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Ongoing Brain Activity Fluctuations Directly Account for Intertrial and Indirectly for Intersubject Variability in Stroop Task Performance

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Recent studies have established a relation between ongoing brain activity fluctuations and intertrial variability in evoked neural responses, perception, and motor performance. Here, we extended these investigations into the domain of cognitive control. Using functional neuroimaging and a sparse event-related design (with long and unpredictable intervals), we measured ongoing activity fluctuations and evoked responses in volunteers performing a Stroop task with color–word interference. Across trials, prestimulus activity of several regions predicted subsequent response speed and across subjects this effect scaled with the Stroop effect size, being significant only in subjects manifesting behavioral interference. These effects occurred only in task relevant as the dorsal anterior cingulate and dorsolateral prefrontal cortex as well as ventral visual areas sensitive to color and visual words. Crucially, in subjects showing a Stroop effect, reaction times were faster when prestimulus activity was higher in task-relevant (color) regions and slower when activity was higher in irrelevant (word form) regions. These findings suggest that intrinsic brain activity fluctuations modulate neural mechanisms underpinning selective voluntary attention and cognitive control. Rephrased in terms of predictive coding models, ongoing activity can hence be considered a proxy of the precision (gain) with which prediction error signals are transmitted upon sensory stimulation.

Keywords: BOLD fMRI, executive function, human brain, neuroimaging, resting state

Introduction

From a behaviorist stance, signal fluctuations during recording of ongoing brain activity have traditionally been considered technical or biological noise and therefore been removed from these recordings so as not to compromise the estimation of paradigm-related responses. However, several studies have shown that accounting for these fluctuations reduces the variability of event-related responses across repeated trials involving the same stimulus or action (Arieli et al. 1996; Fox et al. 2006). At the same time, it has become clear that variability in evoked neural responses is not just a noisy deviation from a fixed veridical response but that it is functionally significant and translates into systematic variations in behavior (e.g., Fox et al. 2007). Finally, several studies have established a direct correlation between ongoing brain activity fluctuations and perception (Boly et al. 2007; Sadaghiani et al. 2009) and shown that the effects of ongoing activity fluctuations are not confined to an additive spillover of prestimulus baseline signal into the strength of the evoked response (Hesselmann, Kell, Eger, et al. 2008; Hesselmann, Kell, and Kleinschmidt 2008).

So far, all these findings have relied on paradigms with simple perceptual and motor tasks because the related predictions are straightforward and simply tested. These predictions involved specific regions related to the processing of sensory input or generation of motor output. Yet, ongoing activity is shared between separate distant regions which has permitted the robust identification of so-called resting state networks (Beckmann et al. 2005). Some studies have shown that activity fluctuations in such networks also impact on behavioral performance, and these observations speak to a role for these networks in underpinning, for instance, attentional or "default mode" functions (Boly et al. 2007; Sadaghiani et al. 2009). We have recently argued that the way in which ongoing activity fluctuations affect behavioral performance is context dependent and will hence vary as a function of which paradigm is used to probe the influence of fluctuations (Sadaghiani et al. 2010).

The present study sought to further test whether synergy can be observed between ongoing activity fluctuations in regions across different networks and antagonism between fluctuations in regions that belong to the same resting state network. A paradigm that may generate such a situation is one where there is conflict between different features of a visual stimulus and where correct task performance requires cognitive control mechanisms. One of the most popular such settings is the Stroop paradigm (Stroop 1935). Color words are presented in conflicting colored fonts—for example, the word RED printed in green font—and participants must name the font color while ignoring the word itself. The task involves attending to a relevant feature (the font color) while suppressing semantic information from a salient, but irrelevant category (the word), which is readily processed automatically and if so interferes.

Previous imaging studies of the Stroop task have investigated the anatomical source of attention and top-down control and have found activation in anterior cingulate cortex, dorsolateral prefrontal cortex (DLPFC), and/or posterior parietal cortex (Pardo et al. 1990; Bench et al. 1993; Carter et al. 1995; Banich et al. 2000; Carter et al. 2000; MacDonald et al. 2000; Milham et al. 2001; van Veen and Carter 2005). Using a sparse event-related design with long variable and unpredictable intervals (20–40 s), we measured ongoing activity fluctuations and evoked responses with functional magnetic resonance imaging (fMRI) in 15 healthy volunteers during a Stroop task with color–word interference. We tested whether variations in

prestimulus activity levels in task-relevant regions could predict the behavioral effects induced by a Stroop paradigm, at the subject's level and on a trial by trial basis. As higher cognitive functions express a greater degree of intersubject variability, the present study also allowed us to investigate the relation between behaviorally relevant intrinsic activity fluctuations and variability in cognitive control across individuals.

Materials and Methods

Subjects

Sixteen right-handed native French speakers gave written informed consent before participation. Data from one subject were discarded because of excessive motion artifact. The remaining 15 subjects (5 females, average age: 22 (±3) years) all had normal or corrected-to-normal visual acuity and no neurological or psychiatric antecedents. They had no color vision defects and were all highly proficient native readers. The study received ethics committee approval as part of a larger ongoing project of cognitive neuroimaging.

Experimental Protocol

The protocol comprised a main experimental session with the Stroop paradigm and a shorter session with the purpose of localizing areas engaged in the processing of color and visual words, respectively. The Stroop variant employed in this study was a 2 word color-naming task with manual response, previously found to reliably induce significant interference effects (Egner and Hirsch 2005). The stimuli consisted of the 2 French color words for RED ("ROUGE") and GREEN ("VERT") (3° visual angle in size) and the neutral noncolor-word CASE, presented either in red or green hue on a medium gray background. A 50 min session covered 88 trials with stimuli presented for 1500 ms and interstimulus intervals ranging unpredictably from 20 to 40 s with a flat distribution. The session was split in 2 by a 1 min pause during which subjects were given permission to close their eyes and rest without moving while image acquisition continued. To optimize sensitivity for neural effects of interest, 80% of the trials were incongruent (e.g., the word GREEN written in red), 10% congruent (e.g., GREEN written in green), and the remaining 10% neutral (e.g., CASE written in red).

The localizer fMRI sessions for mapping regions sensitive to color and visual words, respectively, involved a one-back task and 2 types of stimuli: 1) white words ($n = 10$) and 2) colored words (red, blue, green, and yellow) with a constant number of letters ($n = 6$). Twelve continuous blocks of 7 stimuli and 6.3 s, each alternating between white and colored words, were separated by 10 s intervals. Words were presented for 0.6 s with an ISI of 0.3 s. Subjects were instructed to press a button when 2 consecutive words or colors were repeated. Each block could contain between 0 and 2 repetitions. At the beginning of each block, the instruction "word repetition" or "color repetition" was displayed in French on the screen for 5 s, indicating the nature of the task for the ensuing block.

Stimulus presentation and response recording used MATLAB software (Mathworks Inc.) and the Cogent toolbox (John Romaya, Vision Lab, UCL; www.vislab.ucl.ac.uk). Stimuli were back projected from an LCD projector onto a screen attached to the head coil at a viewing distance of ≈ 20 cm. To avoid motion artifacts associated with speech, subjects were instructed to report word color through button presses with their left- and right-hand index finger as fast as possible, whilst maintaining high accuracy. Before the fMRI session, a brief training period outside the scanner familiarized each subject with the color–button mapping. Subjects were further instructed to maintain their gaze within the boundaries of a line-drawn square (1° visual angle in size) that was centered on the screen during the interstimulus intervals. Although online oculography was not available for this experiment, we informed subjects that we could monitor compliance with the gaze fixation instruction. If within 2 s of stimulus onset, the correct key was pressed, this trial was counted as a hit, if the wrong one was pressed as an error and if none at all was pressed as a miss. No false alarms occurred.

Acquisition and Processing of Whole-Brain Imaging Data

Using a 3 T MRI scanner (Tim Trio, Siemens), we acquired anatomical images with a T_1-weighted magnetization prepared rapid gradient-echo sequence (160 slices, time repetition [TR] = 2300 ms, time echo [TE] = 2.98 ms, Field of View 256, voxel size 1 × 1 × 1 mm). Functional images were acquired by blood oxygen level–dependent (BOLD) T_2^*-weighted gradient-echo echo-planar imaging (25 slices, TR = 1500 ms, TE = 30 ms, voxel size 3 × 3 × 3 mm, interslice gap 20%). Functional neuroimaging involved a main session with 1973 image volumes for the paradigm described above and a 130 volume localizer session. We used statistical parametric mapping (SPM5, http://www.fil.ion.ucl.ac.uk, Wellcome Trust Centre for Neuroimaging) for image preprocessing (realignment, co-registration, normalization to Montreal Neurological Institute stereotactic space, spatial smoothing with an isotropic Gaussian kernel of 6 and 10 mm full-width at half-maximum for single subject and group analyses, respectively) and estimation of the statistical maps.

For conventional event-related analysis, we defined regressors by convolving condition-specific stimulus (unit impulse) functions with a canonical hemodynamic response function. The statistical model included the 5 following events: incongruent, neutral, congruent, errors (including error responses and the rare misses), and the pause. For each subject, we estimated condition-specific effects using a general linear model, then created contrast images and entered these into a second-level one-sample t-test in SPM.

To complement the analyses of prestimulus effects that were performed in regions of interest (ROIs) (see below), we also sought such effects by additional whole-brain mapping. We estimated a finite impulse response (FIR) model using 24 peristimulus stick functions (1.5 s bins) for each of the 5 conditions mentioned above. Nuisance covariates included the realignment parameters. The FIR model was used to generate a map of prestimulus effects on Stroop task performance by contrasting parameter estimates for fast and slow trials averaged over time points 1.5 and 0 s. The corresponding contrast images were entered into a second-level one-sample t-test.

Definition of ROIs

The dorsal part of the anterior cingulate cortex (dACC) and the left DLPFC were identified subject by subject by testing for a simple main effect ("incongruent > baseline") at $P < 0.05$, corrected by familywise error (FWE) rate. This contrast is orthogonal to the subsequent analyses of interest. For regional analysis, we extracted the time course data from a 10 mm sphere centered on the voxel that showed peak activation in proximity to stereotactic coordinates that have been reported in the literature for the dACC and DLPFC (1; 12; 47 [Roberts and Hall 2008] and −36; 38; 20 [Nee et al. 2007], respectively).

We also sought to determine the effects of ongoing activity fluctuations in specialized sensory regions related to the processing of task relevant and of interfering information. As the main experiment involved only colored words and one type of task, we could not use it to define ROIs that are sensitive to color and visual words, respectively. We therefore included the aforementioned localizer sessions that allowed us to functionally and independently identify for each individual participant cortical areas involved in processing colors and words.

Color-sensitive regions were identified by mapping for each subject the contrast "color repetition > white word repetition" from the color repetition blocks of the localizer session at $P < 0.001$, uncorrected. We identified the nearest local maximum relative to coordinates given by the literature (−30; −69; −15 and 30; −75; −19 [McKeefry and Zeki 1997]) extracted data from a 10 mm sphere centered around this peak voxel so as to assess effects in color-sensitive area (CSA). The visual word form area (VWFA), a region specialized for the processing of visual words was identified by mapping for each subject the contrast "word repetition > fixation cross" from the word repetition block of the localizer session at $P < 0.001$, uncorrected. ROIs were selected by identifying the cluster located in the ventral part of the occipitotemporal cortex closest to the published location of the VWFA, with approximate stereotactic coordinates of −43 −54 −12 ± 5 (Cohen et al. 2002; Dehaene et al. 2005). Because this region is fairly small (and to avoid dilution of its signal by response properties form adjacent

cortex), we restricted data extraction to a 5 mm radius sphere centered at the peak of each subject's response in the aforementioned contrast.

For control purposes, further ROIs were defined on the basis of their reactivity (activation or deactivation) to the Stroop paradigm. Activations at the group level from the contrast incongruents > baseline ($P < 0.05$ FWE corrected) in the main experiment included regions such as the anterior insula, right DLPFC, left thalamus, left inferior frontal gyrus, and bilateral intraparietal sulcus (for coordinates of all ROIs, see Supplementary Table S1). A spherical search space of 10 mm was then defined around the peak activation of each cluster and for each subject's corresponding first level contrast, all voxels above a threshold of $P < 0.05$ (uncorrected) within that search space were selected. Finally, regions corresponding to the "default mode" network were defined at the group level by the contrast ("baseline > incongruents") at $P < 0.01$ uncorrected. For each subject, the resulting networks as a whole and each of their clusters in isolation were used as ROI for time course extraction.

Analysis of Regional fMRI Time Series Data

After removing session effects and linear trends from the BOLD signal time series, we extracted the fMRI signal time course from the aforementioned set of ROIs and reconstructed peritrial signal time courses as a function of condition. To do so, the onsets of the target stimuli (rounded with respect to a multiple of scan repetition time) served as time markers to extract segments of the time course data starting 5 scans (7.5 s) before target onset and ending 13 scans (19.5 s) after target presentation. Note that the prestimulus segment was not affected by preceding stimulations even at shortest ISI of 20 s. To test for intersubject variability, we sorted subjects according to the occurrence of a Stroop effect and to test intrasubject but intertrial variability, we sorted the incongruent trials of interest according to the individual subject's median RT into "fast" and "slow" trials. We then analyzed signal at prestimulus time points that are as close as possible to subsequent stimulation but that do not yet carry stimulus- or task-driven signal. Our previous studies had identified such effects at time points 0 and −1.5 s (Hesselmann, Kell, Eger, et al. 2008; Hesselmann, Kell, and Kleinschmidt 2008; Sadaghiani et al. 2009; Hesselmann et al. 2010). We therefore tested as a function of a behavioral Stroop effect the effects of ongoing prestimulus activity at time points −1.5 and 0 s for differences between fast and slow RT trials, correcting for the number (2) of time points tested. Functional considerations permitted the use of one-tailed tests because it was sensible to assume that if there was an effect, prestimulus signal for faster trials should be higher in dACC, DLPFC, and color-sensitive cortex and lower in the VWFA. Finally, we performed parametric analyses in all ROIs to investigate the correlation (Pearson) between the behavioral interference effect (defined by the difference between incongruent and congruent RTs) and the size of the prestimulus effect (as defined by the activity difference between fast and slow trials). For display purposes, but not statistical analyses, signal time courses were temporally smoothed with a (1, 2, 1) kernel.

Results

Behavioral Findings

Mean accuracy for the task was 94% (standard deviation [SD] = 5). Mean absolute reaction times (RTs) for the incongruent, neutral, and congruent conditions were 833 ms (SD = 347), 784 ms (SD = 278), and 789 ms (SD = 306), respectively. Importantly, RTs did not correlate with the length of prestimulus ISIs ($r = -0.06$). To permit comparisons of Stroop effect size between subjects, we normalized absolute RTs to the mean of all trials and rank ordered subjects according to the relative difference of RTs between incongruent and congruent trials (Fig. 1). The specific design we employed with long interstimulus intervals, low proportion of congruent words, 2 color–words only, and nonverbal responses yielded high intersubject variability in Stroop effect size (Supplementary Table S2). In contrast to most Stroop experiments (MacLeod 1991), our paradigm yielded fairly small or even inverse behavioral Stroop effects in some subjects which we exploited when studying intersubject variability.

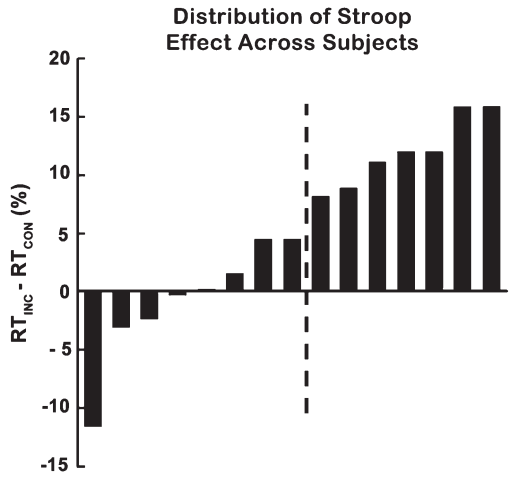

Figure 1. Normalized RT differences between incongruent and congruent trials. Each bar represents a subject and subjects were ordered according to effect size. The vertical line represents the post hoc partition of subjects into the "Stroop effect" and "No-Stroop effect" group.

fMRI Data

In addition to a full group analysis, the aforementioned behavioral results allowed us to interrogate the fMRI data in 2 complementary ways. We could split our sample into a group of subjects with and without a clear behavioral Stroop effect according to the median of RT difference between normalized incongruent and congruent trials ($m = 5.4\%$). There was no difference in mean RT nor in accuracy between these 2 groups ($t_{13} = 0.72$, $P = 0.48$ and $t_{13} = 0.86$, $P = 0.41$, respectively). The second approach relied on the continuous distribution of the RT difference between incongruent and congruent trials and called upon a parametric analysis.

Our analysis was based on assessing effects in suitable candidate regions. Informed by our previous studies (Hesselmann, Kell, Eger, et al. 2008; Hesselmann, Kell, and Kleinschmidt 2008; Sadaghiani et al. 2009), we interrogated effects both in sensory areas sensitive to the visual content of the stimuli (color–words) as well as in central task-relevant regions involved in cognitive control. To delineate regions contributing to task execution, we computed statistical parametric maps of responses evoked by correct incongruent trials compared with baseline (Fig. 2). These trials yielded distributed activation in areas comprising the dACC, anterior insula, thalamus, DLPFC, and intraparietal sulcus. Responses in posterior areas processing the visual input of this paradigm were less extensive and less consistent, hence confirming post hoc, the need for independent localizer procedures to identify regions related to stimulus features (for mean coordinates, see Supplementary Table S1).

In these regions, we then examined the effect of prestimulus activity levels on RTs of ensuing trials. When pooling across all subjects, no significant effects of prestimulus activity on RT in incongruent trials were seen in any of the regions (for the data from dACC, see Fig. 3*A*). This negative finding is in accord with

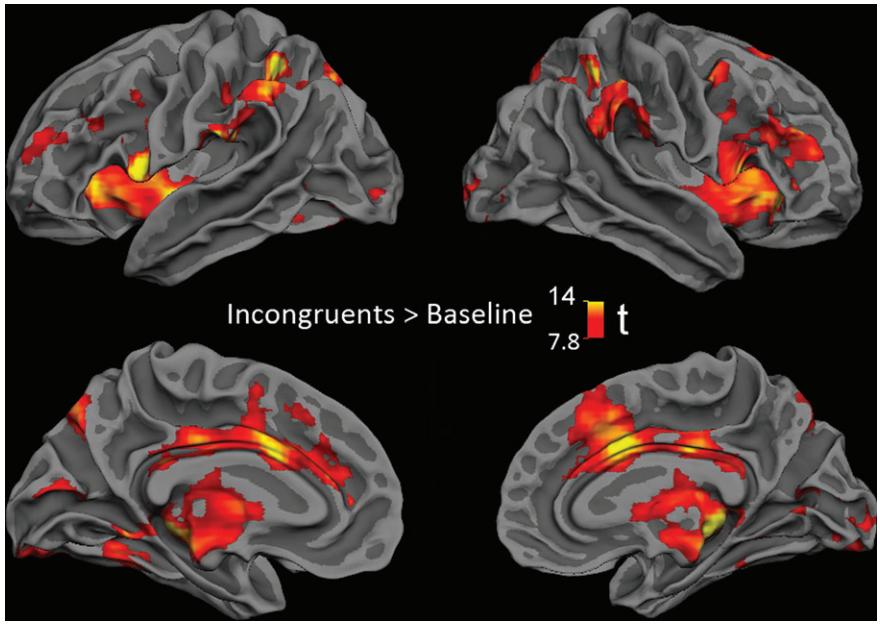

Figure 2. Spatial distribution of cortical responses evoked by incongruent trials with correct responses versus baseline. Activations are shown at a threshold level of $P < 0.01$, FWE corrected at the cluster level. Results of the random effects group analysis ($n = 15$) are superimposed onto the lateral and medial aspects of a cortical surface of a canonical average brain.

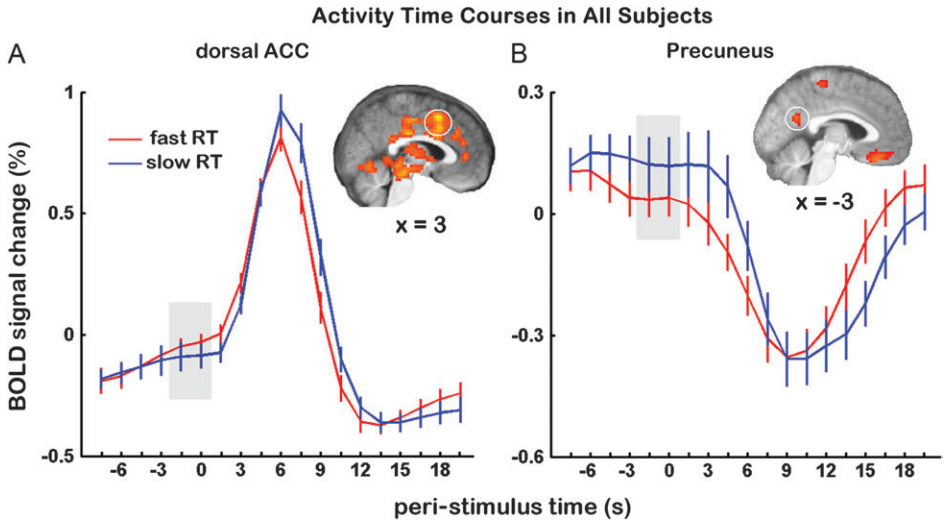

Figure 3. Peristimulus fMRI signal time courses from anterior cingulate cortex (*A*) and precuneus (*B*) averaged across all 15 subjects, with error bars representing ±standard error of the mean. The gray rectangles cover the prestimulus period submitted to statistical testing. The left and right insets illustrate by a white circle the approximate location of the dorsal anterior cingulate region and the precuneus overlaid onto the underlying average anatomy and the group statistical parametric map for the contrast "incongruent > baseline" ($P < 0.01$ FWE corrected) and the contrast "baseline > all trials" ($P < 0.05$), respectively.

the absence of a consistent Stroop effect across the entire subject sample but makes a generic, for instance attentional modulation of RT by prestimulus dACC or other regional activity unlikely. As behavioral correlation has also been established with signal in regions undergoing task-related deactivation we also analyzed time courses from such regions (Singh and Fawcett 2008; Mayer et al. 2010). The overall spatial pattern of task-related deactivation closely resembled what has generally become known as the default mode network (Gusnard and Raichle 2001). The time courses from these regions showed the typical deactivation but there was no significant difference in prestimulus signal between trials with fast and slow RTs (Fig. 3*B*). Qualitatively, there was a trend toward lower activity and an earlier response slope in trials with faster RTs.

In the next step, we constrained the same analysis to those subjects with a Stroop effect. In these subjects, variations in prestimulus signal in several regions predicted very significant performance speed differences on the upcoming incongruent trials. In accord with our intuitive prediction, faster responses followed greater prestimulus activity in dACC ($t_6 = 2.48$, $P = 004$) (Fig. 4*A*), left DLPFC ($t_6 = 4.34$, $P = 0.004$) (Fig. 4*B*), and the right color-sensitive visual area ($t_6 = 2.48$, $P = 0.04$) (Fig. 4*C*). Conversely, but again in accord with

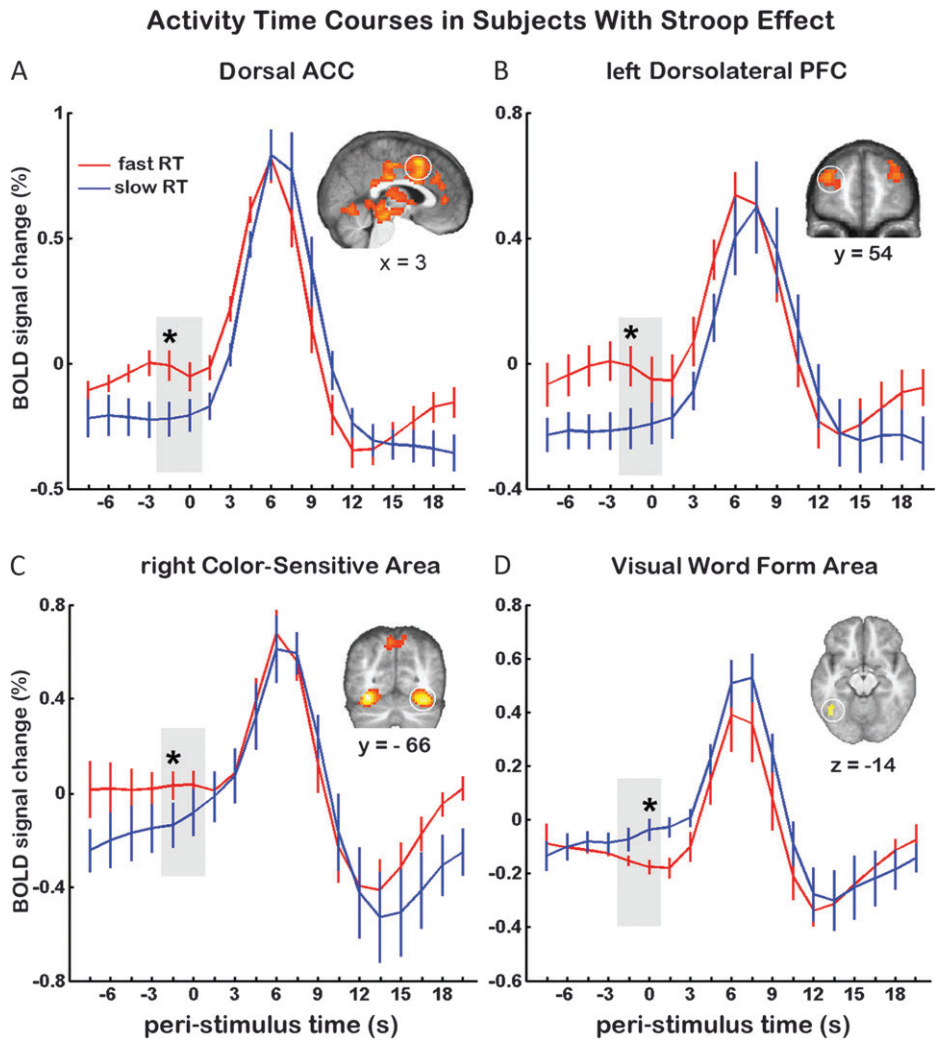

Figure 4. Peristimulus activity time courses averaged across subjects showing a behavioral interference effect ($n = 7$) from dACC (*A*), left DLPFC (*B*), right color-sensitive area (*C*), and VWFA (*D*). Images inserted in each panel illustrate the functionally defined region of interest for which the peristimulus signal time course is plotted. While higher signal levels in the dACC (*A*), DLPFC (*B*), and color-sensitive area (*C*) were found before fast correct incongruent trials, higher signal in the VWFA (*D*) preceded slower correct incongruent trials. The gray rectangles cover the prestimulus period submitted to statistical testing. Asterisks indicate significant RT-dependent time course difference at time point −1.5 s for the dACC, left CSA, and left DLPFC and at time point 0 s for the VWFA. Error bars indicate ±standard error of the mean. Time courses were filtered with a [1 2 1] kernel for display purposes.

our prediction, faster responses were preceded by lower activity in a region sensitive to visual words ($t_6 = 2$, $P = 0.03$) (Fig. 4*D*).

To explore the spatial specificity of the prestimulus signal effect on task performance, we supplemented our analysis in the subjects with a Stroop effect to cover time courses from a set of control regions. We chose as candidate regions those that activated during incongruent trials (see Fig. 2) but none of them exhibited significant effects at time points of interest (for all regions never lower than $P > 0.24$). These regions included areas involved in early visual processing, as well as attention and perceptual decision making (right DLPFC, bilateral intraparietal sulcus, left inferior frontal gyrus, anterior insula, and left thalamus). Finally, using a FIR model, we conducted a whole-brain mapping analysis contrasting signal at time points –1.5 and 0 s between fast and slow incongruent trials and vice versa. Despite the clear effects seen in ROI analyses and in line with our overall experience from the previous related studies, this extended (whole brain and voxelwise) search space reduced sensitivity and we could not identify significant effects in any other regions.

Our analyses of the behavioral results had established a continuous variability in the degree of Stroop effect across subjects. The aforementioned analyses of the imaging results addressed this variability by splitting the study group into 2 halves as a function of the behavioral effect size. In a final step, however, we probed whether the size of the Stroop effect as a subject variable (defined by comparing RTs with 2 conditions) was associated with the size of the prestimulus difference between trials with fast and slow responses to the incongruent trials alone. We computed these correlations for those regions which had shown a prestimulus effect in the group-splitting approach comparing Stroop and no-Stroop subjects and used the signal activity values from the time bin (–1.5 or 0 s) yielding significant findings in that analysis. Across all subjects, the prestimulus effects in these regions, in other words the activity difference between fast and slow trials, were the stronger the more the subjects expressed a behavioral

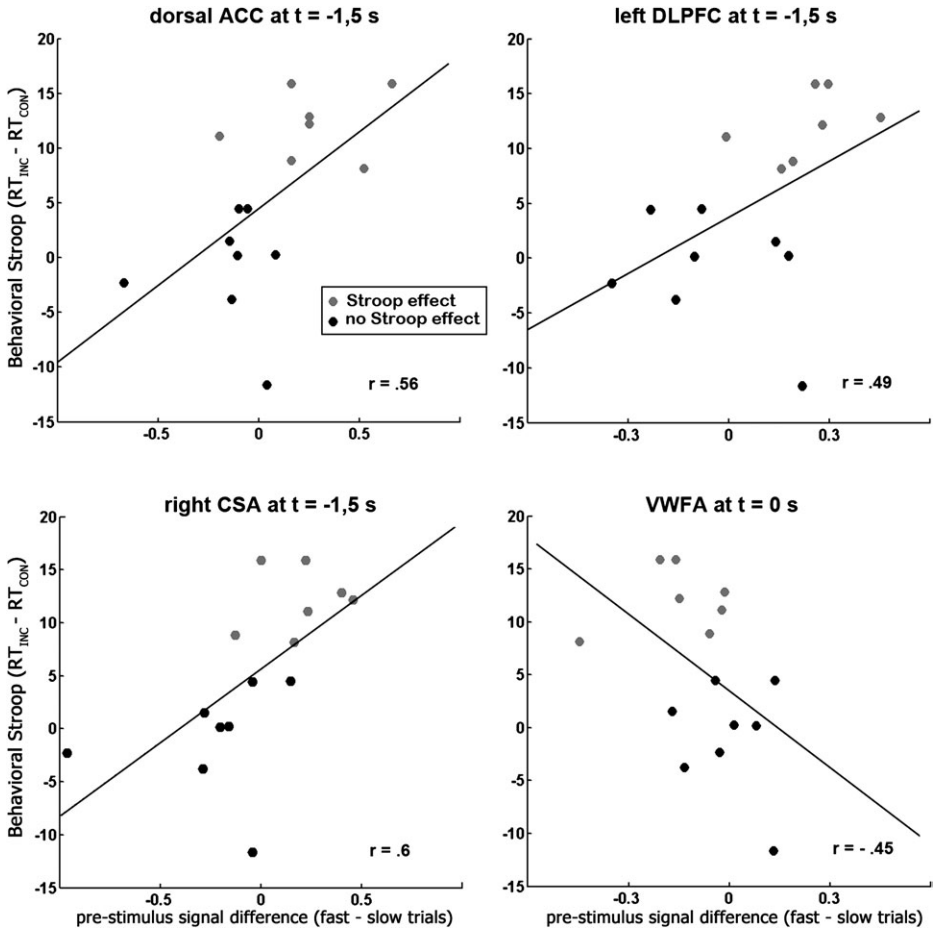

Figure 5. Correlation plots for the dACC (upper left), left DLPFC (upper right), right color-sensitive area (lower left) at time point $t = -1.5$ s and for the VWFA (lower right) at time point $t = 0$ s. Plots represent the correlation between prestimulus difference of BOLD signal change between fast and slow trials and the degree of behavioral Stroop effect (as defined by the difference between incongruent and congruent RTs). Each dot represents a single subject, subjects with a Stroop effect as gray dots and without as black dots. Black lines indicate estimation of the best linear fit.

interference effect (dACC: $r = 0.56$, $P = 0.03$; right CSA: $r = 0.6$, $P = 0.016$ left DLPFC: $r = 0.49$, $P = 0.06$; VWFA: $r = -0.45$, $P = 0.09$) (Fig. 5). This effect was not due to the RT normalization procedure but held when recurring to absolute RT values.

Discussion

The specific question addressed by our experiment is whether ongoing activity fluctuations impact subsequent behavioral performance. Using a classical cognitive control task, we extended previous findings from perceptual and motor paradigms to higher cognitive function (Fox et al. 2006; Boly et al. 2007; Hesselmann, Kell, Eger, et al. 2008; Hesselmann, Kell, and Kleinschmidt 2008; Sadaghiani et al. 2009). We show that ongoing activity fluctuations, both in task-relevant sensory areas as well as interference control regions impact on behavioral performance and hence account for within-subject trial by trial variability, providing strong evidence that those fluctuations are more than simple physiological artifacts. Furthermore, we find that the degree behavioral relevance of ongoing brain activity fluctuations (for incongruent trials) can explain performance differences between subjects (size of Stroop effect). Together, we thus corroborate the behavioral significance of brain signals that are often considered as noise and treated as a variance of no explanatory value.

Our Stroop effects were smaller than those generally reported. This is because we tailored the paradigm to the needs of our specific questions. Designs where incongruent stimuli are rare events (Carter et al. 2000) or where participants strongly emphasize speed over accuracy (van Veen et al. 2008) yield larger Stroop effects. However, such designs would have compromised the sensitivity of our experiment, which required long interstimulus intervals and hence a relatively small number of trials. This meant we had to use proportionally more incongruent trials. Furthermore, we did not want to compromise accuracy, as errors are known to elicit behavioral and neural adjustments that influence subsequent trials (King et al. 2010). These latter post error adjustments may call on the same mechanisms that also mediate the effects of spontaneous fluctuations detected in our study: just as higher levels of ongoing activity in dACC, DLPFC, and color-sensitive cortex facilitate speeded (correct) responses (and activity in the VWFA delays such responding), incorrect responses could modulate subsequent baseline activity levels in these structures, to avoid further errors and optimize performance.

Our findings suggest that this optimization might be implemented neurally by deliberately modulating background activity in the preparatory period. In other words, by demonstrating the impact of spontaneous activity on task-related

behavior, we have identified a neuronal substrate (ongoing activity) that might be called upon if performance errors suggest a need to change perceptual and response criteria. This view fits nicely with the functional notion that spontaneous activity or "noise" serves to explore "the brain's dynamic repertoire"; in other words, preclude neuronal systems from being locked into a single processing state that may only be locally optimal (Ghosh et al. 2008). This interpretation may account for the relationship that we observed between behavior across subjects and the impact of variability in ongoing activity on behavior as determined across trials within these subjects. In other words, greater fluctuations in (behaviorally relevant) prestimulus activity (reflecting a greater range of dynamic exploration) may translate into greater (average) interference effects in a given subject. This relationship also adds to the growing literature linking subject traits to intrinsic functional brain properties (Hampson, Driesen, et al. 2006; Hampson, Tokoglu, et al. 2006; Hampson et al. 2010) and extends it from connectivity measures (between areas) to activity measures (within areas). The key point here is that what appears optimal in a given cognitive setting, that is, a certain "rigidity" of mind set that underpins task compliance and avoids interference effects, is not optimal under changing or incompletely transparent task requirements, as encountered in the real world (Sadaghiani et al. 2010).

The main aim of our experiment was to address the impact on cognitive performance that arises from spontaneous variations in ongoing activity. Using the Stroop paradigm, this question was pursued for a single class of behavioral event; that is, for incongruent trials yielding correct responses. This question was grounded in our earlier studies, where we have examined the effect of spontaneous or endogenous activity fluctuations on perceptual inference and categorization (Hesselmann, Kell, Eger, et al. 2008; Hesselmann, Kell, and Kleinschmidt 2008; Sadaghiani et al. 2009). In particular, we have previously evaluated different accounts of the role of spontaneous (stimulus free) activity in optimizing perception and subsequent responses (Hesselmann et al. 2010). Our empirical results favored predictive coding as the best explanation that linked observed physiological and behavioral responses. Briefly, we concluded that high levels of spontaneous activity in cortical areas processing a stimulus attribute of interest increase the efficiency of subsequent processing and the ensuing accuracy of behavioral responses. Physiologically, this is consistent with a local increase in synaptic gain that, functionally, may encode the precision for processing bottom-up sensory information and feeding forward the associated prediction error (Sadaghiani et al. 2010). In a more general setting, this is consistent with free-energy formulations of perception, in which prediction errors report the free-energy or surprise inherent in sensory information (Friston 2009, 2010).

In the present study, we have generalized the role of spontaneous fluctuations to cognitive control and attentional interference. Again, our empirical results are consistent with predictive coding. In this case, attention can be associated with the selective increase in the synaptic gain of task-relevant sensory channels and a consequent increase in the precision of the information that they carry in the form of prediction errors (Feldman and Friston 2010). Crucially, in the Stroop paradigm, the attentional bias to one sensory attribute (e.g., color) relative to another (e.g., visual word form) places the required and prepotent attentional bias in opposition. In terms of predictive coding, we assume a prepotent tendency to increase the precision (synaptic gain) of neuronal populations encoding prediction errors on word form; however, the Stroop paradigm (during incongruent trials) requires this top-down gain to be redeployed in areas reporting color. Fluctuations in the top-down control and maintenance of regionally specific increases in synaptic gain are a possible explanation for our findings. In other words, when autonomous activity maintains a high level of synaptic gain and precision in the color area, prediction errors reporting color are boosted selectively and enable a speeded and more accurate response (cf., the speed responses in the Posner paradigm simulated in Feldman and Friston (2010)). Conversely, if the prediction errors from the VWFA enjoy a greater selective gain, behavioral interference may be more evident. This is exactly what we observed; a speeded RT when prestimulus activity in the color-sensitive area was higher and a longer RT when activity in the VWFA was higher. The effect is specific to interference because its size scaled with the degree of a behavioral Stroop effect, being absent in a subgroup of subjects without and present in the other subjects with a Stroop effect.

A plausible mechanism for modulating synaptic gain (precision) is fast synchronous interactions associated with attention (Borgers et al. 2005; Womelsdorf and Fries 2006; Fries et al. 2008). The associated increase in local gamma band activity is necessarily accompanied by increased levels of population activity that are both supported by and support synchrony (Chawla et al. 1999; Salinas and Sejnowski 2001). The selective increase in gain and firing of prediction errors in our task-relevant extrastriate cortex may reflect underlying fast synchronization and explain the increase in fMRI signals observed in our study (Logothetis et al. 2001; Niessing et al. 2005). In summary, we again obtain results that are consistent with high regional activity being associated with an increase in the precision of bottom-up sensory information as predicted by generalizations of predictive coding. In this work, we have established that intrinsic or spontaneous fluctuations in gain or precision modulate attentional control mechanisms of a top-down nature.

Supplementary Material

Supplementary material can be found at: http://www.cercor.oxfordjournals.org/

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Notes

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