Published in final edited form as:

Behav Brain Res. 2016 January 01; 296: 100–108. doi:10.1016/j.bbr.2015.08.020.

Reaction Time-Related Activity Reflecting Periodic, Task-Specific Cognitive Control

Anita D. Barber, Ph.D.^{a,b},

716 North Broadway, Baltimore, MD 21205; Phone: 1-443-923-9278; Fax: 1-443-923-9279

James J. Pekar, Ph.D.^{a,b}, and

707 N. Broadway, Baltimore, MD, 21205; 1-443-923-9510

Stewart H. Mostofsky, M.D.^{a,b}

716 N. Broadway, Baltimore, MD, 21205; 1-443-923-9266

Abstract

Reaction time (RT) is associated with increased amplitude of the Blood Oxygen-Level Dependent (BOLD) response in cognitive control regions. The current study examined whether the Primary Condition (PC) effect and RT-BOLD effect both reflect the same cognitive control processes. In addition, RT-BOLD effects were examined in two Go/No-go tasks with different demands to determine whether RT-related activity is task-dependent, reflecting the recruitment of task-specific cognitive processes. Data simulations showed that RT-related activity could be distinguished from that of the primary condition if it is mean-centered. In that case, RT-related activity reflects periodically-engaged processes rather than “time-on-task” (ToT). RT-related activity was mostly distinct from that of the primary Go contrast, particularly for the perceptual decision task. Therefore, RT effects can reflect additional cognitive processes that are not captured by the PC contrast consistent with a periodic-engagement account. RT-BOLD effects occurred in a separate set of regions for the two tasks. For the task requiring a perceptual decision, RT-related activity occurred within occipital and posterior parietal regions supporting visual attention. For the task requiring a working memory decision, RT-related activity occurred within fronto-parietal regions supporting the maintenance and retrieval of task representations. The findings suggest that RT-related activity reflects task-specific processes that are periodically-engaged, particularly during less demanding tasks.

Correspondence to: Anita D. Barber.

^aKennedy Krieger Institute, Baltimore, MD, USA

^bJohns Hopkins University School of Medicine, Baltimore, MD

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Conflict of Interest

Dr. Pekar serves as Manager of the F.M. Kirby Research Center, which receives support from Philips Health Care, which makes the MRI scanners used in this study.

Keywords

cognitive control; reaction times; attention; fMRI

1 Introduction

), “...recent data have suggested that the duration of a subject’s decision process, or time on task, can have large effects on the size of the elicited hemodynamic response, independent of the nature of the decision (Grinband et al., 2008).” This account suggests that RT-related activity reflects the amount of time that underlying neural computations take to perform the decision process. On fast RT trials, this is relatively brief; while on slow RT trials it is relatively long.

Modeling RT-effects involves the creation of condition regressors for all conditions present, and separate RT-regressors for those conditions requiring a response. The PCregressor and its RT regressor share the same stimulus onset times, but differ in the amplitude (or in some cases, the duration) of the hemodynamic response function. The PCregressor has a constant amplitude, while the RT regressor amplitude is scaled by the RT on each trial. The RT regressor is generally orthogonalized with respect to the PCregressor. Even without orthogonalization, the RT regressor reflects additional variance not accounted for by the PCregressor. Despite this, many studies have found that RT effects occur across most of the same regions as the PC effect (Yarkoni et al., 2009; Weissman and Carp, 2013).

Such co-occurring PC and RT effects may be necessitated by the ToT account. According to ToT, RT-related activity reflects process time. Therefore, it always results in BOLD increases from baseline, which produces both significant RT, as well as significant PC, effects. However, RT-BOLD effects could occur in the absence of a PC effect. This scenario would only happen if the actual RT-activity in a region is suppressed on some trials (e.g. fast RT trials) and is positively active on other trials (e.g. slow RT trials). In this case, RT-related stimulus-evoked activity would still be linearly related to RTs, consistent with previous findings in the literature, but would be mean-centered instead of always positive. This type of RT-related activity, which results in a significant RT effect but not a PC effect, may reflect periodic-engagement of task processes rather than the length of the process time.

The current study examined RT-BOLD effects using two Go/No-go tasks with differing demands. The Simple task required a perceptual decision (green=Go, red=No-go), while the Repeat task required working memory to guide the decision (color switch=Go, color repeat=No-go). The aim was to determine whether the same regions show significant effects of both the primary Go and the RT contrast in each task, supporting a ToT account; or whether the two contrasts are non-overlapping, supporting a periodic-engagement account. RT-BOLD effects were also compared for the two tasks to determine whether they reflect task-specific cognitive control.

2 Materials and Methods

2.1 Participants

22 healthy, right-handed adults (10 males), aged 20 – 40 years (mean = 28.97, SD = 5.22) participated in the study. Participants were recruited through local advertisements and had no history of mental illness or substance abuse. The study was approved by the Johns Hopkins Medicine Institutional Review Board. Informed consent was signed before task participation.

2.2 fMRI Behavioral Paradigm

Two Go/No-go tasks (Barber et al., 2013) were performed by all participants. For each trial, spaceship stimuli were presented for 300 milliseconds followed by a 1500 millisecond inter-stimulus interval. 10 second blocks of rest occurred at the beginning, end, and four times throughout each run. Separation of hemodynamic events was achieved through the use of a trial epoch (1.8 seconds) that was not a multiple of the TR (2.5 seconds) and through the use of the occasional rest blocks. The use of incoherent trial and TR epochs is an effective alternative to jittering the interval between trials and allows the BOLD response to be sampled at different intervals from trial onset for each trial (Henson, 2007).

The proportion of Go/No-go trials was 3:1, with 78 Go trials and 26 No-go trials occurring in each run. Participants performed two runs each of the two Go/No-go tasks. Each run was preceded by instructions and 20 practice trials. Half of the participants performed the two Simple runs first and the other half performed the two Repeat runs first.

For the Simple task paradigm, stimulus-response associations were well-ingrained and easy to remember. Go stimuli were green while No-go stimuli were red. For the Repeat task, a more complex task rule that required working memory was used. Participants were required to remember the color of the previous stimulus. A change in the stimulus color signaled a Go trial, while a repetition of the stimulus color signaled a No-go trial. For this task, 50% of stimuli were blue and 50% of stimuli were yellow.

2.3 fMRI Acquisition and Preprocessing

Imaging data were acquired on a Philips 3T scanner. This included a high-resolution anatomical scan (MPRAGE, 8-channel head coil, TR = 7.99 milliseconds, TE = 3.76 milliseconds, Flip angle = 8°). The behavioral task was performed during four fMRI runs (2 DSENSE EPI, 8-channel head coil, TR = 2500 milliseconds, TE = 30 milliseconds, Flip angle = 70°). Each run was 4 minutes and 5 seconds in duration.

Preprocessing of functional data was performed using SPM8 and included: slice timing correction, motion correction, co-registration of the first functional image in the run to the MPRAGE image, segmentation of gray matter, white matter and cerebrospinal fluid using SPM probabilistic tissue priors, normalization to standard MNI space, resampling of voxels to 2 mm³, and 8 mm full-width-at-half-maximum spatial smoothing.

2.4 fMRI Data Analysis

2.4.1 Go and RT Data Simulation—Before examination of the Go and RT-related activity, data simulations were performed to determine whether RT-related activity that is mean-centered (i.e. activity consistent with the periodic engagement account) produces a different pattern of results than RT-related activity that is positive linear (i.e. activity consistent with the ToT account). Time-courses were created to simulate data for five scenarios: 1. Go activity in the absence of a linear RT effect, 2. Linear RT-related activity centered around 0 in the absence of Go activity, 3. Positive linear RT-related activity in the absence of Go activity, 4. Go activity and linear RT-related activity centered around 0, and 5. Go activity and positive linear RT-related activity. Table 1 lists these scenarios and the type of cognitive process that each reflects. RT-related activity was simulated using both a zero-mean centered RT-regressor and a positive RT-regressor, in which RT-scaling on each trial was always greater than zero. This was done in order to determine whether the GLM model could separate Go and RT-related activity in both cases.

Data simulations for the five scenarios were derived from the actual SPM GLM regressors (see the following section, 2.4.2 Go RT Analysis, for details) for the 22 subjects. For the RT regressors, the RT values for each block were standardized by subtracting the mean and dividing by the standard deviation. This created a 0-mean centered regressor with standardized values for each block. For those simulations examining a positive RT effect, the absolute value of the minimum standardized RT value was added to all standardized RT values, thereby creating an RT time-course in which activity for the minimum RT trial was near 0 and activity positively increased with RT on all other trials. Activity for this positive RT simulation was never negative, whereas activity for the 0-mean RT simulation was negative for trials with RT less than the mean and positive for trials with RT greater than the mean. The data simulations were initially sampled at SPM's "micro-time", or the time-scale that is used to create the SPM model regressors, in which a time point occurs 16 times per TR ($2.5/16 = 0.15625$ seconds). The Go and RT-scaled events were convolved with the canonical HRF. To simulate data in which Go and RT-related activity occurred in the same voxel time-course, the Go and RT micro-time regressors were summed. For all simulated data, Gaussian random noise (mean = 0, SD = 0.1) was added to every time-point. The time-courses were then down-sampled to the TR resolution (every 2.5 seconds). The effects of Go, RT, and RT-Go for both the Simple and Repeat tasks were tested using the actual SPM model (see the Go RT analysis section below) for each subject. The full SPM model, including all task events and nuisance covariates, was then pre-colored and filtered (Friston et al., 1995; Worsley and Friston, 1995; Friston et al., 2000) and fit to the simulated data for each subject. Second-level effects of Go, RT, and RT-Go were tested for each of the five scenarios for each task, by performing t-tests to determine whether the Go and RT betas were significantly different from 0.

2.4.2 Go RT analysis—SPM8 was used to create general linear models. First-level models included up to seven condition trial onset regressors (Post-Rest Go, Standard Go, Go RT, No-go, Commission Error, Omission Error, and Anticipatory Error Trials on which the RT was less than 200 msec). Since Post-Rest Go trials were significantly slower than Standard Go trials, these trials were included as a separate regressor and were not examined

in group contrasts. For simplicity, the “Standard Go” contrast will be referred to as just the “Go” contrast for the remainder of the paper. RT on Go trials was modeled as a parametric modulation regressor in which the Go regressor was scaled by RT. All regressors were created in SPM’s micro-time in which a sample occurs every 0.15625 seconds. Events were impulse responses with a duration of zero that were convolved with the canonical hemodynamic response function (HRF). Separate regressors were created for the temporal and dispersion derivative terms of each condition. The regressors were then re-sampled to the TR interval. In addition, each functional run included nuisance regressors (six motion parameters, mean white matter, mean cerebrospinal fluid, and mean whole-brain time-courses) and a block regressor.

First-level contrasts were created for the Go and Go RT regressors. Second-level one-sample t-tests were performed to determine those regions that showed a significant effect of the canonical HRF-convolved regressors (i.e. positive Simple Go, positive Simple Go RT, positive Repeat Go, or positive Repeat Go RT). These tests were voxel-wise thresholded ($p < 0.001$ for Go and $p < 0.01$ for RT contrasts). Because the RT contrast accounted for variance in the BOLD signal that was not already accounted for by the Go contrast, a more liberal voxel-level threshold was chosen for that contrast. All tests were multiple comparisons corrected at a cluster-level of $p < 0.05$ according to Random Field Theory (Worsley et al., 1996; Kiebel et al., 1999). To determine whether there is an effect of task on RT-related activity, the RT regressors for the two tasks were directly contrasted (i.e. Repeat RT > Simple RT and Simple RT > Repeat RT). To determine whether the fMRI findings corresponded with the simulation findings, RT > Go contrasts were also examined for both tasks. These tests were thresholded in the same manner as the primary RT contrasts.

2.4.3 Overlap With RT Contrasts—To determine whether the spatial distribution was the same for the primary Go condition and the RT contrast in each task, a conjunction analysis was performed for the two contrasts within each task. In addition, the number of voxels that were significant for both contrasts (i.e. voxels with overlapping effects) was summed and divided by the total number of significant voxels in each contrast (i.e. both overlapping and non-overlapping effects). This was done both at the initially-chosen voxel-wise thresholds ($p < 0.001$ for Go and $p < 0.01$ for RT contrasts) and a more liberal threshold ($p < 0.05$ for both contrasts) to ensure that the degree of spatial overlap was not just due to the threshold. The latter threshold was chosen as the most-liberal significance threshold.

To determine whether the spatial distribution was the same for both the Simple and Repeat task RT contrasts, a conjunction analysis was performed for the two tasks’ RT contrasts. Here also, the percent of overlapping significant voxels for both contrasts was computed at both the initially-chosen thresholds and the more liberal threshold.

2.4.4 Follow-up Analysis Examining Go Expectancy—To examine whether RT-related activity may be due to expectancy of the Go trial, another GLM was created that included all of the regressors described in the Go RT analysis and additionally included the canonical and derivative terms for Go trial expectancy. For this analysis, Go trial expectancy was indexed by the number of Go trials performed consecutively. It was assumed that expectancy for a Go trial would decrease as the number of Go trials in a row increased. The

Go Expectancy regressors were parametric modulation regressors and were included in the model after the primary Go condition terms and before the Go RT terms. Including Go Expectancy before Go RT in the model insured that the Go RT regressor was orthogonalized with respect to Go Expectancy. Therefore, any RT-related activity found for this model would be robust even after accounting for Go Expectancy. First- and second-level contrasts were set up as described in the Go RT analysis with Go RT as the contrast of interest.

3 Results

3.1 Behavioral Results

Behavioral results are displayed in Tables 2 and 3. Post-Rest Go RTs were significantly slower than Go RTs in both tasks (Table 3). Post-Error Go RTs were not significantly slower than non-Post-Error Go RTs for either task (Table 3). For this reason, the imaging analyses separated Post-Rest Gos, but included Post-Error Gos with Other Go trials.

3.2 fMRI Results

3.2.1 Go and RT Data Simulation—Table 4 displays the results for the five simulated scenarios. The SPM model correctly detected a significant effect of both Go and RT for all scenarios except the third. In scenario 3, there was a linear positive RT effect, but no primary Go effect. In that case, significant effects of both RT and Go were found. The erroneous detection of a primary Go effect in that scenario is because the Go-related activity was, on average, greater than 0. The results suggest that Go effects will be erroneously detected if the RT effect is positive linear; however, Go and RT effects will be effectively distinguished if the actual RT effect is centered around 0 or if there is no RT effect present. Importantly for the interpretation of the current results, an RT effect only occurs in the absence of a Go effect when the actual RT-related activity is zero-mean centered (scenario 2), but not when it is positive linear (scenario 3).

For the RT-Go contrast, the only scenario in which the RT estimate was greater than the Go estimate was scenario 2 (i.e. the scenario in which RT activity was 0-mean centered). It is critical that only 0-mean centered RT-related activity resulted in a significantly greater RT contrast estimate than Go contrast estimate. For all other scenarios, the RT-Go contrast was negative, which indicates that Go activity is greater than RT activity. Therefore, the RT-Go contrast was incorrectly identified as negative in scenario 3, 5, and, for the Repeat Task, scenario 4. The only scenario in which the RT-Go contrast was correctly identified as negative was scenario 1 (i.e. the scenario in which Go activity existed in the absence of RT-related activity). The RT-Go contrast had also distinguished scenario 2 from the other scenarios. Scenario 2 is the only case in which RT-related activity will be found in the absence of Go activity and it is the only scenario in which the RT parameter estimate is significantly greater than the Go parameter estimate.

3.2.2 Go RT Results—Table 5 reports those regions with significant activity for the Go and RT fMRI contrasts in the two tasks. Simple Go activity occurred across a distributed set of regions that are consistent with a motor execution circuit (Mostofsky et al., 2009; Barber et al., 2012). Simple RT-related activity occurred in a region spanning superior and medial

parietal cortex and superior and middle occipital cortex. Figure 1 displays the spatial overlap between the Simple Go and RT contrasts. Overlap between the two occurred in a restricted area of the pre- and post-central gyrus, however, the majority of significant voxels are distinct for the two contrasts (Figure 2).

For the Repeat Task, significant activity for the Go condition contrast also occurred within distributed motor circuit regions (Mostofsky et al., 2009; Barber et al., 2012), but additionally extended into fronto-parietal and dorsal attention regions (Table 5). Repeat RT-related activity was found primarily within fronto-parietal regions. Figure 2 displays the spatial overlap between the Repeat Go and RT contrasts. For this task, overlap occurred in a more extensive set of regions, including fronto-parietal, superior medial parietal, and dorsal pre-motor.

Examination of the RT contrasts for the two tasks revealed that there was also little overlap in RT-related activity for the two tasks (Figure 3). A few voxels overlapped between the two on the boundary of both of the contrasts in the superior medial parietal cortex. The results suggest that RT-related activity reflects task-specific cognitive processes.

Table 6 displays the number and percentage of significant voxels that overlapped for the Go, RT, and RT-Go contrasts in each task. For the Simple Go and Simple RT contrasts, overlap occurred in less than 5% of those voxels that were active for the two contrasts. This was true even when the voxel-wise thresholds were reduced to the liberal p-value of 0.05. For the Repeat task, overlap between the two contrasts was greater, but was still confined to less than 20% of significant voxels. Again, this was true even at the $p < 0.05$ liberal threshold. Therefore, PC and RT effects occurred in a largely independent set of regions particularly for the Simple task. Examination of the RT-Go contrasts confirms this result and shows that a number of voxels have significantly greater parameter estimates for RT-related activity than for mean Go activity. Table 6 also displays the overlap for the RT contrasts in both tasks. The RT contrast overlap for the two tasks was less than 10% of active voxels even at the more liberal threshold, confirming that RT-related activity reflected task-specific cognitive processes.

To further determine whether RT-related activity was distinct for the two tasks, the RT-regressors for the two tasks were directly contrasted. The regions with significantly different activity for the two tasks are displayed in Table 7. RT-related activity was significantly greater in the Simple than Repeat task primarily within Visual regions and within the DAN. RT-related activity was significantly greater in the Repeat than Simple task in regions of the FPN and extending into the DMN. The networks that were differentially engaged by the two tasks are consistent with the specific cognitive demands for the two tasks and therefore, may reflect specific cognitive control processes that are periodically engaged by the task at hand. The Simple task involved a perceptual decision which engages regions involved in visual discrimination and visuo-motor representations; whereas, the Repeat task, involved a decision that recruited working memory, which engages FPN regions involved in working memory retrieval and representation.

3.2.3 Follow-up Analysis Examining Go Expectancy—The Go RT effects were examined in models that included Go Expectancy to determine whether it could account for RT-related activity. Table 8 displays the regions that showed significant RT-related effects, even when Go Expectancy was included in the model. RT-related activity occurred within the same set of regions as those found in the previous models without Go Expectancy included. However, RT-related activity was somewhat attenuated in the models with Go Expectancy. This attenuation may be due to collinear Go Expectancy effects occurring within the same voxels, however, it may also be due to reduced power due to a greater number of model regressors. Either way, RT-related activity occurred within the same set of regions and therefore was not due to Go trial expectancy.

4 Discussion

RT-related activity has previously been attributed to ToT, but could also reflect periodic engagement of cognitive processes. The ToT account suggests that RT-BOLD effects are always due to positive stimulus-evoked activity for regions that contribute to decision processing. Activity of this nature would result in co-occurring PC and RT effects. The periodic engagement account, on the other hand, suggests that RT-BOLD effects are not always positively active and therefore, RT-BOLD effects occur in the absence of a PC effect. Data simulations confirmed that positive linear RT-related activity always results in both significant PC and RT effects, which supports the ToT account. An RT effect occurs in the absence of a PC effect only when the BOLD amplitude decreased with RT for trials with mean < 0 and increased with RT for trials with mean > 0 (i.e. when RT-related activity is 0-mean centered). In that case, there is a significant RT effect, but not a significant PC effect, which supports the periodic engagement account.

Support for the two accounts of RT-related activity was examined in two Go/No-go tasks. For the Simple task, RT-BOLD effects overlapped with the Go condition effect in a region of the somatomotor cortex; however, the two effects occurred, for the most part, in a distinct set of regions. For the Repeat task, there was a greater degree of overlap between PC and RT-BOLD effects; however, again, the two effects had a mostly distinct spatial distribution.

Examination of the RT-BOLD effects for the Simple and Repeat tasks, revealed that RT-related activity was mostly distinct and reflected the specific cognitive demands of each task. For the Simple task, RT-BOLD effects occurred in Visual and Dorsal Attention Network (DAN) regions consistent with the perceptual decision-making demands of that task. Whereas, for the Repeat task, RT-related activity occurred primarily in Ventral Attention Network (VAN) and Fronto-Parietal Network (FPN) regions, consistent with the working memory decision-making demands of that task. The results suggest that RT-BOLD effects can reflect periodic engagement of cognitive control regions particularly during low cognitive demand. In addition, RT-related activity reflects task-specific cognitive functions.

4.1 Periodic Engagement Versus Time on Task

ToT is the most well-established account of RT-BOLD effects. According to this view, increased activity on longer RT trials reflects the length of the underlying cognitive process. The ToT account is well-supported by findings in which RT-related activity is always

positive (i.e. positive linear RT effects or RT effects in conjunction with PC effects), but not by findings in which an RT effect occurs in the absence of a PC effect (i.e. when RT-related activity is 0-mean centered). Negative activity, as would be found on fast RT trials when RT-related activity is 0-mean centered, does not make sense in the context of this theory. For the current study, the majority of RT-related activity fit this latter description and therefore is not well-supported by the ToT account. Activity that is suppressed on fast RT trials is better supported by a periodic engagement account.

Periodic engagement may reflect cognitive processes that are not necessary for task performance on every trial but are instead recruited only occasionally. This type of engagement may be more relevant for sustained attention tasks or situations in which task performance is relatively easy or automatic as was the case in the current study for the Simple task. During this task, the same stimulus-response mapping was relevant for every trial and the Go response was correct on the majority of trials. Thus, Go trials had relatively low demands for attention, monitoring, interference control, and response selection. This low cognitive demand may be the reason that PC and RT-related overlap was less extensive than previously reported (Yarkoni et al., 2009; Carp et al., 2010; Grinband et al., 2011a; Prado et al., 2011; Weissman and Carp, 2013; Neta et al., 2014).

The majority of studies examining RT-BOLD effects have employed complex tasks that recruit a number of cognitive control processes. For example, Yarkoni and colleagues (2009) examined RT effects across a number of different tasks (e.g. working memory and decision-making tasks) in which the mean RT ranged from 642 – 1247 msec and found common RT-related activation for all tasks across an extensive set of regions. Given the relatively high mean RTs for the tasks examined, these tasks likely required the recruitment and coordination of a number of cognitive control processes for response selection. Therefore, greater overlap between the PC and RT contrasts in previous studies may be due to the complexity of the cognitive processes recruited for task performance. However, this is speculative as one previous study used a Simple RT task with minimal response selection (Weissman & Carp, 2013) and found much more extensive RT-related activation. In addition, the RT-related activity showed more overlap with PC activity than was present in the current study. Although this previous study had minimal response selection demands, other cognitive demands may have contributed to the discrepant findings. For example, the previous study used event timings which were less predictable, had much longer time in between events (2.5 – 6.25 seconds in the previous study versus 1.8 seconds in the current study), and had a much more difficult second task that was performed in the same testing session than the current study. Any of these task differences may have contributed to this discrepancy in findings. While the current results suggest that periodic engagement occurs during sustained attention tasks with minimal cognitive demand, more research is necessary to determine the precise experimental conditions that lead to this type of activity.

4.2 Task-Specific RT-Related Activity

The current study found circumscribed RT-related activation primarily in Visual areas and the DAN for the Simple task and the VAN and FPN for the Repeat task. This activation is consistent with the specific cognitive demands for the two tasks. The Simple task requires a

perceptual decision, which involves regions that play a role in visual discrimination and visuo-motor representations (Corbetta et al., 2002; Corbetta et al., 2008); whereas the Repeat task requires working memory to make a decision, which involves regions that play a role in the maintenance and/or retrieval of task information (Vincent et al., 2008; Power and Petersen, 2013). Therefore, the current finding of task-specific RT-related activity is consistent with the cognitive demands for each particular task.

Previous studies have found that RT-related activity can account for condition differences in activity (Grinband et al., 2011b, a; Weissman and Carp, 2013). The difference in dorsal medial frontal cortex activity between two conditions was found to be due to RT-related differences between the two conditions, which reflected ToT rather than additional cognitive processes for the more difficult condition. The findings for the current study suggest RT-related activity is not limited to a particular region or brain system, but instead occurs across a number of cognitive networks, dependent on task demands. Further, the current findings suggest that this task-specific RT-related activity reflects cognitive processes that are not consistently engaged on all trials. It is not clear from the current study whether this periodically-engaged activity reflects the specific cognitive processes that are recruited during the Simple task or whether it reflects the level of cognitive demand. It may be that periodic engagement only occurs when cognitive demand is relatively low and neural activity is not necessary on every trial. For instance, if a region is involved in updating task representations, this may be done only periodically during a sustained attention task, but more frequently during a working memory task. Future research is necessary to determine the circumstances that distinguish these two types of activity.

Acknowledgments

Funding for this research was provided by NIH R01 MH078160, R01 MH085328, and P41 EB015909.

References

- Barber AD, Caffo BS, Pekar JJ, Mostofsky SH. Effects of working memory demand on neural mechanisms of motor response selection and control. *J Cogn Neurosci*. 2013; 25:1235–1248. [PubMed: 23530923]
- Barber AD, Srinivasan P, Joel SE, Caffo BS, Pekar JJ, Mostofsky SH. Motor "dexterity"? Evidence that left hemisphere lateralization of motor circuit connectivity is associated with better motor performance in children. *Cereb Cortex*. 2012; 22:51–59. [PubMed: 21613469]
- Carp J, Kim K, Taylor SF, Fitzgerald KD, Weissman DH. Conditional Differences in Mean Reaction Time Explain Effects of Response Congruency, but not Accuracy, on Posterior Medial Frontal Cortex Activity. *Front Hum Neurosci*. 2010; 4:231. [PubMed: 21212836]
- Corbetta M, Kincade JM, Shulman GL. Neural systems for visual orienting and their relationships to spatial working memory. *J Cogn Neurosci*. 2002; 14:508–523. [PubMed: 11970810]
- Corbetta M, Patel G, Shulman GL. The reorienting system of the human brain: from environment to theory of mind. *Neuron*. 2008; 58:306–324. [PubMed: 18466742]
- Friston KJ, Josephs O, Zarahn E, Holmes AP, Rouquette S, Poline J. To smooth or not to smooth? Bias and efficiency in fMRI time-series analysis. *Neuroimage*. 2000; 12:196–208. [PubMed: 10913325]
- Friston KJ, Holmes AP, Poline JB, Grasby PJ, Williams SC, Frackowiak RS, Turner R. Analysis of fMRI time-series revisited. *Neuroimage*. 1995; 2:45–53. [PubMed: 9343589]
- Grinband J, Wager TD, Lindquist M, Ferrera VP, Hirsch J. Detection of time-varying signals in event-related fMRI designs. *Neuroimage*. 2008; 43:509–520. [PubMed: 18775784]

- Grinband J, Savitskaya J, Wager TD, Teichert T, Ferrera VP, Hirsch J. The dorsal medial frontal cortex is sensitive to time on task, not response conflict or error likelihood. *Neuroimage*. 2011a; 57:303–311. [PubMed: 21168515]
- Grinband J, Savitskaya J, Wager TD, Teichert T, Ferrera VP, Hirsch J. Conflict, error likelihood, and RT: Response to Brown & Yeung et al. *Neuroimage*. 2011b; 57:320–322. [PubMed: 21554960]
- Henson, R. Analysis of fMRI Timeseries: Linear Time-Invariant Models, Event-related fMRI and Optimal Experimental Design. In: William Penny, KF.Ashburner, JohnKiebel, Stefan, Nichols, Thomas, editors. *Statistical Parametric Mapping: The Analysis of Functional Brain Images*. London: Elsevier; 2007.
- Kiebel SJ, Poline JB, Friston KJ, Holmes AP, Worsley KJ. Robust smoothness estimation in statistical parametric maps using standardized residuals from the general linear model. *Neuroimage*. 1999; 10:756–766. [PubMed: 10600421]
- Mostofsky SH, Powell SK, Simmonds DJ, Goldberg MC, Caffo B, Pekar JJ. Decreased connectivity and cerebellar activity in autism during motor task performance. *Brain*. 2009; 132:2413–2425. [PubMed: 19389870]
- Neta M, Schlaggar BL, Petersen SE. Separable responses to error, ambiguity, and reaction time in cingulo-opercular task control regions. *Neuroimage*. 2014; 99C:59–68.
- Power JD, Petersen SE. Control-related systems in the human brain. *Curr Opin Neurobiol*. 2013; 23:223–228. [PubMed: 23347645]
- Prado J, Carp J, Weissman DH. Variations of response time in a selective attention task are linked to variations of functional connectivity in the attentional network. *Neuroimage*. 2011; 54:541–549. [PubMed: 20728549]
- Vincent JL, Kahn I, Snyder AZ, Raichle ME, Buckner RL. Evidence for a frontoparietal control system revealed by intrinsic functional connectivity. *J Neurophysiol*. 2008; 100:3328–3342. [PubMed: 18799601]
- Weissman DH, Carp J. The congruency effect in the posterior medial frontal cortex is more consistent with time on task than with response conflict. *PLoS One*. 2013; 8:e62405. [PubMed: 23638070]
- Worsley KJ, Friston KJ. Analysis of fMRI time-series revisited—again. *Neuroimage*. 1995; 2:173–181. [PubMed: 9343600]
- Worsley KJ, Marrett S, Neelin P, Vandal AC, Friston KJ, Evans AC. A unified statistical approach for determining significant signals in images of cerebral activation. *Hum Brain Mapp*. 1996; 4:58–73. [PubMed: 20408186]
- Yarkoni T, Barch DM, Gray JR, Conturo TE, Braver TS. BOLD correlates of trial-by-trial reaction time variability in gray and white matter: a multi-study fMRI analysis. *PLoS One*. 2009; 4:e4257. [PubMed: 19165335]

Highlights

- RT-related BOLD activity can reflect periodic engagement of cognitive processes.
- RT-related BOLD activity depends on task-specific demands.
- Periodic engagement is particularly evident during less-demanding tasks.

Figure 1. Regions Showing an Effect of Go, RT, or Both in the Simple Task. Significance is assessed at a voxel-level threshold of $p < 0.001$ for Go contrasts and $p < 0.01$ for RT contrasts and multiple comparisons-corrected at a cluster-level of $p < 0.05$.

Figure 2. Regions Showing an Effect of Go, RT, or Both in the Repeat Task. Significance is assessed at a voxel-level threshold of $p < 0.001$ for Go contrasts and $p < 0.01$ for RT contrasts and multiple comparisons-corrected at a cluster-level of $p < 0.05$.

Figure 3. Regions Showing an Effect of RT in the Simple Task, in the Repeat Task, or in Both. Significance is assessed at a voxel-level threshold of $p < 0.01$ for RT contrasts and multiple comparisons-corrected at a cluster-level of $p < 0.05$.

Table 1

Five scenarios captured by the data simulations.

primary condition	consistently active for all condition trials
periodic engagement	periodically engaged; more engaged when RTs are slower
time on task	active on all condition trials; greater activity when RTs are slower

Reaction Times (RTs), Intra-Subject Variability (ISV = SD RT / mean RT), and Accuracy for each task. At the bottom, the t- and p-values report differences between the Simple and Repeat tasks. Significant results are highlighted.

Table 2

373.12 (107.52)	365.94 (110.35)	0.20 (0.05)	3.59 (4.72)	0.36 (1.04)	0.615 (2.60)
454.01 (128.03)	441.96 (126.99)	0.25 (0.05)	11.87 (10.37)	4.97 (10.87)	1.00 (4.53)
5.36	5.31	3.80	6.03	3.52	0.92
<0.001	<0.001	<0.001	<0.001	0.002	0.37

Table 3

Reaction Times (RTs) for Post-Rest Go, Post-Error Go, and Commission Error trials. The t- and p-values report differences between each condition and Go trial RTs. Significant results are highlighted.

463.33 (118.84)	8.76	<0.001	412.95 (141.81)	1.52	0.14	343.86 (86.00)	0.2	0.84
546.31 (118.78)	5.22	<0.001	428.24 (119.08)	0.94	0.38	442.32 (126.82)	0.5	0.62

Table 4

The model fit for data simulations in five scenarios. The parameter estimates for the group-level contrasts are displayed. The parameter estimates that were found to be positive significant are highlighted in green ($p < 0.001$). The parameter estimates that were found to be negative significant are highlighted in red ($p < 0.001$).

Simple Task	1.08	0.00	-0.49
	-0.01	1.08	0.49
	1.91	1.07	-0.38
	1.11	1.09	-0.01
	3.03	1.09	-0.88
Repeat Task	1.10	0.01	-0.63
	0.01	1.03	0.42
	1.73	1.03	-0.57
	1.11	1.04	-0.20
	2.82	1.03	-1.19

Table 5

Regions with Significant Activation for Go and RT Contrasts

Precentral Gyrus/Postcentral Gyrus	B	6/4/3/2/32	0.000	5141	9	0	6	56
Supplementary Motor Area/ Superior Temporal Gyrus		40/9/13/8			8.85	-60	-16	20
Supramarginal Gyrus/Inferior Parietal Lobule		43/1/44/24			8.55	2	0	64
Rolandic Operculum/Inferior Frontal Operculum								
4th, 5th, and 6th Lobules of the Cerebellum	B		0.000	1600	6.71	18	-52	-20
4th, 5th, and 6th Lobules of the Cerebellar Vermis					5.72	30	-50	-26
					5.7	28	-60	-22
Putamen/Insula/Rolandic Operculum	L	13/22	0.000	717	5.25	-48	6	0
Superior Temporal Gyrus					4.82	-40	-4	10
					4.76	-24	8	-2
Precentral Gyrus/Middle Frontal Gyrus	R	6/9	0.000	405	5.21	54	2	44
					4.45	42	-2	60
Superior Temporal Gyrus	R	42	0.023	178	4.91	66	-34	16
			0.005	250	4.53	-40	-58	-32
					4.43	-32	-62	-26
Superior Parietal Lobule/Precuneus/Middle Occipital Gyrus	B	7/19/4/3	0.000	4327	4.78	-10	-50	54
Postcentral Gyrus/Superior Occipital Gyrus/		40/5/18			4.69	-18	-60	66
Cuneus/Precentral Gyrus/Inferior Parietal Lobule					4.49	8	-54	54
Precentral Gyrus/Inferior Parietal Lobule/Supplementary	B	6/40/9/32/4	0.000	9730	9.74	0	6	56
Motor Area/Postcentral Gyrus/Superior Parietal Lobule		7/44/3/8/13			8.28	2	12	50
Inferior Frontal Operculum/Supramarginal Gyrus		47/22/45/2			7.82	-50	4	40
Middle Frontal Gyrus/Superior Temporal Gyrus								
Superior Frontal Gyrus/Middle Cingulate Cortex/Insula								
Rolandic Operculum/Superior Medial Frontal Gyrus								
Superior Temporal Pole/Inferior Frontal Trigeminal								
4th, 5th, 6th, and 7th Lobules of the Cerebellum	B		0.000	2628	7.52	-34	-58	-30
4th, 5th, and 6th Lobules of the Cerebellar Vermis					6.96	6	-64	-16
Crus I Lobule of the Cerebellum					6.46	6	-74	-16

Middle Frontal Gyrus	R	9/10	0.000	688	6.13	44	36	34
					5.02	34	48	32
Superior Temporal Gyrus/Middle Temporal Gyrus	R	40/42	0.000	461	5.61	66	-34	18
					4.62	46	-40	2
					3.55	50	-24	-2
Inferior Parietal Lobule/Supramarginal Gyrus	R	40/7	0.000	1300	5.54	34	-44	42
Superior Parietal Lobule/Angular Gyrus					5.41	42	-42	44
					4.98	50	-38	50
Postcentral Gyrus/Superior Temporal Gyrus	L	43	0.004	257	5.35	-58	-16	20
					3.44	-62	-28	10
Middle Frontal Gyrus/Inferior Frontal Trigeminal	L	9	0.001	342	5.26	-48	32	28
					3.7	-38	42	36
Supramarginal Gyrus/Inferior Parietal Lobule	R	40/7	0.000	1971	5.37	56	-44	34
Angular Gyrus/Superior Parietal Lobule					4.35	54	-40	42
Superior Occipital Gyrus/Precuneus					3.5	34	-52	44
Middle Frontal Gyrus/Inferior Frontal Trigeminal	R	9/10/47/45	0.000	2957	5.1	22	50	26
Inferior Frontal Opercular/Insula/Inferior Frontal Orbitalis		46/44/8			4.28	48	18	-2
Superior Frontal Gyrus/Precentral Gyrus					4.22	52	14	22
Inferior Parietal Lobule/Supramarginal Gyrus	L	40	0.002	870	5	-52	-48	28
Angular Gyrus					3.56	-34	-50	30
					3.24	-50	-44	44
Supplementary Motor Area/Middle Frontal Gyrus	B	6/8/32	0.000	1097	4.36	4	22	50
Superior Medial Frontal Gyrus/Superior Frontal Gyrus					3.9	4	26	40
Middle Cingulate Gyrus					3.71	34	6	64

Table 6
Number of Significantly Active Voxels for Each Contrast and the Number and Percentage of Overlapping Voxels.

8291	15406	4327	6895	14308	21782	468	2890	246
						3.85	14.89	2.24
24709	40566	15207	15700	20780	35596	1819	9256	2699
						4.77	19.69	9.57

Table 7

Regions with Significantly Greater Activity for the Repeat RT > Simple RT Contrast and for the Simple RT > Repeat RT Contrast.

Angular Gyrus/Inferior Parietal Lobule	R	40	0.000	1118	5.34	46	-54	34
Supramarginal Gyrus					4.98	46	-60	46
					4.90	62	-54	28
Angular Gyrus/Inferior Parietal Lobule	L	40	0.004	793	5.33	-46	-58	34
Supramarginal Gyrus					4.91	-50	-50	30
					4.77	-34	-52	32
Superior Frontal Gyrus/Middle Frontal Gyrus	R	10/9	0.015	623	5.24	22	44	28
					4.93	22	52	24
					3.49	14	52	40
Inferior Frontal Trigeminal/Inferior Frontal Opercular	R	45	0.021	585	4.53	52	16	22
Middle Frontal Gyrus					4.24	34	34	12
					4.01	52	22	16
Superior Frontal Gyrus/Superior Medial Frontal Gyrus		6/8	0.026	560	4.05	4	38	54
Supplementary Motor Area					3.86	4	32	60
					3.60	22	10	64
Middle Occipital Gyrus/Lingual Gyrus	B	19/18/39	0.000	3728	6.95	-42	-76	2
Superior Occipital Gyrus/Fusiform Gyrus/Cuneus		37/7			5.99	42	-76	2
Calcarine Sulcus/Middle Temporal Gyrus					5.45	28	-84	18
Inferior Occipital Gyrus/6th Lobule Cerebellum								
Superior Parietal Lobule/Precuneus/Postcentral Gyrus	B	7/5	0.006	727	5.09	-26	-42	54
					5.00	-10	-46	56
					4.35	-26	-52	58
Fusiform Gyrus/Lingual Gyrus/6th Lobule Cerebellum	L	18/19	0.006	726	4.74	-32	-62	-18
					4.38	-32	-70	-16
					3.93	-16	-60	-26

Table 8
Regions with Significant Activation for RT Contrasts in Models that Included Go Expectancy Regressors.

Middle Occipital Gyrus/Precuneus/Superior Parietal Lobule	B	7/19/5	0.000	3268	4.41	8	-56	54
Superior Occipital Gyrus/Cuneus/Inferior Parietal Lobule					0.60	-16	-58	68
					0.60	-30	-86	10
Supramarginal Gyrus/Inferior Parietal Lobule	R	40/7	0.000	1993	4.78	56	-46	34
Angular Gyrus/Superior Parietal Lobule					4.29	54	-40	44
					4.26	46	-42	46
Middle Frontal Gyrus/Inferior Frontal Opercular	R	9/10/45/44	0.000	3516	4.65	52	14	22
Inferior Frontal Trigeminal/Insula/Inferior Frontal Orbitalis		47/46/8/13			4.65	28	48	28
Precentral Gyrus/Superior Frontal Gyrus					4.56	36	30	22
Inferior Parietal Lobule/Precuneus/Superior Parietal Lobule	L	40/7	0.000	1876	4.58	-54	-46	28
Supramarginal Gyrus/Angular Gyrus					4.19	-34	-48	34
					4.08	-48	-46	46
Superior Frontal Gyrus/Supplementary Motor Area	B	6/8/32	0.000	1453	4.36	2	20	50
Superior Medial Frontal Gyrus/Middle Frontal Gyrus					4.35	24	14	64
Middle Cingulate Gyrus					4.29	4	26	40