned that the organization of motivation in the MFC parallels the posterior-anterior architecture of cognitive control in the LPC; posterior MFC regions (typically the pre-supplementary motor area, pre-SMA) are assumed to subserve contextual

motivation by modulating the engagement of post-LPC regions implementing contextual control, whereas middle MFC regions (typically the dorsal anterior cingulate cortex, dACC) subserve episodic motivation by modulating the engagement of mid-LPC regions implementing episodic control. Furthermore, according to previous studies (for a review, see refs. 8,9), motivational processes in MFC regions operate according to rewarding values of action sets rather than to demands of cognitive control. We therefore reasoned that contextual motivation energizes contextual control according to immediate contextual incentives signaling the rewards/penalties at stake in immediate action, whereas episodic motivation energizes episodic control according to the rewards/penalties at stake in the ongoing behavioral episode (see **Supplementary Fig. 1** online). Overall, these putative gain modulation mechanisms implementing motivation are consistent with psychological models that describe motivation as including a global energization factor that varies independently of control demands and behavior direction^{16,17}. Furthermore, the proposed functional segregation between post- and mid-MFC regions subserving contextual and episodic motivation, respectively, is consistent with previous results; the pre-SMA is preferentially involved in endogenous initiation/intention^{18–20} or inhibition^{14,21} of immediate action, possibly in relation to rewards^{22,23}, whereas the dACC is associated with behavioral adjustments in episodes following or preceding motivationally salient events (for example, errors, rewards and penalties)^{22,24–29}.

Our hypothesis first predicts that the modulation exerted by contextual and episodic motivation onto cognitive control is independent of the demands of contextual and episodic control. Second, a gain modulation mechanism, which enhances neuronal activity without altering the functional selectivity of neuronal computations underlying cognitive control, predicts that variations of contextual/episodic

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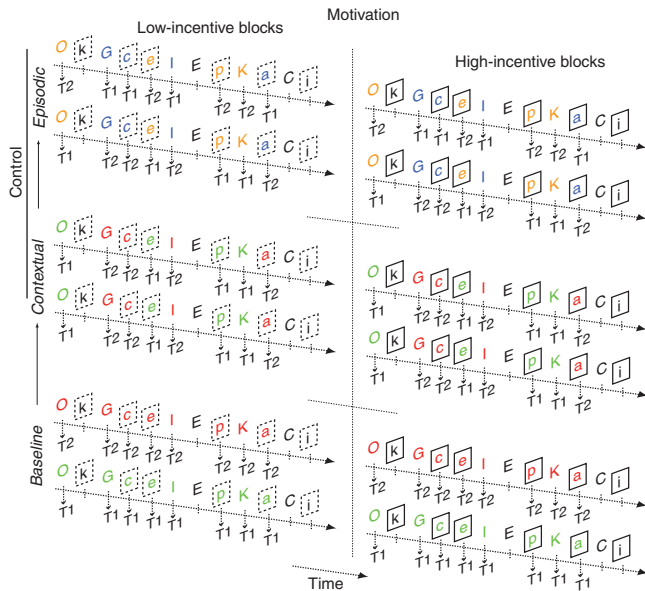


Figure 1 Behavioral protocol. Stimuli consisted of visually and successively presented letters. Series of letters were broken down into successive blocks (represented by horizontal arrows) preceded by distinctive instruction cues (not shown). The colors of the letters were contextual cues indicating the appropriate task set (T1 and T2 indicate vowel/consonant and lower/upper case discrimination tasks, respectively). Green and red were invariably associated with T1 and T2, respectively. Yellow and blue were associated with T1 or T2 according to instruction cues. Baseline blocks included either green or red cues, contextual blocks included a mixture of green and red cues (in equal proportion), and episodic blocks included a mixture of yellow and blue cues (in equal proportion). In half of the episodic blocks, yellow and blue cues were associated with T1 and T2, respectively. The converse associations were used in the remaining half of episodic blocks. In all blocks, black letters were distracters that subjects ignored by producing a fixed response (33% of trials). In each block, subjects received a monetary payoff for correct performance (or a monetary loss for errors). In half of the trials, letters were presented in frames. These additional contextual cues indicated bonus trials that were associated with an extra payoff for correct performance in these trials (or extra losses for errors). Dashed and solid frames indicated bonus trials associated with negligible and substantial extra payoffs, respectively. Blocks included either dashed or solid frames, thereby defining low- versus high-incentive blocks, respectively. See Online Methods for further details.

motivation and control demands should independently alter behavioral reaction times. Third, given that functional magnetic resonance imaging (fMRI) measures metabolic/energetic activity underlying neuronal activity rather than neuronal activity itself³⁰, we expected that the modulation exerted by contextual/episodic motivation and selection processes implementing cognitive control should have additive effects on fMRI activations recorded in the LPC. In summary, we predicted that post-MFC activations and lateral interactions between post-MFC and LPC regions would vary as a function of contextual motivation only, whereas post-LPC activations would vary as an additive function of contextual motivation and control. Similarly, mid-MFC activations and lateral interactions between mid-MFC and LPC activations would vary as a function of episodic motivation only, whereas mid-LPC activations would vary as an additive function of episodic motivation and control.

RESULTS

To test these predictions, we scanned 16 healthy people using fMRI while they were responding to successive visual stimuli by pressing left and right response buttons (task trials). Stimuli were randomly intermixed with task-irrelevant distracters to which participants had to respond by pressing the left button only (default trials). As previously described³, series of stimuli/distracters were broken down into successive blocks (that is, behavioral episodes preceded by distinct instruction cues) that varied the demand of contextual and episodic control (see Fig. 1 and Online Methods). On baseline blocks, subjects responded to stimuli in task trials using fixed sensorimotor associations (that is, a single task set). On contextual blocks, subjects had to additionally select the appropriate task set on every task trial according to fixed contextual cues accompanying stimulus occurrences. Thus, demand of contextual control increased from baseline to contextual blocks on task trials, but remained unchanged on default trials. Finally, in episodic blocks, subjects performed as in contextual blocks. However, associations between contextual cues and task sets were variable across episodic blocks and contingent on instruction cues preceding these blocks. Thus, demand of episodic control increased from contextual to episodic blocks irrespective of trial type, corresponding to the passing of information from instruction cues to subsequent trials for adjusting task set selection.

Cognitive control in the prefrontal cortex

Accordingly, we first conceived of our procedure as a 2×3 factorial design crossing trial type (default versus task) and block type (baseline versus contextual versus episodic) factors to identify the previously described cascade of control processes in the LPC³. Activations associated with contextual control were specified as an interaction between both factors, increasing from baseline to contextual blocks on task trials only (transient effect). In contrast, activations associated with episodic control were specified as a main effect of block type, increasing only in episodic compared with contextual blocks, irrespective of trial type (sustained effect, see Online Methods).

Consistently with previous data³, we found contextual control activations in the left post-PFC (inferior frontal gyrus, Brodmann's area 44; Fig. 2a). Analyses of variances (ANOVAs) showed that activations on default trials remained unchanged across blocks in this region ($F < 1$), but activations increased from baseline to other blocks on task trials ($F = 19.4$, $P < 0.001$; interaction of trial type \times block type, $F = 7.02$, $P = 0.003$; Fig. 2a). In contrast, we identified episodic control activations in the left mid-LPC (middle frontal gyrus, Brodmann's area 46/9; Fig. 2a). In this region, activations showed only a main effect of block type ($F = 8.9$, $P < 0.001$); activations were virtually identical on baseline and contextual blocks ($F < 1$), but significantly increased from contextual to episodic blocks ($F = 18.1$, $P < 0.001$), irrespective of trial type (main effect and interaction, both F s < 1.1 , $P > 0.31$). No other frontal regions, including MFC regions, showed activations associated with contextual and/or episodic control (see **Supplementary Data** online).

Effective connectivity analyses³¹ further confirmed that episodic control was exerted through top-down interactions from mid- to post-LPC regions (see below). Consistent with such top-down interactions integrating episodic information into contextual control, left post-LPC activations increased on task trials in episodic compared with contextual blocks ($F = 11.3$, $P = 0.004$; Fig. 2a). Moreover, consistent with the hierarchical hypothesis that contextual control regions exert top-down influence on premotor regions involved in response selection³, cognitive control factors affected behavioral performance in the same way as post-LPC activations (Fig. 2b); reaction times and error rates on default trials did not significantly differ across blocks (both F s < 2.4 , $P > 0.11$), but on task trials, they gradually increased from

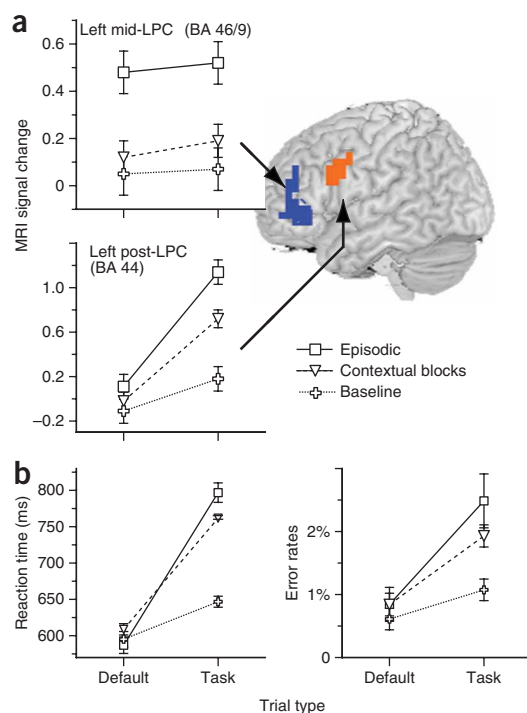


Figure 2 Cognitive control in the prefrontal cortex. **(a)** fMRI activations in the prefrontal cortex superimposed on a three-dimensional rendering of the left hemisphere are shown on the right. Orange indicates regions showing the effects of contextual control (Montreal Neurological Institute coordinates of maximal random-effect T scores, $x, y, z = -45, 15, 30, T = 3.92$). Blue indicates regions showing the effects of episodic control ($x, y, z = -40, 40, 25, T = 3.90$). Factorial analyses of fMRI activations crossing the trial type (default versus task trials) and block type (baseline versus contextual versus episodic blocks) factors are shown on the left. Data points are mean activations (\pm s.e. across subjects) computed over each region shown on the right (arrows). **(b)** Factorial analyses of behavior performances (mean performance \pm s.e. across subjects, reaction times were measured on correct trials only) crossing the same factors.

to 98.4%, indicating that subjects made no errors and received extra payoffs in more than 90% of blocks.

These manipulations constituted an additional 2×2 factorial design crossing trial type (standard versus bonus) and block-incentive value (low versus high) factors. Accordingly, activations associated with contextual motivation were specified as an interaction between the two factors, increasing from low- to high-incentive blocks on bonus trials only (transient effect). Activations associated with episodic motivation, however, were specified as the main effect of block-incentive value, increasing from low- to high-incentive blocks independent of trial type (sustained effect, see Online Methods).

fMRI results confirmed the predictions (**Fig. 3a**). We identified contextual motivation activations in the post-MFC (pre-SMA), the right post-LPC (inferior frontal gyrus, Brodmann's area 44/45) and the left post-LPC involved in contextual control. In contrast, we found episodic motivation activations in the mid-MFC (dACC), the right mid-LPC (middle frontal gyrus, Brodmann's area 46/9) and the left mid-LPC involved in episodic control. No other frontal regions had activations associated with contextual and/or episodic motivation (see **Supplementary Data**).

baseline to contextual and episodic blocks (both $F_s > 14.9, P < 0.001$; interaction trial type \times block type, both $F_s > 15.6, P < 0.001$).

Motivation in the frontal cortex

We used additional contextual cues to manipulate participants' motivation. These incentive cues modified rewards/penalties at stake across trials and blocks and were manipulated independently of the control factors described above. In each block, incentive cues signaled bonus trials associated with extra monetary payoff for correct performance on these trials (or extra losses for incorrect performance; see **Fig. 1** and Online Methods). Notably, these extra payoffs differed across blocks associated with distinct incentive cues. In low-incentive blocks, extra payoffs at stake were negligible ($\sim 5\%$ of regular payoffs), whereas in high-incentive blocks, extra payoffs were very large ($\sim 200\%$). Thus, the rewards and penalties at stake in immediate action (contextual motivation) increased from standard to bonus trials, especially in high-compared with low-incentive blocks, whereas the rewards and penalties at stake in block performance (episodic motivation) increased from low- to high-incentive blocks, irrespective of trial type. These motivational manipulations affected reaction times (see below), but had no effects on performance accuracy (all $F_s < 1$). Mean accuracy was equal

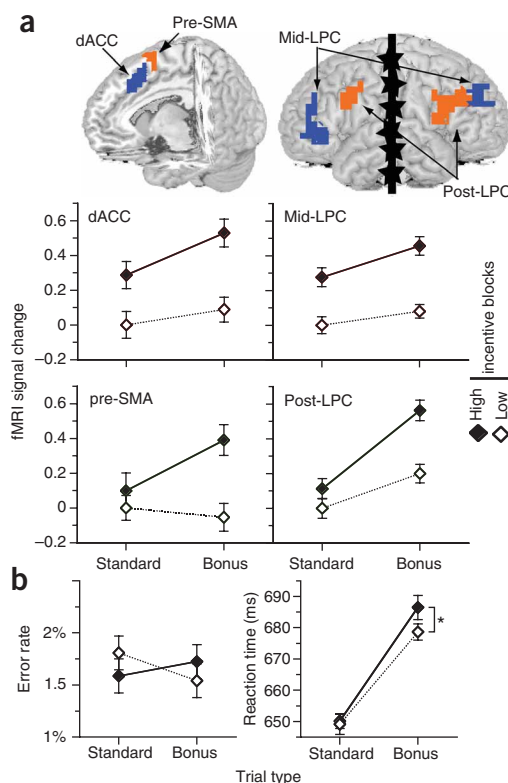


Figure 3 Motivational processes in the prefrontal cortex. **(a)** Top, fMRI activations superimposed on three-dimensional renderings of the left and right prefrontal cortex. Orange indicates regions showing the effects of contextual motivation (MNI coordinates of maximal random-effect T scores, $x, y, z = -5, -5, 55, T = 4.46$; $x, y, z = -45, 5, 25$ and $45, 30, 25, T = 3.77$ and 4.01). Blue indicates regions showing the effects of episodic motivation ($x, y, z = 10, 20, 40, T = 5.39$; $x, y, z = -35, 45, 0$ and $20, 45, 30, T = 3.77$ and 4.72). In the left hemisphere, activations were found in the regions reported in **Figure 2**. Bottom, factorial analyses of fMRI activations crossing trial type (standard versus bonus trials) and block type (low- versus high-incentive blocks) factors. Data points are mean activations (\pm s.e. across subjects) computed over each region shown above (left and right activations are averaged together). **(b)** Factorial analyses of behavior performances (mean performance \pm s.e. across subjects, reaction times were measured on correct trials only) crossing the same factors.

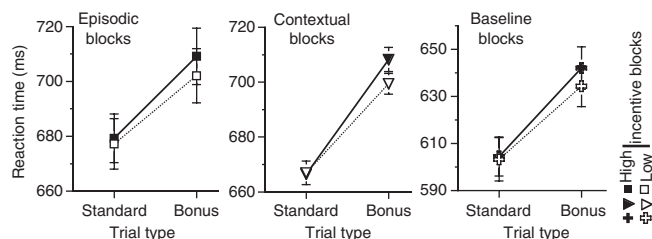


Figure 4 Motivational effects on reaction times according to control demands. Data points are mean reaction times for correct trials in baseline, contextual and episodic blocks. Error bars are s.e. across subjects. Note that motivational effects were independent of control demands.

ANOVAs showed that these motivational activations were similar in the left and right LPC (interactions with hemisphere, $F_s < 2.3$, $P > 0.15$). *Post hoc* analyses further confirmed that post-LPC and pre-SMA activations had interaction effects of contextual motivation: In the post-LPC and pre-SMA, activations increased from low- to high-incentive blocks on bonus trials (all $F_s > 11.2$, $P < 0.004$), but remaining unchanged on standard trials (all $F_s < 1.9$, $P > 0.19$; interaction trial type \times block-incentive value, all $F_s > 8.9$, $P < 0.009$; **Fig. 3a**). In contrast, dACC and mid-LPC activations had a main effect of episodic motivation (all $F_s > 35$, $P < 0.001$; **Fig. 3a**), increasing from low- to high-incentive blocks irrespective of trial type (interaction, all $F_s < 1.7$, $P > 0.20$). *Post hoc* analyses including cognitive factors confirmed that the pre-SMA and dACC showed no effects of contextual and episodic control (see Discussion), whereas the posterior region in the right LPC consistently showed a marginal effect of contextual control (interaction cognitive trial type by block type, $F = 3.31$, $P = 0.05$).

As for cognitive control factors, motivational factors modulated reaction times in the same manner as post-LPC activations (**Fig. 3b**). Reaction times increased from low- to high-incentive blocks on bonus trials ($F = 7.8$, $P < 0.01$), but remained unchanged on standard trials ($F < 1$; interaction trial type \times block-incentive value, $F = 4.8$, $P = 0.034$). There was also a main effect of trial type on reaction times ($F = 58$, $P < 0.001$), reflecting longer reaction times in bonus than in standard trials. The same main effect of motivational trial type was also significant in post-LPC ($F = 25$, $P < 0.001$), but not pre-SMA ($F = 1.1$, $P = 0.31$) activations.

Integration of motivation and cognitive control

Overall, our protocol formed a $2 \times 3 \times 2 \times 2$ factorial design crossing the cognitive and motivational factors described above (**Fig. 1**) to test the prediction that motivational incentives and cognitive control are essentially independent factors of prefrontal executive function. Our results confirmed our prediction. First, the contextual motivation effects (two-way interaction between block-incentive value (low/high) \times trial type (standard/bonus)) that we observed on reaction times were independent of cognitive blocks (three-way interaction with block type, $F < 1$); the increases in reaction times from low- to

high-incentive blocks that we observed on bonus trials were virtually identical across baseline, contextual and episodic blocks (**Fig. 4**). Motivational factors had no effects on error rates in any of the cognitive blocks (all $F_s < 1$).

Second, we found no frontal regions in which the effects of contextual or episodic motivation varied with the demands of cognitive control (**Fig. 5**). For the frontal activations described above, *post hoc* analyses further revealed no significant four-way interactions (all $P_s > 0.1$). In addition, in the pre-SMA, contextual motivation activations did not significantly vary across cognitive blocks (three-way interaction, $F < 1$) and trial type (default versus task, three-way interaction, $F = 1.4$, $P > 0.25$), whereas episodic motivation activations (main effect of block-incentive value) were unchanged across cognitive blocks and trial type in the dACC (both two-way interactions, $F < 1$) (**Supplementary Fig. 2** online). We obtained the same results in right LPC regions (all interactions, $F_s > 1.6$, $P > 0.21$). Furthermore, activations reflecting cognitive control were independent of motivational factors in the left LPC (**Supplementary Fig. 3** online). In the post-LPC, contextual control activations (showing two-way interactions between cognitive block type \times trial type) did not significantly differ across block-incentive values (three-way interaction, $F = 1.1$, $P > 0.37$) and motivational trial types (standard versus bonus, three-way interaction, $F < 1$). In the left mid-LPC, episodic control activations (main effect of cognitive block type) were independent of block-incentive value and motivational trial type (both two-way interactions, $F = 1.3$, $P > 0.3$).

Finally, we examined whether the motivational effects that we observed in LPC regions specifically resulted from lateral interactions between MFC and LPC regions. Accordingly, we reformulated our hypothesis as a model of structural linear equations with path coefficients quantifying variations of effective connectivity between the frontal regions reported above with respect to both motivational and cognitive control factors. The structural equation model included reciprocal paths linking MFC and LPC regions and oriented paths from mid- to post-LPC regions modeling top-down control (see **Fig. 6** and Online Methods).

As predicted, effective connectivity from the left mid- to post-LPC significantly increased with the demands of episodic control (episodic versus contextual blocks, $\chi^2 = 4.2$, $P = 0.04$) rather than contextual control (interaction block type \times trial type, $\chi^2 < 1$, $P > 0.5$) (**Fig. 6**). In contrast, effective connectivity between MFC and LPC regions was unrelated to the demands of episodic (all $\chi^2 < 1.7$, $P > 0.19$) and contextual (all $\chi^2 < 2.6$, $P > 0.11$) control but varied with

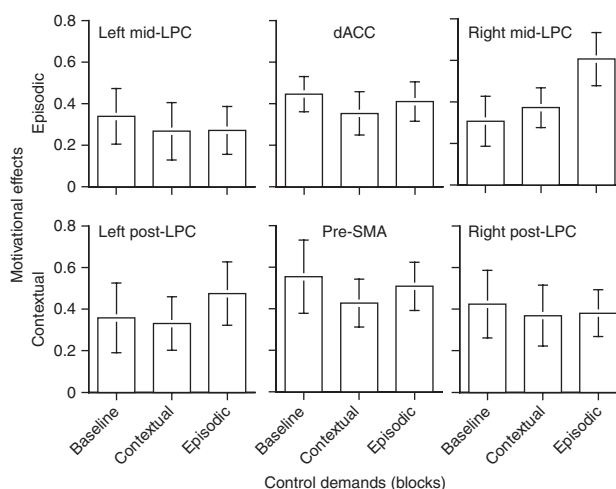
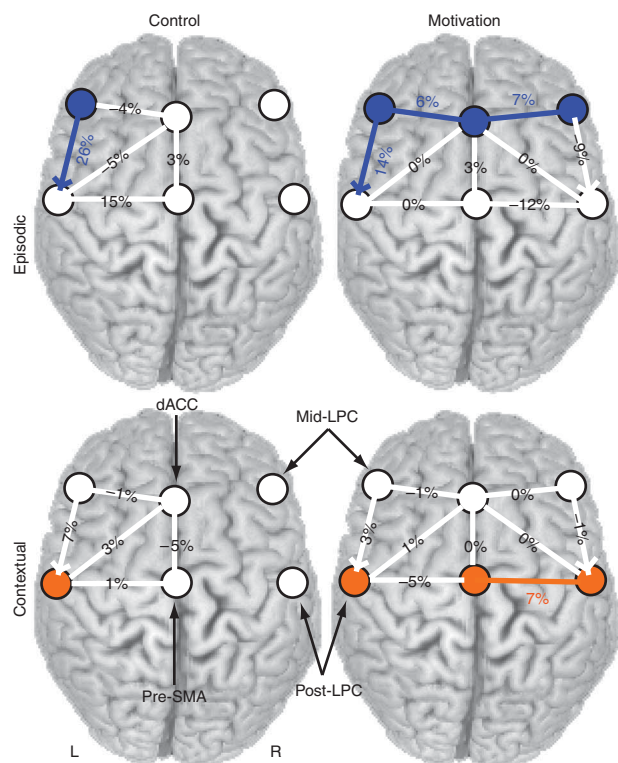


Figure 5 Motivational activations in medial and lateral frontal regions according to control demands. Magnitudes of motivational activations observed in baseline, contextual and episodic blocks in the frontal regions reported in **Figures 2** and **3**. The histograms show the contrasts of parameter estimates in the multiple regression model averaged over each region (\pm s.e. across subjects). In the bottom panel, the effects of block-incentive values (high minus low) are shown for bonus trials (sustained effects), whereas in the top panel, the effects of block-incentive values (high minus low) are shown on both standard and bonus trials (sustained effects). Note that the magnitudes of motivational activations were unrelated to control demands.



motivational incentives (Fig. 6). Contextual motivation increased effective connectivity between the pre-SMA and right post-LPC (interaction trial type \times block-incentive values, $\chi^2 = 4.04$, $P = 0.045$; elsewhere, all $\chi^2 < 1.9$, $P > 0.17$), whereas episodic motivation increased effective connectivity between the dACC and bilateral mid-LPC (main effect of block-incentive values, both $\chi^2 > 6.7$, $P < 0.01$) and from the left mid- to post-LPC ($\chi^2 = 5.6$, $P = 0.02$; elsewhere, all $\chi^2 < 2.3$, $P > 0.13$).

DISCUSSION

Our results support the idea that the LPC is functionally organized as a posterior-anterior, top-down cascade of control processes with posterior and anterior regions subserving contextual and episodic control, respectively^{3,4}. The transient versus sustained activations that we observed in post- and mid-LPC regions in relation to contextual and episodic control, respectively, provide further evidence that cognitive control is primarily organized from posterior to anterior LPC regions according to the temporal structure, rather than to the relational complexity of events involved in action selection^{4,6}. Moreover, consistent with this top-down cascade of control processes, behavioral performance varied according to post-LPC rather than to mid-LPC and MFC activations (Figs. 2, 3 and 7). Note that such a cascade was

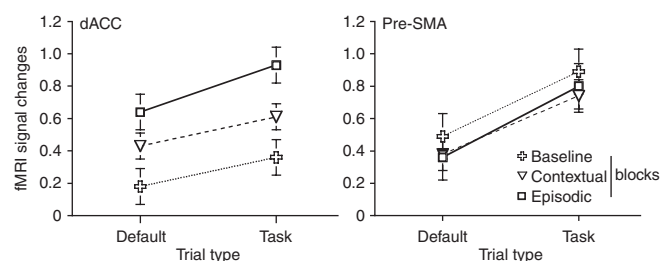
Figure 6 Diagram of effective connectivity between frontal regions. The structural equation model included the paths (lines, arrows indicate oriented top-down paths) connecting frontal regions described in the text (circles, neurological convention, approximate locations). The structural model estimates the path coefficients quantifying effective connectivity as partial correlations between related regional activations. Relative variations of path coefficients with contextual and episodic control (left) and with contextual and episodic motivation (right) are shown. Colors indicate significant variations of frontal activations and path coefficients ($P < 0.05$; see details in Online Methods). Note that statistics were appropriately performed on absolute variations of path coefficients, whereas relative variations are shown. This explains why relative variations appear large for a few path coefficients that were especially low compared with others but actually corresponded to weak, nonsignificant variations of effective connectivity.

previously observed to operate bilaterally³; the left lateralization of control processes described here probably results from the exclusive use of verbal material (letter stimuli), which is preferentially processed in the left hemisphere³².

In contrast, MFC activations and lateral interactions between MFC and LPC regions were unassociated with the demands of contextual and episodic control (see Results and Fig. 7). Consistent with previous studies^{8,12,21,33–36} (for a review, see refs. 7,37), pre-SMA and dACC activations varied with response conflict and performance difficulty, respectively. Indeed, the pre-SMA and, to a lesser extent, the dACC showed larger activations on task than on default trials (main effects of trial type, both $F_s > 13.1$, $P < 0.001$) that were virtually identical across baseline, contextual and episodic blocks (interaction trial type \times block type, $F < 1$; Fig. 7). In the pre-SMA, this pure main effect with no additional effects of control demands ($F < 1$; Fig. 7) reflected the response conflict that occurred irrespective of control demands in task trials requiring subjects to choose between the left or right response compared with default trials, which were invariably associated with the left response. dACC activations varied according to performance difficulty across blocks because dACC activations linearly increased as average performance from baseline to contextual and episodic blocks (main effect of block type, $F = 6.5$, $P < 0.001$; Fig. 7), regardless of trial type.

According to a prominent view^{12,36,37}, the MFC monitors response conflict and error-prone situations for subsequent regulation of cognitive control resources in the LPC. However, we found no evidence that MFC activations associated with response conflict and performance difficulty had an influence on LPC activations. Indeed, effective connectivity, especially between the pre-SMA and LPC regions, remained virtually constant when computed within a trial or across successive trials and even tended to decrease with increased response conflict (main effect of default versus task trials, all $\chi^2 < 1.1$, $P > 0.29$; see Fig. 8 and Online Methods). Similarly, effective connectivity between the dACC and LPC regions did not vary across cognitive blocks according to performance difficulty (baseline versus contextual versus episodic blocks, all $\chi^2 < 1.7$, $P > 0.19$). Consistent with this, we found in a

Figure 7 Factorial analyses of medial frontal activations according to cognitive factors. Data points are mean activations computed over the pre-SMA and dACC (regions shown in Fig. 3) in baseline (crosses), contextual (triangles) and episodic (squares) blocks. Error bars represent s.e. across subjects. The effects of trial type (default versus task trials) and block type (baseline versus contextual versus episodic) factors were additive in both regions (interaction, both $F_s < 1$), indicating that pre-SMA and dACC activations were unrelated to the demands of contextual control. Furthermore, pre-SMA activations were identical across cognitive blocks (main effect, $F < 1$), whereas dACC activations showed a strong linear increase from baseline to contextual and episodic blocks (main effect, $F = 6.5$, $P < 0.001$) with virtually identical increases from baseline to contextual blocks and from contextual to episodic blocks (difference, $F < 1$). Consequently, pre-SMA and dACC activations were also unrelated to the actual demands of episodic control, which varied only between contextual and episodic blocks. As explained in the Discussion, these activations instead reflected response conflict (pre-SMA) and performance difficulty (dACC).





Altogether, our results support the idea that MFC regions implement cost-benefit computations for regulating cognitive control resources in

In summary, our results support a model that describes the prefrontal executive function as a dual hierarchical system of executive processes extending from posterior to anterior regions in the MPC and LPC (**Supplementary Fig. 1**). In the posterior sector, medial regions (pre-SMA) evaluate immediate contextual incentives for action and energize (or inhibit) lateral prefrontal resources that guide action selection according to immediate contextual signals. In the more anterior sector, medial regions (dACC) retain incentive values of past events and energize/inhibit lateral prefrontal resources that guide action selection according to past events. In this system, functional interactions from medial to lateral regions convey motivational incentives rather than control demands and regulate the relative influence of immediate and past information in the cascade of top-down selection processes operating in the LPC.

Notably, the model describes the prefrontal architecture of selection processes that are contingent on external events rather than those that are based on the relative rewarding values of action sets. On the basis of our results, the model indicates that such selection processes are confined to LPC regions, which is consistent with lesion studies in monkeys^{42,43}. In contrast, reward-based selection of action sets could not be observed in our protocol, given that all action sets were equally rewarding, and there was therefore no intrinsic bias toward specific responses or task sets. Nevertheless, single-unit recordings in monkeys provide evidence that MFC regions are involved in reward-based selection, as MFC regions comprise neurons encoding associations between action sets and their rewarding values in addition to neurons coding for the rewards at stake in trials^{8,25,44}. Similar neurons have been found in the LPC²⁵, and the issue remains open whether reward-based selection is confined to MFC regions or whether MFC regions only bias selection processes in the LPC according to relative rewarding values of action sets through medial-to-lateral interactions. Both views are compatible with our results. In both cases, the MFC may globally scale rewarding values of action sets according to external cues without altering their relative values (gain control mechanism) to process external incentives regulating the engagement of cognitive control resources in the LPC that subserve action selection that is contingent on external cues.

As postulated by psychological theories^{16,17,45}, our findings confirm that reward-based energization of higher cognitive resources independently of cognitive demands and behavior direction is a central component of human motivation. We found, however, that this motivational function includes distinct incentive levels that are intimately related to cognitive stages of decision-making.

METHODS

Methods and any associated references are available in the online version of the paper at <http://www.nature.com/natureneuroscience/>.

Note: Supplementary information is available on the Nature Neuroscience website.

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AUTHOR CONTRIBUTIONS

F.K. and E.K. designed the experiments. F.K. and S.C. conducted the experiments. F.K. analyzed the data. E.K. supervised the project and wrote the paper.

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ONLINE METHODS

Subjects. Subjects (eight females and eight males aged 19–35 years) had no general medical, neurological, psychiatric or addictive history. They provided written informed consent that was approved by the French National Ethics Committee. Subjects were paid for their participation.

Behavioral protocol. Stimuli/distracters (duration, 1,500 ms; stimulus onset asynchrony, 2,500 ms) were letters that were pseudo-randomly chosen from the set A, E, I, O, a, e, i, o, C, G, K, P, c, g, k and p. Series of stimuli/distracters were broken down into successive blocks. Each block included a series of eight stimuli and four randomly intermixed distracters that were preceded 5,000 ms earlier by an instruction cue (duration, 2,000 ms) and followed 1,000 ms later by a visual feedback (duration, 2,000 ms) indicating the payoff obtained from the block. Feedback offsets were followed by a delay period (duration, 3,000 ms) before the next block.

We chose letters pseudo-randomly so that the ratio of left versus right responses in task trials and the ratio of congruent versus incongruent trials (same versus different responses for the two task sets) were equal to 1 in every block. Thus, we maintained the response conflict that occurred in task trials requiring subjects to choose between left and right responses constant across blocks compared with default trials invariably associated with left responses. We also maintained the proportions of two successive trials including identical contextual cues constant across contextual and episodic blocks, so that task switching remained constant across contextual and episodic blocks.

Before training, we instructed subjects that payoffs could vary according to their own performance as follows. Subjects earned a monetary reward for each block completed with no errors (1 €). They earned no reward if an error was made and each additional error incurred a loss (–1 €). Bonus trials (signaled by frames, pseudo-randomly chosen and forming 50% of trials in every block) were associated with extra payoffs. Subjects earned an extra monetary reward for each block completed with no errors occurring in the bonus trials. They earned no extra reward with one error and each additional error in the bonus trials incurred a loss (equal to the extra reward). Extra monetary rewards varied across blocks. In high-incentive blocks (bonus trials with solid frames, 50% of blocks), extra rewards were equal to 2 €. In low-incentive blocks (bonus trials with dashed frames, 50% of blocks), extra rewards were equal to 0.05 €. Thus, the total payoffs at stake in high-incentive blocks (1 + 2 €) were approximately three times as large as in low-incentive blocks (1 + 0.05 €). In high-incentive blocks, the total payoffs at stake in bonus trials (1 + 2 €) were three times as large as in standard trials (1 €, trials with no frames). In low-incentive blocks, the total payoffs at stake were virtually identical in bonus and standard trials (1 + 0.05 € versus 1 €, respectively).

Baseline, contextual and episodic blocks included low- and high-incentive blocks in equal proportion. Occurrences of frames were pseudo-randomized so that frames appeared in equal proportion in default and task trials, as well as in congruent and incongruent trials.

We used dashed versus solid frames for low- versus high-incentive blocks, respectively. We used a separate behavioral control experiment to ensure that these distinct visual frames did not affect reaction times independently of associated reward values (see **Supplementary Data**).

Data acquisition. For practical reasons (duration of fMRI sessions and subjects' fatigue), we carried out the experiment in two sessions; one session included only baseline and contextual blocks, whereas the other included only contextual and episodic blocks. We counterbalanced the order of sessions across subjects and genders. We trained subjects on the tasks a few days before each session by practicing the protocol once. The two sessions were administered in 2 successive weeks.

Each experimental session formed an 8×8 latin square consisting of eight series of stimuli (fMRI scanning runs) divided into eight blocks. In each scanning run, the eight blocks formed the four experimental conditions crossing control and motivation block factors. Thus, in one experimental session, each scanning run included one low-incentive baseline block with only green cues and one with only red cues, one high-incentive baseline block with only green cues and one with only red cues, two low-incentive contextual blocks, and two-high incentive contextual blocks. In the other experimental session, each scanning run included two low-incentive contextual blocks, two

high-incentive contextual blocks, one low-incentive episodic block with yellow and blue cues associated with T1 and T2, respectively, and one with the converse associations, and one high-incentive episodic block with yellow and blue cues associated with T1 and T2, respectively, and one with the converse associations. We administered the behavioral protocol using the Labview6 software package (<http://www.ni.com/labview/>).

We used a 3T Bruker whole-body and radio frequency coil scanner to perform a structural scan for each subject followed by eight series of 172 functional axial scans (time of repetitions, 2,000 ms; time of echos, 35 ms; flip angle, 78 deg; field of view, $192 \times 192 \text{ mm}^2$; acquisition matrix, 64×64 ; thickness, 5 mm; 24 interleaved and joint slices; voxel size, $3 \times 3 \times 5 \text{ mm}^3$). Note that TR were not multiples of stimulus onset asynchronies to maximize temporal sampling of event-related hemodynamic responses.

Computations of brain activations. We processed fMRI data using the SPM2 software package (<http://www.fil.ion.ucl.ac.uk/spm/>) with standard interslice temporal rephasing, standard realignment, nonlinear normalization to the stereotaxic Talairach atlas (Montreal Neurological Institute echo planar imaging template, images resampled at $5 \times 5 \times 5 \text{ mm}^3$) and spatial (isotropic three-dimensional Gaussian kernel, 10 mm) smoothing. Temporal correlations were estimated using restricted maximum likelihood estimates of variance components using a first-order autoregressive model. The resulting non-sphericity was used to form maximum likelihood estimates of the activations.

We computed brain activations using standard statistical procedures. Statistical parametric maps were obtained from local fMRI signals using a linear multiple regression model with event-related regressors (Dirac functions convolved with the canonical hemodynamic response function) and scanning series as covariates. Distinct event-related regressors modeled correct trials associated with the different cells of the factorial design. Additional event-related regressors factored out error trials, instruction and feedback signals. Scanning series were covariates of no interest factoring out effects of scanning runs. We estimated regression parameters in every voxel for each subject, and then entered parameter estimates in a between-subject, random-effect analysis for obtaining statistical parametric maps. We identified brain activations showing significant contrasts of parameter estimates with a voxel-wise ($T = 2.95$, $P < 0.005$, uncorrected) and cluster-wise (28 voxels = $3,500 \text{ mm}^3$, $P < 0.05$) significance threshold. All reported activations survived false discovery rate correction for multiple comparisons ($P < 0.05$)⁴⁶. Moreover, we observed no additional activations with a lower cluster-wise threshold of 16 voxels ($2,000 \text{ mm}^3$, $P < 0.15$).

Regions associated with contextual control were computed as showing the interaction between trial type (default versus task trials) and block type (baseline versus contextual blocks) factors; that is, larger responses on task trials in contextual than baseline blocks compared with responses on default trials (restricted to the experimental session including the two block types). Regions associated with episodic control were identified as showing the main effect of block type (episodic versus contextual blocks); that is, larger responses on all trials in episodic than in contextual blocks (restricted to the experimental session including the two block types) and by excluding activations associated with contextual control. Regions associated with contextual motivation were identified over the two experimental sessions as showing the interaction between the trial type (standard versus bonus trials) and block type (low-versus high-incentive blocks) factors; that is, larger responses on bonus trials in high-incentive than in low-incentive blocks compared with responses on standard trials. Regions associated with episodic motivation were identified over the two experimental sessions as showing larger activations on all trials in high-incentive than in low-incentive blocks and by excluding activations associated with contextual motivation.

ANOVAs. We carried out additional ANOVAs on the activations identified above to further assess the effects of critical theoretical importance. For that purpose, we averaged regression parameter estimates over each activation cluster. For every subject, the averaged estimates in each cluster were further normalized across experimental sessions using the grand mean of averaged estimates in contextual blocks as the normalization factor (because both experimental sessions included contextual blocks). As a result, all averaged estimates were relative to a common origin across experimental sessions. We

then entered the resulting normalized averaged estimates in each cluster in a repeated-measure $2 \times 3 \times 2 \times 2$ ANOVA with cognitive trial type (default versus task trials), block type (baseline versus contextual versus episodic blocks), motivational trial type (standard versus bonus trials) and block-incentive value (low- versus high-incentive blocks) as within-subject factors. Finally, to remove possible artifacts resulting from the repetition of contextual blocks across the two sessions and to keep the same number of measures in every condition, we only entered contextual block data from the first session performed by subjects in these ANOVAs. We obtained the same results by including contextual block data from both sessions. In particular, when the session order was included as a covariate, we found that this factor did not interact with any cognitive and motivational factors (all $F_s < 1.79$, $P > 0.2$). We computed all ANOVAs using the SPSS15 software package (<http://www.spss.com>). We performed additional interregional ANOVAs, including regions as within-subjects factors, and confirmed the functional segregations described above (data not shown).

Effective connectivity analyses. We used structural equation modeling (SEM) to analyze effective connectivity between prefrontal activations³¹. SEM was preferred to dynamic causal modeling because, in contrast with dynamic causal modeling, SEM does not rely on specific assumptions about the input structure to the prefrontal system (which is poorly known). SEM was processed with the Mx software package (<http://www.vcu.edu/mx/>). In these analyses, activity associated with instruction cues preceding each block and feedbacks following each block were factored out. Subject-specific time series of fMRI signals were collected at activation peaks, averaged over subjects and standardized in each condition (mean and variance were equated across conditions). The resulting time series were then used for structural model estimation and statistical inference on the basis of maximum-likelihood statistics. We assessed significant variations of path coefficients using a nested model approach⁴⁷.

Variations of path coefficients associated with contextual and episodic control were computed from variations in interregional correlation matrices observed between contextual versus baseline blocks and between episodic versus contextual blocks, respectively. This approach has been used previously³. Similarly, coefficient variations associated with episodic motivation were computed from variations of correlation matrices observed between high-versus low-incentive blocks (Fig. 6).

In contrast, contextual motivation in our protocol was only characterized by an interaction between trial type (standard versus bonus trials) and block type (low- versus high-incentive blocks). This case was analyzed previously⁴⁸ by creating 'dummy' regions, which reflect such interaction effects in original activations. A dummy region was computed for each original region and was included in the structural model, with dummy paths reflecting the original

structural model. Thus, the coefficients of dummy paths quantified the influence of contextual motivation on effective connectivity of the original model; positive deviations of dummy path coefficients from zero indicated an increase of effective connectivity with contextual motivation. The resulting model was estimated and statistical inferences were performed as described above. Significant deviations of dummy path coefficients were then assessed using the standard nested model approach. For contextual motivation, Figure 6 shows such deviations relative to estimates of path coefficients connecting original regions. This method was also used for contextual control (interaction trial type \times block type) in addition to the block-related approach described above. Both approaches provided the same results (that is, nonsignificant variations with contextual control).

Finally, we used the dummy region approach proposed previously⁴⁸ to study the effects of response conflict (main effect of default versus task trials). In a first analysis, we used the same structural model as that described in the main text. This analysis therefore tested for variations of effective connectivity with response conflict between medial and lateral activations associated with the same trial. In a second analysis (Fig. 8), we tested the prediction of the conflict-monitoring theory^{12,36,37} that MFC regions monitoring response-conflict in a given trial would modulate LPC activations in the subsequent trial. For that purpose, we used the same structural model as above except that time courses of MFC regions were shifted forward by one trial to account for interactions across two successive trials. The border effects occurring from this manipulation at blocks boundaries (series of trials consisted of blocks of 12 trials) were removed by factoring out the last trial of every block for MFC time courses and the first trial of every block for LPC time courses.

Finally, to account for between-subject variability, to make inferences at the population level and to control that such substantial variations resulted from underlying neuronal interactions, we computed pair-wise psycho-physiological interactions⁴⁹ between prefrontal activations using SPM2. This additional analysis confirmed that all significant variations of path coefficients reported here corresponded to significant variations of PPI related to the same psychological factors ($P < 0.05$).

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