

# 1 The response time paradox in functional 2 magnetic resonance imaging analyses

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9 **Abstract** The functional MRI (fMRI) signal is a proxy for an unobservable neuronal signal, and differences in fMRI  
10 signals on cognitive tasks are generally interpreted as reflecting differences in the intensity of local neuronal activity.  
11 However, changes in either intensity or duration of neuronal activity can yield identical differences in fMRI signals.  
12 When conditions differ in response times (RTs), it is thus impossible to determine whether condition differences in  
13 fMRI signals are due to differences in the intensity of neuronal activity or to potentially spurious differences in the  
14 duration of neuronal activity. The most common fMRI analysis approach ignores RTs, making it difficult to interpret  
15 condition differences that could be driven by RTs and/or intensity. Because differences in response time are one of  
16 the most important signals of interest for cognitive psychology, nearly every task of interest for fMRI exhibits RT  
17 differences across conditions of interest. This results in a paradox, wherein the signal of interest for the psychologist  
18 is a potential confound for the fMRI researcher. We review this longstanding problem, and demonstrate that the  
19 failure to address RTs in the fMRI time series model can also lead to spurious correlations at the group level related to  
20 RTs or other variables of interest, potentially impacting the interpretation of brain-behavior correlations. We propose  
21 a simple approach that remedies this problem by including RT in the fMRI time series model. This model separates  
22 condition differences from RT differences, retaining power for detection of unconfounded condition differences while  
23 also allowing the identification of RT-related activation. We conclude by highlighting the need for further theoretical  
24 development regarding the interpretation of fMRI signals and their relationship to response times.

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## 26 Introduction

27 The goal of task-based functional magnetic resonance imaging (fMRI) studies is to infer the involvement of particular  
28 brain regions or networks in specific cognitive functions. These studies are most often designed using the subtraction  
29 logic first developed by *Donders (1969)* for the analysis of response times (RTs), in which comparisons are made between  
30 different task conditions that are thought to differ with regard to the involvement of some specific cognitive function(s).  
31 For example, in the well known Stroop task, stimuli are presented in which the color and text of the word are either  
32 congruent (e.g. "blue" presented in blue) or incongruent (e.g. "blue" presented in red) (*Stroop, 1935*). Individuals are  
33 consistently slower at naming the color of the stimulus when the written word is incongruent compared to congruent,

34 and this difference in response times is interpreted as indexing the engagement of an additional cognitive process in  
35 the incongruent condition, such as conflict detection or resolution (*Botvinick et al., 2001*). Similarly, greater activation  
36 in regions such as the dorsal medial frontal cortex (dmFC) in fMRI studies of the Stroop task have been interpreted as  
37 reflecting a specific role in these cognitive processes (*Botvinick et al., 1999; MacDonald et al., 2000; Kerns et al., 2004*).

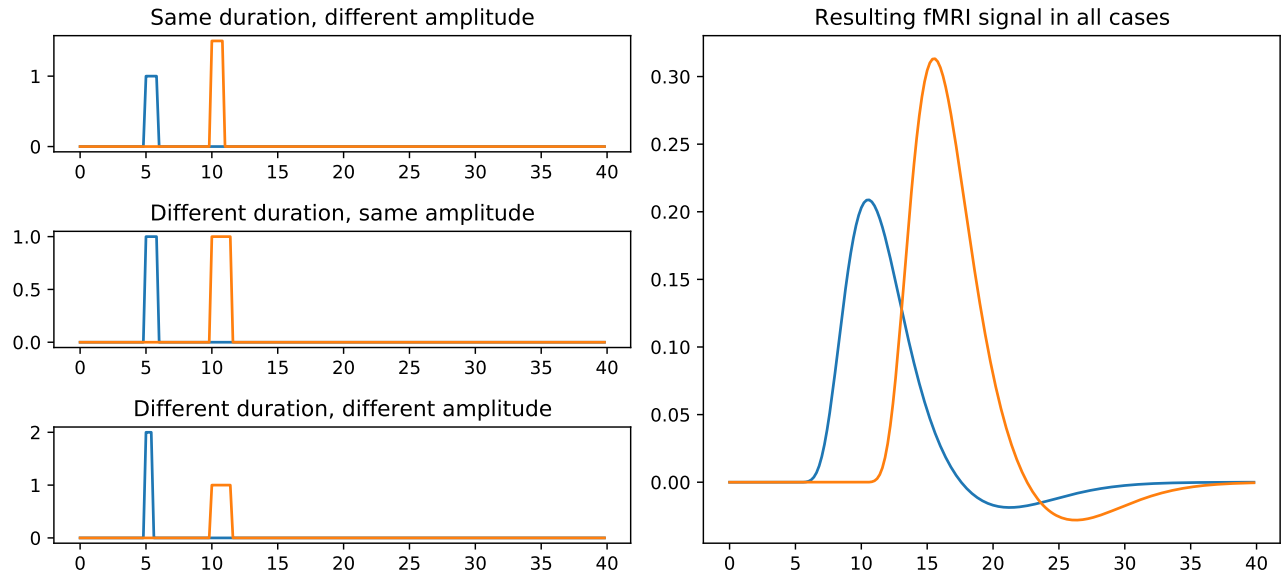
38 The facile nature of the common inference from activation to “involvement” belies the deep complexity of the link  
39 between fMRI signals and underlying neuronal activity (cf. *Logothetis (2008)*). Here we focus on disambiguating these  
40 interpretations of activation: namely, whether a difference in activation reflects the differential engagement of a partic-  
41 ular computation, or engagement of the same computation for a different amount of time. Because of the slow nature  
42 of the blood oxygen-level dependent (BOLD) response that is measured in most fMRI studies, it is nearly impossible to  
43 distinguish the degree to which a difference in evoked BOLD response reflects an increase in the amplitude of neuronal  
44 response versus a difference in the duration of that response (Figure 1). This indeterminacy has been known since the  
45 early days of fMRI (*Savoy et al., 1995; Jezzard et al., 2001*), and establishes the importance of considering the potential  
46 of differences in the duration of neural activity to confound amplitude estimates in some fMRI tasks.

47 Over a decade ago, *Grinband et al. (2008)* started the discussion about modeling of response times in fMRI analysis.  
48 They proposed the use of a variable epoch model, where the trial-by-trial neuronal durations were assumed to track  
49 with RTs as opposed to the common modeling practice at the time that assumed each trial was sufficiently modeled as  
50 a brief impulse of constant duration (e.g., .1s). The impulse model was previously considered to be adequate in rapid  
51 event-related designs due to the belief that differences in RTs would not be detectable in this setting. The proposed  
52 model using RTs as the duration was shown to produce activation estimates that were not confounded by RT differ-  
53 ences and yielded more powerful results than the impulse model or an impulse model that included an RT-modulated  
54 regressor. Importantly, this model’s performance studied within-subject power for a single condition versus baseline  
55 and relied on specific assumptions about the underlying signal, specifically that the duration of neuronal activation  
56 mirrors the RTs, which is not necessarily the case. The behavior of this model when this assumption is not met has  
57 not been well studied nor has the behavior of more commonly used condition difference contrasts in the context of  
58 response time differences between conditions.

59 *Yarkoni et al. (2009)* examined the relationship between RT and fMRI signal across a variety of tasks in an effort to  
60 better understand how RTs were related to the measured BOLD signal. Evidence was found that RT-driven amplitude  
61 differences were likely due to “time on task” or simply duration differences in the neuronal signal across trials, as  
62 opposed to differences in the magnitude of neuronal activity (characterized as “effort” in that paper). These time on  
63 task effects could reflect stimulus-related processes that simply reflect constant neuronal activity that varies in relation  
64 to the duration of the trial, rather than differences in the amplitude of neuronal activity across trials. A compelling result  
65 of this work was the identification of a widespread network of brain regions that showed significant correlation with  
66 RTs across each of a variety of different tasks including the dmFC which was previously described as reflecting conflict  
67 in the Stroop task. This calls into question how RT-based activation differences might be interpreted given that they  
68 are common across many tasks and thus are unlikely to reflect processes that are specific to a particular task.

69 A subsequent series of papers focused on the incongruent versus congruent contrast of the Stroop task and whether  
70 activation in the dmFC reflected conflict, as proposed by a prominent theory (*Botvinick et al., 2001*). This inspiring dis-  
71 course across multiple publications illustrates the challenge of interpreting RT-correlated activation as well as demon-  
72 strating the rigorous work required to combine the behavioral theory of a task with imaging analysis results when  
73 RT-correlated activation is found. Both *Grinband et al. (2011b)* and *Carp et al. (2010)* showed that the difference in  
74 activation between slow and fast congruent trials was similar to the difference between all congruent and incongruent

## Different underlying neuronal signals yield same BOLD signal



**Figure 1.** Illustration of how amplitude and duration of neuronal signal interact to yield similar BOLD responses. The left hand column shows 3 different examples of neuronal signals that evoke the same BOLD response shown in the right hand panel.

75 trials in the dmFC, supporting the idea that the commonly found effect was driven by RTs. The next step to fully under-  
76 stand this RT-driven effect is the difficult step of determining whether this is a time on task effect or an actual difference  
77 in the amplitude of neuronal signaling that correlates with RT and whether these differences align with the underlying  
78 theory of conflict in the Stroop task. This was the focus of follow-up work by **Yeung et al. (2011)** who proposed that the  
79 RT-based effects were a result of differential engagement of specific cognitive processes and not simply due to time  
80 on task. They also argued that the result supported the predictions from the computational model that formalizes the  
81 conflict monitoring theory. Even though this series of papers drew attention to how we model and interpret response  
82 times in the fMRI based Stroop task, a consensus was not reached (**Brown, 2011; Grinband et al., 2011a; Nachev, 2011**)  
83 and it did not have a widespread impact on how the Stroop task is modeled or interpreted in fMRI data. Of the 22  
84 papers published resulting from a PubMed search for "stroop task fmri 2021", only 4 addressed RT in their analyses  
85 and interpretation of their results.

86 It is beyond the scope of the present work to come to an agreement on how to interpret Stroop-based fMRI activation  
87 maps that may be driven by RTs, but we use this example to illustrate challenges of modeling RT-based effects in  
88 fMRI results and the important implications it can have on theoretical conclusions. If a model only evaluates condition  
89 differences, without adjusting for RTs, an observed condition effect has multiple potential interpretations, as the true  
90 effect could be: a simple condition difference in the amplitude of neuronal response (not driven by RTs), an RT effect  
91 with constant amplitude of the neuronal response (with no condition difference) or a relationship where there is both  
92 a condition difference and RT effect. If the result is driven by RTs the question remains as to whether it reflects time  
93 on task versus a difference in the amplitude of neuronal signaling. Therefore, our ability to interpret the finding of an  
94 unadjusted condition difference, without further analysis and theoretical work, is limited at best.

95 For clarity, we define some terms that will be used throughout this paper. Time series-level analysis refers to linear  
96 models of fMRI time series. A group-level analysis refers to an analysis of an estimated fMRI contrast across a set of

97 subjects that could be a single group average (1-sample t-test), group average comparisons (e.g., 2-sample t-test), linear  
98 associations with a covariate (e.g., phenotype) or other group-level models. Between-trial RT adjustment is formally  
99 carried out in the time series-level. Between-subject RT confounds will only impact group-level models involving group  
100 comparisons or associations but not single group averages. Although we focus on “2 stage” models, with only within-  
101 subject and group levels, these ideas extend to three stage models where subjects have multiple runs and so analyses  
102 are done within-run (time series analysis), within-subject (combining runs) and between-subject.

103 Limited focus has been given to the link connecting between-trial RT adjustment in the time series analysis to  
104 between-subject RT confounds in the group-level analysis. For example, if between-trial RT adjustment is ignored,  
105 the incongruent versus congruent Stroop contrast may be correlated with the within-subject difference in average RT  
106 between incongruent and congruent trials. In earlier work (*Carp et al., 2012*), this relationship was illustrated by show-  
107 ing that the correlation between age and the contrast estimate of incongruent versus congruent Stroop conditions  
108 changes based on whether between-trial RT adjustment is performed. Although this work points out the possibility of  
109 between-trial RT adjustment impacting between-subject analyses, the link has not been formally defined.

110 In the present work we extend and improve upon previous attempts to incorporate RT into in fMRI data analysis. We  
111 present a model that separates condition differences, adjusted for RTs, and RT-specific effects. This model is flexible,  
112 obviating the assumption in *Grinband et al. (2008)* that the duration of the neuronal signal necessarily matches the RTs.  
113 When the duration of the signal matches RTs, we refer to this type of BOLD signal as “scaling with RT”. The RT duration  
114 model can bias results when the underlying true signal duration is constant across trials (i.e., does not scale with RT),  
115 whereas the model presented here can adapt to either of these situations. We further quantify the bias in the *Grinband*  
116 *et al. (2008)* model as well as the most commonly used model that ignores RTs completely.

117 We also formally define the relationship between the between-trial RT adjustment, or lack thereof, and potential  
118 between-subject RT confounds. We will show that when between-trial RT adjustment is skipped, the effect size magni-  
119 tude of these potential between-subject RT confounds is on the order of common effects of interest, e.g., correlations  
120 with various behavioral phenotypes. An unexpected, but concerning result occurs if a variable (e.g., age) is associated  
121 with each condition, separately, but this variable is not associated with the condition difference. If RT is ignored in the  
122 time series analysis it can introduce both an RT effect and a false association with the variable (age in this example), and  
123 the only way to remedy this problem is to repeat the time series analysis with a model that adjusts for between-trial RT  
124 differences. This will be a barrier for some when using condition difference estimates supplied in databases for large  
125 neuroimaging studies, since RT adjustment in the times series model is typically skipped and redoing the time series  
126 analyses for thousands of subjects may not be possible for many users of these databases.

127 Finally we replicate and extend the findings of *Yarkoni et al. (2009)* by demonstrating that the widespread association  
128 between RT and fMRI activation is consistent over a set of 7 fMRI tasks, each with approximately 91 subjects.

129 The overarching goal of this work is to revive an interest and curiosity in understanding and addressing RT-correlated  
130 activation to improve our interpretation of fMRI signals and their relationship to underlying theories of RT-based tasks.  
131 The suggestions we present are easy to implement and enable the direct estimation of RT-based effects in parallel with  
132 condition differences, adjusted for RTs. This does not limit the researcher, but instead more clearly defines what is  
133 being studied, thus providing a cleaner link to underlying behavioral theory and improving the ability of fMRI to help  
134 understand brain function.

## 135 Results

### 136 Simulations

137 The statistical models used for fMRI data generally involve the convolution of a vector representing trial or stimulus  
 138 onsets with a canonical hemodynamic response function (as shown in Figure 1) to create regressors for use in linear  
 139 modeling (*Poldrack et al., 2009*). The trials can be represented either as delta functions or as boxcar functions with  
 140 some duration; when a boxcar is used, it is common to set the duration of the boxcar to a constant value such as  
 141 the duration of the stimulus, or to some brief default value (such as 0.1 second). In Figure 2 this model is referred to  
 142 as “Constant duration, no RT” (hereafter as ConstDurNoRT). Because of the indeterminacy described above (Figure 1),  
 143 the specific constant value used for stimulus duration will not generally impact the statistical inferences derived from  
 144 the model, as it will simply scale the values of the parameter estimates along with their variances (assuming the trial  
 145 durations are relatively short). This standard approach does not include any information about response times; thus,  
 146 if two conditions differ in their RTs when the true activation magnitude does not differ, the condition with the longer  
 147 RTs may have higher estimated activation if the signal scales with RT.

Model name		Unconvolved regressor	Duration	Modulation
1	Constant Duration, no RT (ConstDurNoRT)		.1s	None
			.1s	None
2	RT Duration (RTDur)		RT	None
			RT	None
3	Constant Duration, RT (ConstDurRT)		.1s	None
			.1s	None
			.1s	RT*

**Figure 2.** Models assessed in the simulation study described by name, unconvolved regressor visualization, duration used for boxcars of unconvolved regressors and definition of the modulation used, when present. Convolved regressors were used in data generation and modeling. The first model does not include any response time information, the second model addresses RT through the duration of the regressors and the third model adds an RT modulated regressor to the first model. \*See Discussion for details on why RT is not centered and other details about centering.

148 *Grinband et al. (2008)* developed a modeling approach to address the confounding effect of response times in fMRI  
 149 data, in which the duration of the boxcar function for each trial was varied by the response time on that trial (labeled  
 150 as “RT Duration” in Figure 2 and hereafter as RTDur). This approach will appropriately scale the parameter estimates  
 151 for regions in which neural activity duration matches the RT duration, which we will refer to as “the signal scales with  
 152 RT”. Technically, this model implies a restricted condition by RT interaction model, in that it is modeling a separate RT  
 153 slope, by condition, without main condition effects (i.e., constant duration regressors for each condition). Specifically,  
 154 the model implies each condition has a different linear relationship between BOLD activation and RT, but the intercepts  
 155 (BOLD activation when RT is 0) are both zero. Given this, the model has two shortcomings. First, it will not correctly

156 model activation in regions where neural activity does *not* scale with RTs but rather the true duration is an unknown  
157 constant across all trials. Second, it does not allow a separate identification of condition differences versus RT effects;  
158 instead, it only performs well if the restricted interaction model is correct.

159 To address these issues, we created a generalized model of RT that can identify RT effects separately from the task  
160 effect (corrected for RT); this is shown as “Constant Duration, RT” in Figure 2 and hereafter as ConstDurRT. This model  
161 includes a boxcar function with constant duration for each of the task conditions, along with a single regressor that  
162 models the parametric modulation of the response in relation to RT for each trial. Because all RTs are modeled within a  
163 single regressor, any differences in RT between conditions will be removed by this regressor, leaving the condition dif-  
164 ference effects to be interpreted as unconfounded estimates of activation in relation to the experimental manipulation.  
165 This model can be extended to a full interaction model, if an interaction is suspected, and this will be further described in  
166 the Discussion section (“Condition by RT interaction models”) as well as concerns in using an interaction model to study  
167 condition differences if there is not a significant interaction present. We focus on a simpler non-interaction scenario in  
168 the simulation studies to illustrate the results of interest and these results are nontrivial to extend to the interaction  
169 model setting.

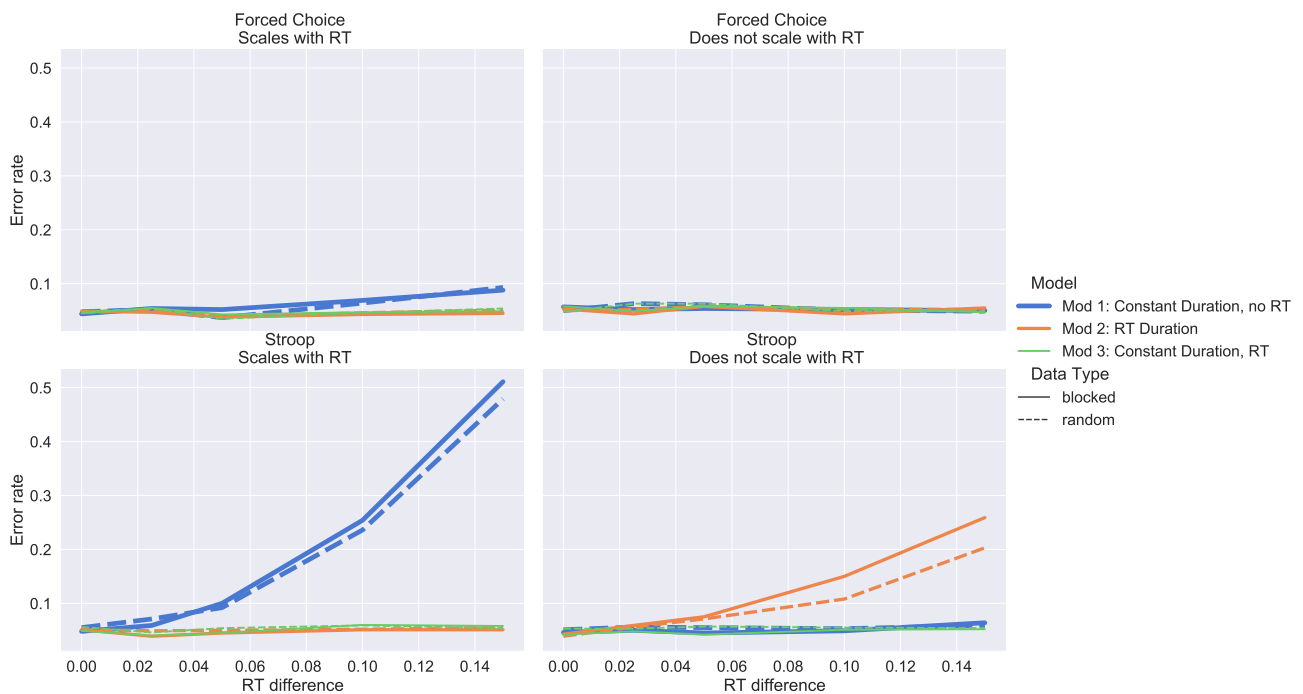
170 Notably we have not mean centered RT or subtracted any value from RT on each trial. This will not have any impact  
171 on the estimate of the contrast of interest (condition difference) and would only impact the condition versus baseline  
172 contrast estimate in this model. If RT is mean centered, within run, the interpretation of some contrasts becomes,  
173 “BOLD activation difference when RT is the mean RT for this run”, necessarily introducing an RT-based confound if this  
174 contrast is used as the dependent variable in higher level analyses. More details about the impact of centering RTs are  
175 included in the Discussion (“Should the RT modulation values be centered?”), including examples where it is necessary  
176 to center in some way and how to do so without introducing a new confound. We also discuss why an RT duration  
177 regressor is not used instead of the RT modulated regressor. For all models the effect of interest was the subtraction  
178 of condition 2 - condition 1, so the RT modulated regressor in ConstDurRT simply serves as a nuisance regressor to pick  
179 up RT variability, when present. Of course if there is interest in the RT effect, the parameter of the RT regressor can  
180 also be analyzed, although that is not the focus of the simulation analyses and will be the focus of the real data analysis.  
181 Further details regarding the modeling approach can be found in Methods; code and data for all analyses are shared  
182 at [https://github.com/jmumford/rt\\_simulations](https://github.com/jmumford/rt_simulations) (simulations) and [https://github.com/jmumford/rt\\_data\\_analysis](https://github.com/jmumford/rt_data_analysis) (real data  
183 analysis).

184 Response time data were simulated based on RTs from two different tasks: the Stroop task (based on real data  
185 analyzed below) and reported RT distribution parameters from a Forced Choice task used by *Grinband et al. (2008)*. In  
186 each case RTs were generated by sampling from an ex-Gaussian distribution (*Ratcliff and Murdock, 1976*); the specified  
187 ex-Gaussian parameters led to RTs that were generally longer for the Forced Choice task (mean = 1337, sd = 706.5)  
188 compared to the Stroop (mean = 690, sd = 177.5). Another difference is that the variance relative to the mean is smaller  
189 for the Stroop task (coefficient of variation of .528 and .257 for the Forced Choice and Stroop tasks, respectively). The  
190 interstimulus interval (ISI) was sampled from a Uniform distribution. Trials were either randomly presented conditions  
191 or blocked conditions, where 4 trials of the same condition were presented in a row. Time series data that scale with  
192 RT were based off of the RTDur regressors and data that did not scale with RT were generated using the ConstDurNoRT  
193 regressors.

194 All simulation-based results correspond to group level analyses with 100 subjects. See the Methods for further  
195 details on effect size and variance settings.

196 Error rates and power

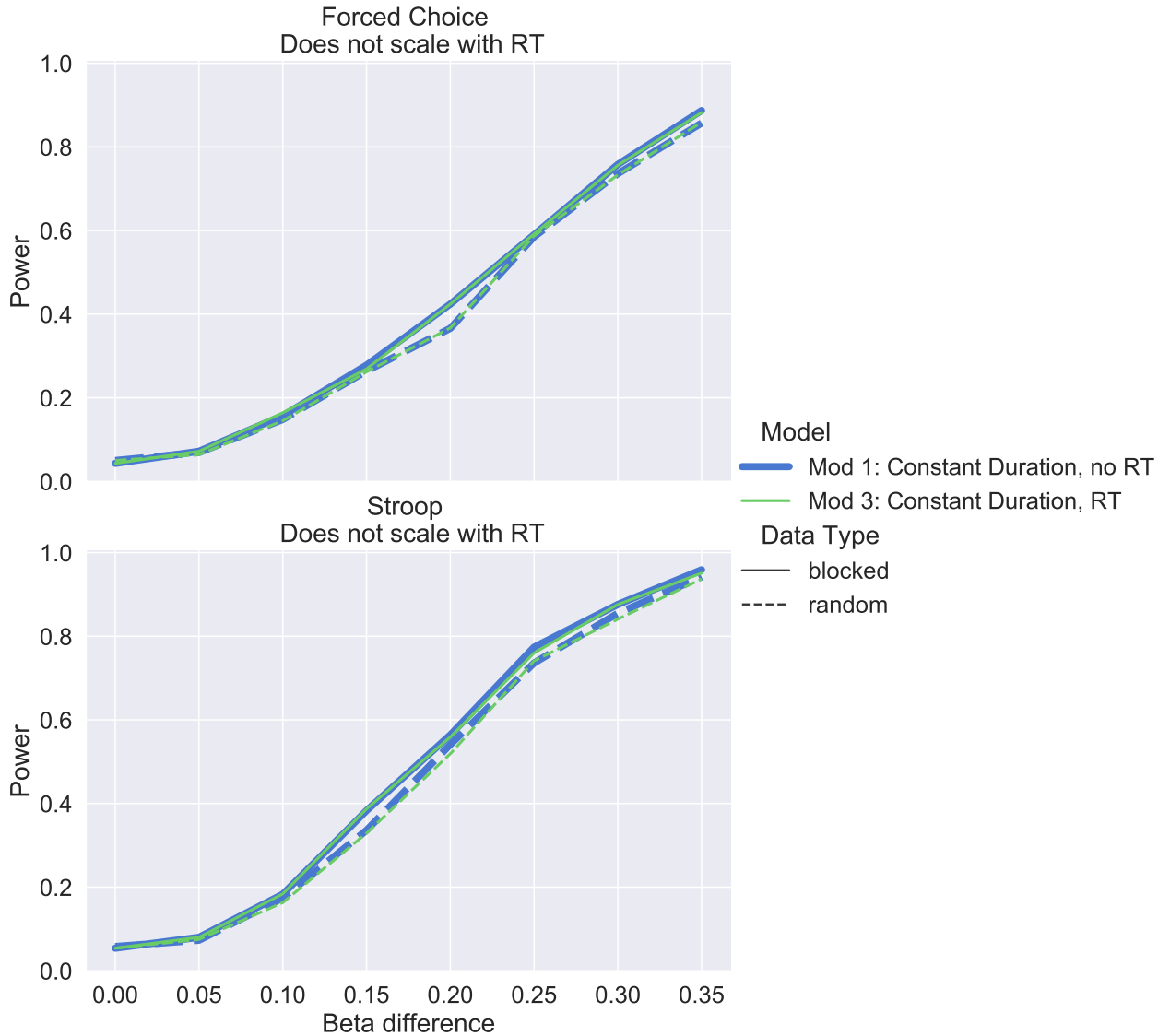
197 We first assessed the false positive rate for each of the models on each of the simulated data sets for the condition  
198 comparison contrast (Figures 3, S1). In all cases the ConstDurRT model appropriately controlled Type I error, but error  
199 rates were inflated when model assumptions regarding the relationship between RT and neural activity were violated  
200 by the data. Specifically, ConstDurNoRT had highly inflated error rates when activation did scale with RT, and RTDur had  
201 inflated error rates when the signal did not scale with RT. Thus, the most commonly used model for task fMRI analysis,  
202 ConstDurNoRT, suffers from substantial inflation of false positives in the face of RT differences between conditions,  
203 because it inaccurately attributes the confounding RT signal to differences in the intensity of the underlying neuronal  
204 signal. The larger Type I error rates observed with the Stroop-based RT reflects that the standard deviation of the RT,  
205 relative to the mean, was lower in this setting and so RT-based differences are easier to detect. The error rates for  
206 blocked designs (solid lines) are slightly higher, likely due to the fact that blocked designs have a higher signal to noise  
207 ratio, making it easier to detect RT differences in the data. Results with a longer ISI, between 3-6s, are similar (Results  
208 shown in Figure S1).



**Figure 3.** Type I error as RT difference between conditions increases. The Forced Choice Task RT distribution was used in the top panels, while Stroop RT distribution was used in the bottom panels, both with an ISI between 2-4s was used and inference of interest was the 1-sample t-test of the condition effect with 100 subjects. 2500 simulations were used to calculate the error rate.

209 When signal does not scale with RT, power can only be considered for the ConsDurNoRT and ConsDurRT models  
210 since the RTDur model did not have controlled error rates. Figure 4 shows that adding an RT-based regressor, when no  
211 RT effect is present, does not impact power at the group level. Thus the flexibility of the ConsDurRT model to adapt to  
212 either the scales with or doesn't scale with RT scenario does not result in a loss in power, which was previously implied  
213 in *Grinband et al. (2008)*, which only studied power at the single subject level for a condition versus baseline contrast  
214 and not the group level condition difference effect as done here. We do not study power in the context of when the  
215 signal scales with RT, since the signal generated by scaling each of the RTDur model regressors by different values

216 would represent an interaction model, where the linear relationship between RT and BOLD differs by condition. In  
217 this case the ConsDurRT model is clearly the incorrect model and power is irrelevant. The more suitable model would  
218 fit an interaction effect by replacing the single RT modulated regressor in the ConsDurRT model by condition-specific  
219 RT modulated regressors. Interaction models will be a topic in the Discussion section (“Condition by RT interaction  
220 models”).



**Figure 4.** Power when RT difference is 0.1s as the condition difference increases when signal does not scale with RT. The ConsDurRT model (green line) has similar power to the true model, ConsDurNoRT, illustrating no power loss occurs due to including an RT regressor in the time series analysis. Results for RTDur are not shown since it did not have controlled error rates. Sample size is 100, with an ISI between 2-4s.

## 221 RT differences can confound group-level analyses and introduce other false associations

222 The foregoing analyses, along with the previous work by Grinband, focused on confounding of RT between-trials, which  
223 impacts average condition effects. Here we introduce a new problem of a between-*subject* RT confound. The within-  
224 subject differences in average RT, corresponding to the contrasted conditions, can confound group level analyses in-



225 volving group comparisons or associations. For example, the incongruent versus congruent BOLD contrast estimate  
226 may correlate with the differences in average RTs for incongruent and congruent conditions. This is of particular inter-  
227 est given the increasing focus on analyses of brain-behavior correlations in fMRI literature (e.g., *Dubois and Adolphs*  
228 *(2016)*).

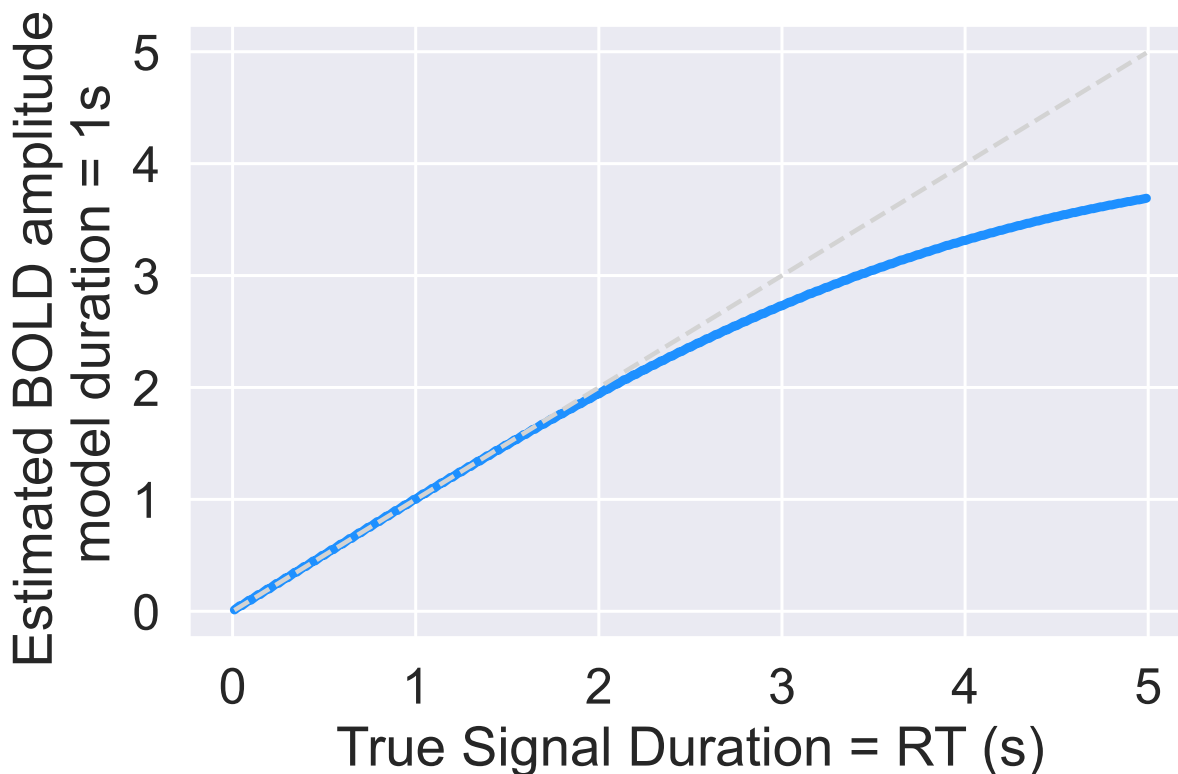
229 The driving factor of correlations between condition differences in brain activation and the corresponding differ-  
230 ences in RTs is simply due to a linear relationship between the activation estimate and RT when the data and model  
231 assumptions are in conflict. In the case where signals scales with RT and the ConstDurNoRT model is used (duration =  
232 1s), the relationship between the estimated activation,  $\hat{\beta}$ , and the true activation,  $B$ , is approximately  $\hat{\beta} = B \times RT$ , for  
233 a single trial. In this illustration, the true activation,  $B$ , is assumed to be the same for both conditions and does not  
234 vary over subjects. Figure 5 shows this linear relationship holds within the range of RTs one would expect to observe  
235 in most data sets (i.e.,  $< 2s$ ). Moving from the activation estimate of a single trial to the BOLD activation across multiple  
236 trials, the relationship becomes  $\hat{\beta} = B \times \overline{RT}$ , where  $\overline{RT}$  is the average RT across trials. Last, for two conditions, 1 and 2,  
237 the relationship for the contrast of conditions is

$$\hat{\beta}_1 - \hat{\beta}_2 = B \times (\overline{RT}_1 - \overline{RT}_2). \quad (1)$$

238 From this it directly follows that in a *group* level analysis there is an expected linear relationship between the estimated  
239 condition difference and the difference in RTs, specifically the between-subject slope would be  $B$ , the true, common  
240 activation of the two conditions that does not vary across subjects. As is the case with all linear trends (equivalently,  
241 correlations) this relationship does not require a non-zero RT difference on average, but is driven by between-subject  
242 RT variability. Therefore the RT difference is an important confound regardless of whether it is significantly different  
243 from 0 on average.

244 The simulation results in Figure 6 show the relationship across all models and data types considered in this work. The  
245 ConstDurNoRT model produces correlations between contrast differences and RT differences when the signal scales  
246 with RT, as does the RTDur model when the signal does not scale with RT while the ConstDurRT model does not induce  
247 correlations for either signal type. In other words, although there is no true relationship between average subject RT  
248 difference and the fMRI contrast estimate, the ways in which these models cannot capture RT (ConstDurNoRT) or intro-  
249 duce RT information (RTDur) cause an RT effect at the group level, which may interfere with the correct interpretation  
250 of group level results (e.g., if group level variable of interest is related to RT). Notably, the data were simulated such  
251 that the variance in RT did not change with RT, whereas in real data the variance of RT often increases with its mean.  
252 The implication is the correlation estimated by our simulations is conservative. Even so, it is within the ballpark of the  
253 expected true correlations between brain and behavior measures (*Marek et al., 2022*).

254 Importantly in this scenario, the linear relationship at the group level is simply,  $B$ , the common activation for both  
255 conditions and all subjects. If the activation differs between conditions or across subjects the confound will potentially  
256 be more complex in the between-subject analysis and can even introduce new artifactual associations into a group  
257 analysis. A simple extension to illustrate how false associations can be introduced is to only relax the assumption  
258 that  $B$  is the same across subjects, but preserve the assumption that  $B$  is the same for both conditions. For example,  
259 assume age is equally related to both conditions through the relationship,  $B = \gamma_0 + \gamma_1 age + \epsilon$  and note that this does not  
260 introduce an association of age with the true activation difference. If the signal scales with RTs and the ConstDurNoRT  
261 model is used to estimate the condition difference, not only is an RT effect introduced to the group level analysis, but  
262 an artifactual age effect is also introduced. This can be seen in the following derivation that extends the earlier defined  
263 relationship with the new definition of  $B$ :

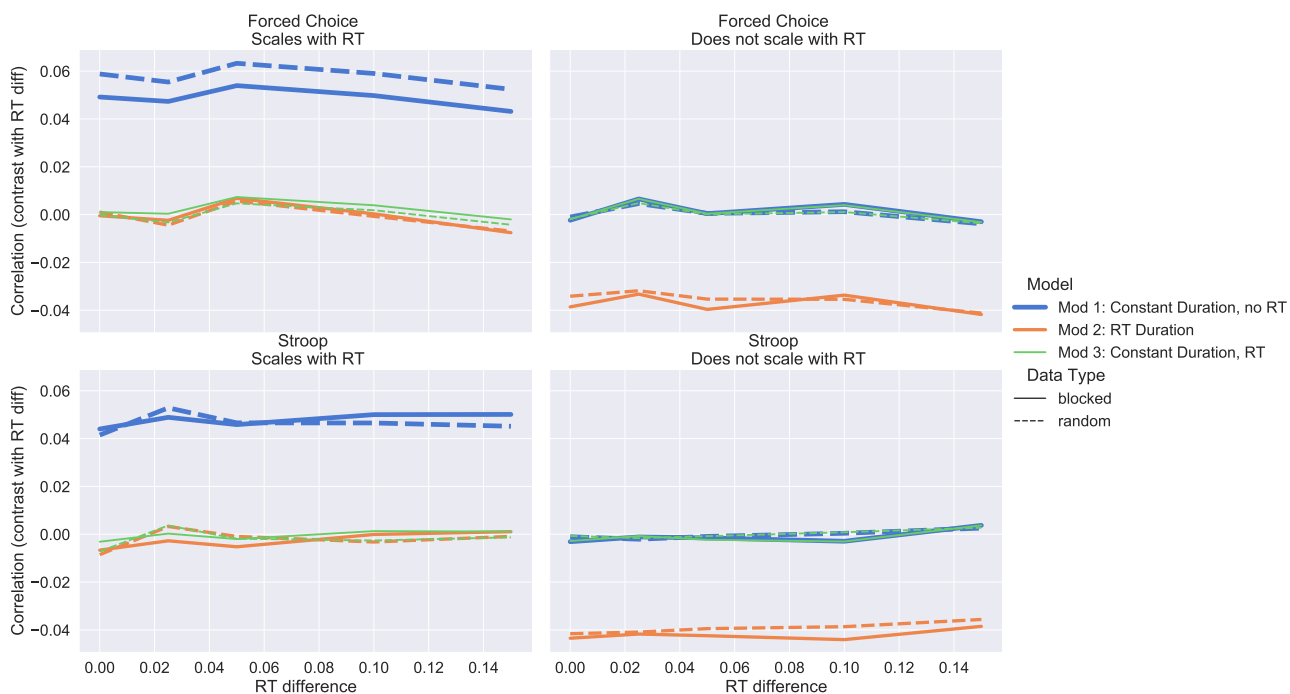


**Figure 5.** Relationship between trial RT and the trial-specific BOLD activation estimate when a constant duration of 1s regressor is assumed and signal scales with RT (blue). Gray dashed line is a line with a slope of 1 and intercept of 0. The true BOLD activation is 1, but the model estimates the BOLD activation to be  $1 \times RT$  for RTs < 2s.

$$\begin{aligned} \hat{\beta}_1 - \hat{\beta}_2 &= (\gamma_0 + \gamma_1 age) \times (\overline{RT}_1 - \overline{RT}_2) \\ &= \gamma_0 (\overline{RT}_1 - \overline{RT}_2) + \gamma_1 age (\overline{RT}_1 - \overline{RT}_2). \end{aligned} \quad (2)$$

264 This result is concerning because there is not a true relationship of the condition difference with either the RT  
 265 difference or age, but the use of ConsDurNoRT when the data scale with RT introduces an age association to the group  
 266 level analysis through an interaction with the RT difference. The implication is if the RT difference is nonzero, on average,  
 267 an age association will be present in the group level when there is not a relationship between age and the true activation  
 268 difference. Adding RT difference as a confound regressor to the group model will not remedy these issues and should  
 269 be avoided as it may inflate the significance of the false association with age. This calls into question the interpretation  
 270 of between-subject analyses where the signal may scale with RT and ConsDurNoRT is used.

271 The relationship between RT and potential variables of interest will be different and more complex if, say, the RT  
 272 difference is correlated with that variable or if there is a correlation between the true activation difference and the  
 273 variable of interest. Just as in the example above, it is clear that adding an RT confound regressor to the group level  
 274 model is not an adequate fix. The recommendation is to repeat the time series level analyses using ConsDurRT to  
 275 avoid these issues. This is unsettling news for those using fMRI activation databases, since the ConsDurNoRT model is  
 276 typically used to generate activation estimates.



**Figure 6.** Correlation between the contrast difference and difference in average condition RT across subjects as a function of the average difference in RT between conditions. Since the correlation is driven by between-subject variability in the *difference* in RT, there is no requirement that RTs differ between tasks and the correlation is constant regardless of the RT difference.

## 277 **Widespread RT activation is not specific to task, revisited**

278 Our real data analyses were modeled to include separate regressors for each condition as well as a single RT regressor  
279 to control for RT effects in our contrasts between conditions, similar to the ConsDurRT model. A total of 7 tasks,  
280 with sample sizes ranging from 86 to 94, were analyzed. The cognitive processes involved in these tasks include atten-  
281 tion, temporal discounting, proactive control, reactive control, response inhibition, resisting distraction, and set shifting.  
282 Brief descriptions are given in Table 1 and more detailed summaries are provided in the Methods section. Compara-  
283 tively, *Yarkoni et al. (2009)* used tasks including 3-back, decision making, emotion ratings and memory in sample sizes  
284 of 50, 102, 26, 35 and 39. Our seven tasks emphasize cognitive control to a greater extent and emotional processing  
285 and working memory to a lesser extent, compared to *Yarkoni et al. (2009)*. The focus here is on the average RT-related  
286 effect across subjects. Notably, this effect estimate will be slightly diminished from a full RT effect, since it is adjusted for  
287 condition difference and so the interpretation would be the average within-condition RT effect. Group statistics maps  
288 were thresholded using the TFCE p-value (from FSL Randomise) less than 0.05 with 5000 permutations. The conjunc-  
289 tion in Figure 7 shows voxels where the average RT-modulated effects were significant across all 7 tasks. Our maps are  
290 consistent with *Yarkoni et al. (2009)*, but with a more spatially widespread effects, which may reflect the fact that our  
291 sample sizes were larger. In particular, the present comparison demonstrated substantially more signal in the lateral  
292 superior parietal cortex.

## 293 **Discussion**

294 The problem of potential response time confounds for fMRI activation estimates has been discussed for more than a  
295 decade, but there has been little resulting change in how the community approaches the analysis and interpretation of  
296 fMRI contrasts when RT differences between task conditions are present. There are three takeaways from the present

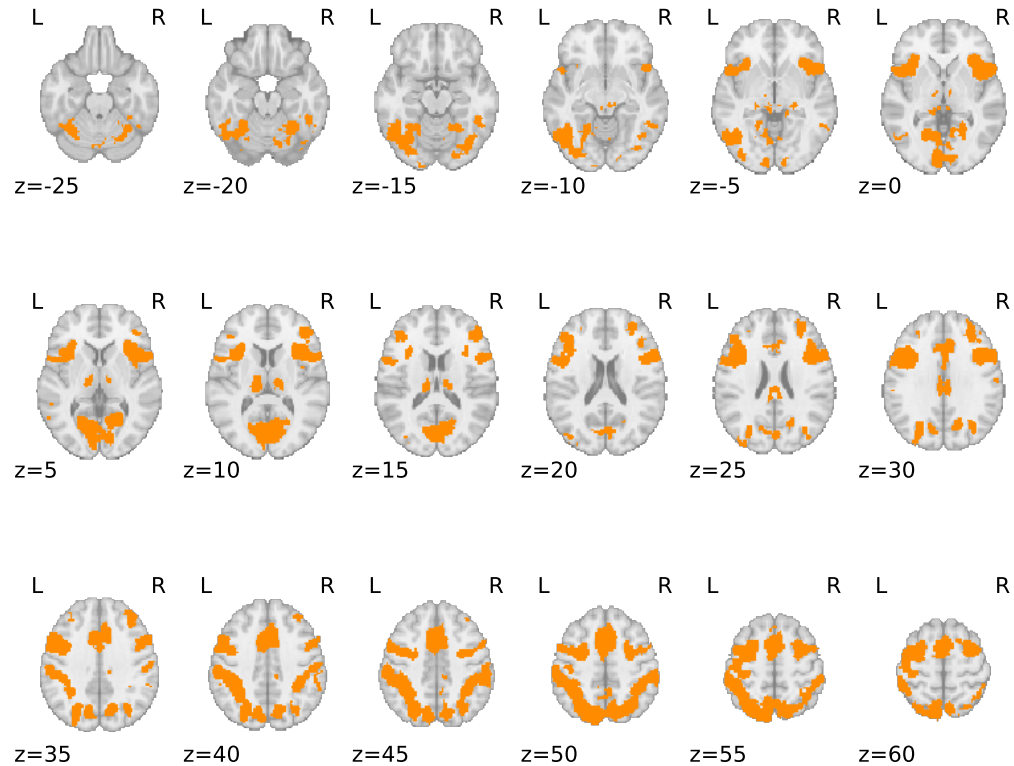
**Table 1.** fMRI task summaries

Name	Description	N
Attention Network Test (ANT)	Tests three aspects of attention or “attentional networks”: alerting, orienting, and executive control	91
Delay-Discounting Task (DDT)	Measure of temporal discounting, the tendency for people to prefer immediate monetary rewards over delayed rewards	86
Dot Pattern Expectancy (DPX)	Measure of individual differences in cognitive control including proactive and reactive control modes	91
Motor Selective Stop Signal	Measures the ability to engage response inhibition selectively to specific responses	91
Stop-Signal Task	Measure of response inhibition	91
Stroop	Measure of cognitive control perhaps including resisting distraction or attentional filtering	94
Cued Task-Switching Task (CTS)	Indexes the processes involved in reconfiguring the cognitive system to support a new task	94

297 work. First, we propose a modeling approach that more effectively adjusts within-subject contrast estimates for re-  
298 sponse time differences, so that group average estimates of contrasts are adjusted for between-condition response  
299 time differences. Importantly this model does not remove the ability to also study RT-specific effects, if they are of  
300 interest. Second, this work highlights an important problem that has not been discussed previously: the presence of a  
301 between-subject analysis confound of the average RT differences and the potential to introduce artificial associations  
302 with variables of interest at the group level. Finally, we replicate previous work showing that RT-related effects are not  
303 task specific (*Yarkoni et al., 2009*).

304 This work presents a model that can adapt to data whether or not the signal scales with RT, without losing perfor-  
305 mance. By adding an RT modulated regressor to the most commonly used model that only contains condition-specific  
306 regressors, the ConstDurRT model reduces RT-driven type I errors in average condition comparison effects without  
307 a reduction in power. The commonly used ConstDurNoRT model assumes the signal does not scale with RT and the  
308 RTDur model assumes the signal must scale with RT, hence both models fail to control error rates when these model  
309 assumptions are violated (Figure 3).

310 We have also uncovered that subject-specific differences in average RT represent an important group-level con-  
311 found. This confound is only present if the time series model follows the ConsDurNoRT or RTDur approaches, whereas  
312 the ConsDurRT model produces condition difference effects that are free of this confound. Notably, the average dif-  
313 ference in RT across subjects does not impact the strength of the correlation, since the correlation is driven by the  
314 variability in RT differences across subjects. Thus, even if the RT difference is 0, the first level models should include  
315 a between-trial RT adjustment. We have also shown that when the signal scales with RT and the ConsDurNoRT model  
316 is used, other false associations can be introduced at the group level. Specifically we have shown that when there is a  
317 common association between a variable of interest (e.g., age) and each condition, separately, but no association of this



**Figure 7.** Conjunction of the average, within-condition RT effect across ANT, DDT, DPX, motor selective stop, stop signal, stroop, and CTS. On average, each analysis included around 91 subjects and maps were corrected for multiple comparisons using a TFCE p-value thresholded at 0.05 using 5000 permutations.

318 variable with the true condition difference, the ConsDurNoRT condition difference estimates can have false associations  
319 with this variable. This is an especially concerning result for users of neuroimaging databases of condition difference  
320 estimates, since ConsDurNoRT is typically used.

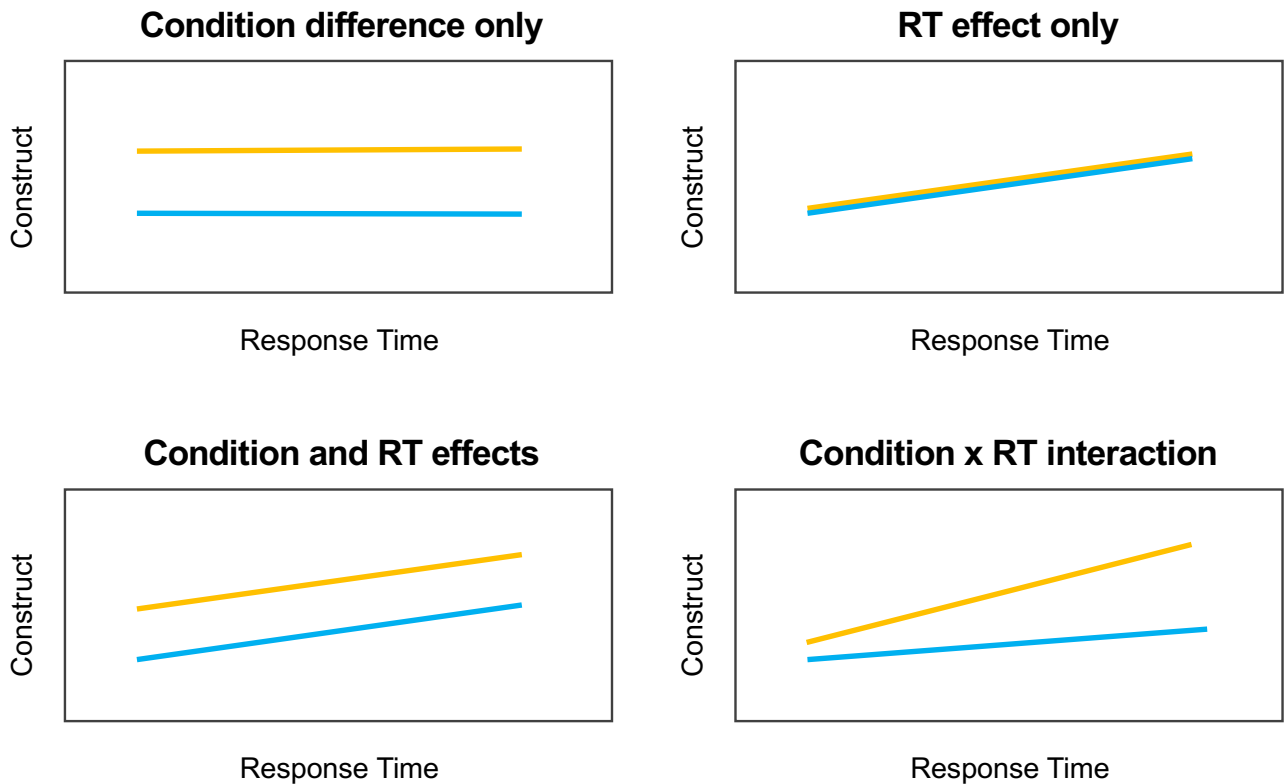
321 Last, our updated RT-effect conjunction analysis across 7 tasks tapping into different mental processes show widespread  
322 shared activation in the so-called “task-positive” network, replicating the previous results of *Yarkoni et al. (2009)*. This  
323 highlights the generality of the RT effect across tasks, and motivates the need to model these effects across all tasks.

### 324 **The paradox that RT is the effect of interest in fMRI studies**

325 Our recommendation here is to focus separately on RT-based effects and condition differences, adjusted for RT. There  
326 can be resistance to this idea, since RT is the measure of interest in behavioral studies and removing RT effects from  
327 condition differences is argued to be “throwing the baby out with the bathwater”. This argument is paradoxical since  
328 if RT effects are the effects of interest, then why not study the RT effects directly? Studying unadjusted condition  
329 differences does not directly reflect RT effects and may reflect differences that are completely unrelated to RTs. In fact

330 the condition difference effect, when unadjusted for RTs, may be driven by any of the underlying models shown in  
331 Figure 8 and this fact should be made clear when presenting any results focused on averages of condition differences  
332 estimated with the ConsDurNoRT model. If the RT based effect is the effect of interest, it should be studied directly using  
333 a model that mirrors the underlying theoretical model of RTs relationship with the construct of interest to maximize  
334 power. A significant finding of an RT-based effect is just the beginning and further work is necessary to establish whether  
335 the RT-based effect reflects time on task or an amplitude-driven effect, as was argued for the Stroop task by *Yeung*  
336 *et al. (2011)*. If this important extra work is not done, then conclusions for unadjusted RT effects must be presented  
337 acknowledging the limitations in their interpretation.

338 Overall our recommendation of focusing on RT-based effects and condition differences, adjusted for RTs, separating  
339 the two effects so they can be more accurately interpreted, ultimately improving our understanding of the brain.



**Figure 8.** The ConsDurNoRT model assumes the underlying relationship between the construct of interest follows the “Condition difference only” model. Since the condition difference model can yield significant results when *any* of these models is the true underlying model, only nonspecific interpretations can be made from the ConsDurNoRT model results. To strongly link brain activation to a specific construct of interest, the fMRI model should mirror the underlying behavioral theoretical model.

### 340 **Modeling considerations**

341 Should the RT modulation values be centered?

342 We did not center RT in our models, as it would not have any impact on the condition difference estimate since trials in  
343 both conditions involve RTs and the model implies the same condition difference effect occurs for all RTs. A common  
344 practice is to center by the mean RT for that subject and run of data, but this can introduce RT information into some  
345 contrast estimates. For example, if RT is centered, the interpretation of a condition versus baseline effect is specifically

**Table 2.** Whether or not centering of the RT modulated regressor is necessary when using ConsDurRT to study adjusted condition differences. When centering is required do not use the mean RT for the run, but use the same centering value for all subjects and runs to prevent incorporating an RT confound in between-subject analyses.

Contrast type	Example (stop signal task)	Interpretation without centering RT	RT centering necessary with ConsDurRT model?
Condition (RTs) vs. baseline	Go vs. baseline	Go activation when RT is 0	Yes
Condition (RTs) vs. Condition (no RTs)	Go vs. Successful Stop	Condition difference when Go RT is 0	Yes
Condition (RTs) vs. Condition (RTs)	Go vs. Unsuccessful Stop	Condition difference	No

346 for that subject/run's mean RT. In this case there is an RT confound introduced at the group level since each subject's  
347 activation reflects their own RT. The same will occur for any contrast where one condition involves RTs and another  
348 does not. For example, in the stop signal task the go trials have a response time whereas successful stop trials do not.  
349 Therefore if RT is centered within-subject and run, the go versus successful stop contrast estimate corresponds to the  
350 magnitude of the effect for mean RT of that subject/run, such that a correlation between this contrast and the average  
351 go RT will leak into the group level analysis. A summary of contrast types that are impacted by centering RT is given in  
352 Table 2.

353 To avoid this issue simply center by the same value for all subjects and runs. This value can either be the mean RT  
354 across *all* subjects and runs or a value that is roughly what one would expect the average RT to be for that task. In this  
355 case the RT confound at the group level should not be present. If all condition comparisons involve conditions with RT  
356 effects (as is most often the case for contrasts of interest in cognitive fMRI studies), then centering RT in the modulated  
357 regressor will have no effect on the contrast estimates of interest.

### 358 Why an RT modulation is used instead of RT duration

359 It may seem counterintuitive that we model RT through a parametrically modulated regressor in the ConsDurRT model,  
360 instead of a single RT duration style regressor. This is because the RT centering, described in the previous section, is a  
361 special type of orthogonalization that is not possible to carry out directly with the RT duration style regressors in most  
362 fMRI software packages in a straightforward way. Efforts to do so will typically reflect an unintended orthogonalization  
363 that removes condition difference information from the RT regressor, which should be avoided. Even if orthogonal-  
364 ization could be done properly, it will cause the condition-based activation to reflect subject-specific RT averages in  
365 the same way as mean centering was described to have issues in the previous section. Generally the RT modulated  
366 regressor is a very close approximation to the RT duration regressor, so it is an excellent substitute with more flexibility  
367 so we can properly adjust it to improve the interpretation of condition difference contrasts without introducing a new  
368 between-subject RT confound.

### 369 Avoiding common pitfalls when adding RT to a time series model

370 When adding RT to the time series model, there are some common mistakes that should be avoided. Most of the  
371 problem relates to the intuition that collinearity between regressors is problematic and thus that mean centering or

372 orthogonalization is always necessary. Once the data have been collected, collinearity with regressors of interest often  
373 cannot be resolved, but may have been preventable with a different study design. If the RT regressor is highly collinear  
374 with the task contrast, this should not be altered by orthogonalization or centering RT within task, as that is in conflict  
375 with the motivation for adding RT in the first place: controlling condition differences for RT differences or time on task  
376 effects. If RT is mean centered within-condition, then it is misleading and incorrect to claim the condition effects have  
377 been adjusted for RT differences. If RT is split into separate regressors by condition, this model implies an interaction  
378 effect between condition and task is suspected. In this case, if the interaction is significant, then that is the contrast to be  
379 studied in detail as it indicates the magnitude of the condition difference varies by RT. One should not use an interaction  
380 model to study main condition effects, even if the interaction is not found to be significant, which is discussed in the  
381 next section. Our recommendation is if there is not an expected interaction between different conditions and RT, then  
382 a single RT regressor should be used.

### 383 Condition by RT interaction models

384 If the underlying theory about the relationship between the psychological measure of interest and RT implies a condition  
385 by RT interaction, then an interaction model should be used in the fMRI analysis. Specifically the single RT regressor  
386 from ConsDurRT would be split by condition and no RT centering should be applied. In this case the effect of interest is  
387 the difference in the parameters corresponding to the RT modulated regressors for each condition. If the interaction  
388 is not found to be significant, we discourage using the interaction model to then study the main condition effects, as  
389 recommended in *Carp et al. (2010)*. Although finding the interaction is not significant means the estimated slopes  
390 between RT and BOLD activation are not statistically different between conditions, the estimated slopes will  
391 be different and this adds noise into the condition difference estimate, which reduces power. Instead, to study main  
392 condition differences when the interaction is not found to be significant, we recommend simplifying to the ConsDurRT  
393 model. A group level power analysis (Figure S2) indicates that the additional noise introduced when using the interaction  
394 model results in a loss in power as high as 9.5% compared to the ConsDurRT model (Figure S2). Of course, to avoid  
395 inflated error rates, p-value thresholds should use a correction for multiple comparisons (e.g., Bonferroni correction) to  
396 correct for testing both the interaction and then the main condition effect if the interaction is not found to be significant.

### 397 Limitations of this work

398 This work consists of real data analyses as well as simulated data analyses. Simulations are required in cases where  
399 we need to know the ground truth and link the theoretical problems with how these problems might surface in real  
400 data analyses (e.g., how strong the results are and whether they persist at the group level). As such, the simulations  
401 require specifying a large number of parameters including the RT distribution for each condition, effect size for each  
402 condition, stimulus length, ISI, within-subject variance and between-subject variance. We specifically focus on the RT  
403 distribution used in previous work (*Grinband et al., 2008*) to broaden those conclusions to more models and add an  
404 RT distribution based on our own Stroop data, which is quite different. In an effort to set the rest of the parameters to  
405 realistic values we focused on the size of the within-subject condition effect, aiming for correlations 0.07-0.08, ratio of  
406 total variance to within-subject variance,  $\frac{SD_{total}}{SD_{within}}$ , ranged between 2-3 and the Cohen's D for the average of task versus  
407 baseline across subjects was approximately 0.85. Higher between-subject variance (lower  $\frac{SD_{total}}{SD_{within}}$ ) would yield smaller  
408 time on task effects. Additionally we only shifted the mean parameters of the Exponential Gaussian distributions used  
409 to define the RT differences between conditions, whereas our analysis of our own Stroop data showed the variance in-  
410 creased with average within-subject RT. This was done intentionally to isolate how mean RT differences impact different



411 analyses while holding the RT variance constant. This increased variance in RT as RT increases would only strengthen  
 412 the between-subject correlation between the condition contrast and RT difference at the group level. Even though  
 413 these limitations exist, we believe our results to be accurate representations of the RT effect based on consistencies  
 414 with other studies focusing on the RT effect (*Yarkoni et al., 2009; Brown, 2011; Grinband et al., 2011b*).

## 415 Methods

### 416 Models considered

#### 417 Data generation and modeling

418 The interstimulus interval (ISI) was sampled from a Uniform distribution and RT was sampled from an ex-Gaussian  
 419 distribution. For RT, a subject specific  $\mu_{sub}$  was obtained by sampling an ex-Gaussian with parameters  $\mu_{rt}$ ,  $\sigma_{rt}$  and  $1/\lambda_{rt}$  and  
 420 subtracting the sampled value by  $1/\lambda_{rt}$ . The subject-specific RTs were then sampled from an ex-Gaussian distribution  
 421 with  $\mu_{sub}$ ,  $\sigma_{rt}$  and  $1/\lambda_{rt}$ . When RT differed between conditions, each Condition 1's RT mean was  $\mu_{sub} - \Delta RT/2$  and Condition  
 422 2's was  $\mu_{sub} + \Delta RT/2$ , where  $\Delta RT$  was the RT difference. Values of  $\mu_{rt}$ ,  $\sigma_{rt}$  and  $\lambda_{rt}$  were based on our Stroop data and  
 423 the Forced Choice Task in *Grinband et al. (2008)*. In both cases distributions were fit to subject-specific data and then  
 424 parameters were averaged over subjects. The Forced Choice RT distribution was defined by a Gamma distribution with  
 425 shape parameter = 1.7, beta = 0.49. Sampling from this distribution and fitting an ex-Gaussian to that sample resulted  
 426 in ex-Gaussian parameters of  $\mu_{rt} = 638$ ,  $\sigma_{rt} = 103$ , and  $1/\lambda_{rt} = 699$  (mean = 1337, sd = 706.5). The Stroop data had faster  
 427 RTs with less variability, with ex-Gaussian parameters of  $\mu_{rt} = 530$ ,  $\sigma_{rt} = 77$ , and  $1/\lambda_{rt} = 160$  (mean = 690, sd = 177.5). The  
 428 distribution functions from Python's Scipy module were used to simulate and estimate the distribution parameters.  
 429 Trials were either randomly presented conditions or blocked conditions, where 4 trials of the same condition were  
 430 presented in a row.

431 Simulated data that scaled with RT were created with the convolved RT duration regressors (RTDur) and data that did  
 432 not scale with RT used the constant duration regressors (ConsDurNoRT). The BOLD activation sizes for the  $i^{th}$  subject  
 433 for each condition,  $\beta_{i,1}$  and  $\beta_{i,2}$ , were sampled from a Gaussian distribution,  $N(\beta, \sigma_b^2)$ , where  $\beta$  is the true activation  
 434 magnitude and  $\sigma_b^2$  is the between-subject variance. The time series data for the  $i^{th}$  subject, of length  $T$ , was created  
 435 according to

$$435 \mathbf{Y}_i = \mathbf{X}_1\beta_{i,1} + \mathbf{X}_2\beta_{i,2} + \epsilon, \quad \epsilon \sim N(0, \sigma_w^2), \quad (3)$$

436 where  $\mathbf{X}_1$  and  $\mathbf{X}_2$  are either the Model 1 or 2 regressors ( $T \times 1$ ) and  $\sigma_w^2$  is the within-subject variance.

437 In an effort to choose realistic values for  $\beta_1$ ,  $\beta_2$ ,  $\sigma_w^2$  and  $\sigma_b^2$ , we considered the first level effect size (converting the true  
 438  $\beta_i$  to a correlation), second level effect size for a 1-sample t-test (Cohen's D) as well as the ratio of the total mixed effects  
 439 variance to the within-subject variance. Following the definitions of parameters as given in the model above, the total  
 440 mixed effects variance for a first level contrast of parameter estimates is

$$440 \sigma_{mfx}^2 = \mathbf{c}(\mathbf{X}'\mathbf{X})^{-1}\mathbf{c}'\sigma_w^2 + \mathbf{c}\mathbf{c}'\sigma_b^2, \quad (4)$$

441 where  $\mathbf{X}$  and  $\mathbf{c}$  are the first level design matrix (based on models in Figure 2) and contrast of interest (*Mumford and*  
 442 *Nichols, 2006*). The contrast of interest for each model corresponded to condition 2 > condition 1 ( $\mathbf{c} = [-1, 1]$ ) for the 2  
 443 regressor models and  $\mathbf{c} = [-1, 1, 0]$  for the three regressor model). The ratio of total standard deviation (SD) to within-  
 444 subject SD is defined by

$$444 \frac{SD_{total}}{SD_{within}} = \frac{\sqrt{\mathbf{c}(\mathbf{X}'\mathbf{X})^{-1}\mathbf{c}'\sigma_w^2 + \mathbf{c}\mathbf{c}'\sigma_b^2}}{\sqrt{\mathbf{c}(\mathbf{X}'\mathbf{X})^{-1}\mathbf{c}'\sigma_w^2}}, \quad (5)$$

445 Our within-subject effect size for condition versus baseline was between 0.07-0.08 (correlation), ratio of total vari-  
446 ance to within-subject variance,  $\frac{SD_{total}}{SD_{within}}$ , ranged between 2-3 and the Cohen's D for the average of task versus baseline  
447 across subjects was approximately 0.85.

448 Each run contained 40 trials of each condition and a time resolution (TR) of 1s. Time course length varied, as it was  
449 set to extend 50s past the last stimulus offset. Group analyses included 100 subjects. A total of 1000 data sets were  
450 simulated to calculate power and error rates.

451 Regressors were constructed by convolving boxcar functions with a Double Gamma hemodynamic response func-  
452 tion (HRF) using the `compute_regressor` function from the Nilearn module in Python.

453 Least squares regression was used to estimate the models described in Figure 2 at the first level including a set of  
454 cosine basis functions (0.1 Hz cutoff) for high-pass filtering generated with the `cosine_drift` function from Nilearn in  
455 Python. At the group level, 1-sample t-tests were used to assess type I error and power. A correlation of the average  
456 difference in RT between conditions and the fMRI contrast (condition 2 vs condition 1) was estimated for each group  
457 analysis.

458 Since RT and ISI values are random, the contribution of the design matrix,  $X$ , to the overall variance varies between  
459 samples (Equation 4) and the true effect size was variable. Therefore, to calculate the first level true effect size 100 data  
460 sets were simulated and the partial correlation coefficient for one condition, controlling for the other condition and  
461 cosine basis set, was estimated and then averaged over the 100 data sets to serve as the true within-subject effect. The  
462 variance ratio,  $SD_{total}/SD_{within}$ , was estimated by simulating 100 design matrices. Cohen's D estimates were based on  
463 5000 simulated within-subject model estimates for the task versus baseline contrast.

#### 464 Real data analysis

465 A total of 110 subjects completed each of the following fMRI tasks: Stroop (**Stroop, 1935**), Attention Network Test (ANT,  
466 **Fan et al. (2002)**), Dot Pattern Expectancy task (DPX, **MacDonald et al. (2005)**), Delayed-Discounting task (DDT, **Kirby**  
467 **(2009)**), cued task-switching task (CTS, **Logan and Bundesen (2003)**), stop signal task (**Logan and Cowan, 1984**) and a  
468 motor selective stop signal task (**Dejong et al., 1995**). Brief summaries are provided in Table 1 and more detailed  
469 descriptions are provided in the Supplementary materials. Data were acquired using single-echo multi-band EPI. The  
470 following parameters were used for data acquisition: TR = 680ms, multiband factor = 8, echo time = 30 ms, flip angle =  
471 53 degrees, field of view = 220 mm,  $2.2 \times 2.2 \times 2.2$  isotropic voxels with 64 slices.

472 Data were preprocessed in Python using fmriprep 20.2.0 (**Esteban et al., 2019**). First, a reference volume and its skull-  
473 stripped version were generated using a custom methodology of fMRIPrep. A B0-nonuniformity map (or fieldmap) was  
474 directly measured with an MRI scheme designed with that purpose (typically, a spiral pulse sequence). The fieldmap was  
475 then co-registered to the target EPI (echo-planar imaging) reference run and converted to a displacements field map  
476 (amenable to registration tools such as ANTs) with FSL's `fugue` and other SDCflows tools. Based on the estimated suscep-  
477 tibility distortion, a corrected EPI (echo-planar imaging) reference was calculated for a more accurate co-registration  
478 with the anatomical reference. The BOLD reference was then co-registered to the T1w reference using `bbregister`  
479 (FreeSurfer) which implements boundary-based registration (**Greve and Fischl, 2009**). Co-registration was configured  
480 with six degrees of freedom. Head-motion parameters with respect to the BOLD reference (transformation matrices,  
481 and six corresponding rotation and translation parameters) are estimated before any spatiotemporal filtering using  
482 `mcflirt` (FSL 5.0.9, **Jenkinson et al. (2002)**). BOLD runs were slice-time corrected using `3dTshift` from AFNI 20160207 (**Cox**  
483 **and S (1997)**, RRID:SCR\_005927). The BOLD time-series (including slice-timing correction when applied) were resampled  
484 onto their original, native space by applying a single, composite transform to correct for head-motion and susceptibility

485 distortions. These resampled BOLD time-series will be referred to as preprocessed BOLD in original space, or just pre-  
486 processed BOLD. The BOLD time-series were resampled into standard space, generating a preprocessed BOLD run in  
487 MNI152Nlin2009cAsym space. First, a reference volume and its skull-stripped version were generated using a custom  
488 methodology of fmripRep. Automatic removal of motion artifacts using independent component analysis (ICA-AROMA,  
489 *Pruim et al. (2015)*) was performed on the preprocessed BOLD on MNI space time-series after removal of non-steady  
490 state volumes and spatial smoothing with an isotropic, Gaussian kernel of 6mm FWHM (full-width half-maximum). Cor-  
491 responding “non-aggressively” denoised runs were produced after such smoothing. These data were used in our time  
492 series analysis models.

493 Data were analyzed using `FirstLevelModel` from `nilearn` in Python (*Abraham et al., 2014*). A double gamma HRF  
494 was used for convolution and an AR(1) model addressed temporal auto correlation. Regressors were included for each  
495 condition, versus baseline, as well as a single RT modulated regressor, similar to the simulation analysis model Cons-  
496 DurRT. The RT modulated regressor included the uncentered RT values. The contrast of the RT modulated regressor  
497 was the contrast of interest in our models and represents the average relationship between BOLD activation and RT  
498 within condition, since condition specific regressors were also included. Nuisance regressors in the time series analysis  
499 included the following from the `fmripRep` output: cosine basis functions (corresponding to a highpass filter cutoff of  
500 128s) and the average time courses for the CSF and WM as estimated by `fmripRep`.

501 Subjects were excluded within-task for the following general reasons: missing 1 or more files required to analyze the  
502 data, having more than 20% high motion time points (measured by Framewise Displacement > .5 or SD of DVARS > 1.2),  
503 having more than 45% missing responses, a subjective poor performance rating assessing high choice and/or omission  
504 error rates in at least one condition of the task, and when subjects omitted most of their responses towards the end  
505 of the task scan. Specific exclusion for the stop signal tasks are less than 25% successes for stop trials or more than  
506 a 75% successful stop rate. For the Delay-Discounting tasks, subjects were excluded if they made the same choice on  
507 all trials. Last, if there were exclusions on more than half the tasks for a subject, that subject was completely excluded.  
508 For Stroop 9 subjects had missing data files, 1 subject had more than 45% missing responses, 2 subjects had >20% high  
509 motion volumes, 1 subject had exclusions on more than half the tasks, 1 subject had exclusions

510 Group models were estimated using `Randomise` (*Smith and Nichols, 2009*) and included either a single column  
511 of 1s (group mean) or a column of 1s along with the difference in mean RTs. Statistics maps were thresholded, con-  
512 trolling for family-wise error rate, using the `Randomise` TFCE statistic below 0.05, based on 5000 permutations. Two  
513 sided hypotheses were studied using an F-contrast. A conjunction map was constructed by taking the overlap of the  
514 thresholded, binarized map for each of the 7 tasks (*Nichols et al., 2005*).

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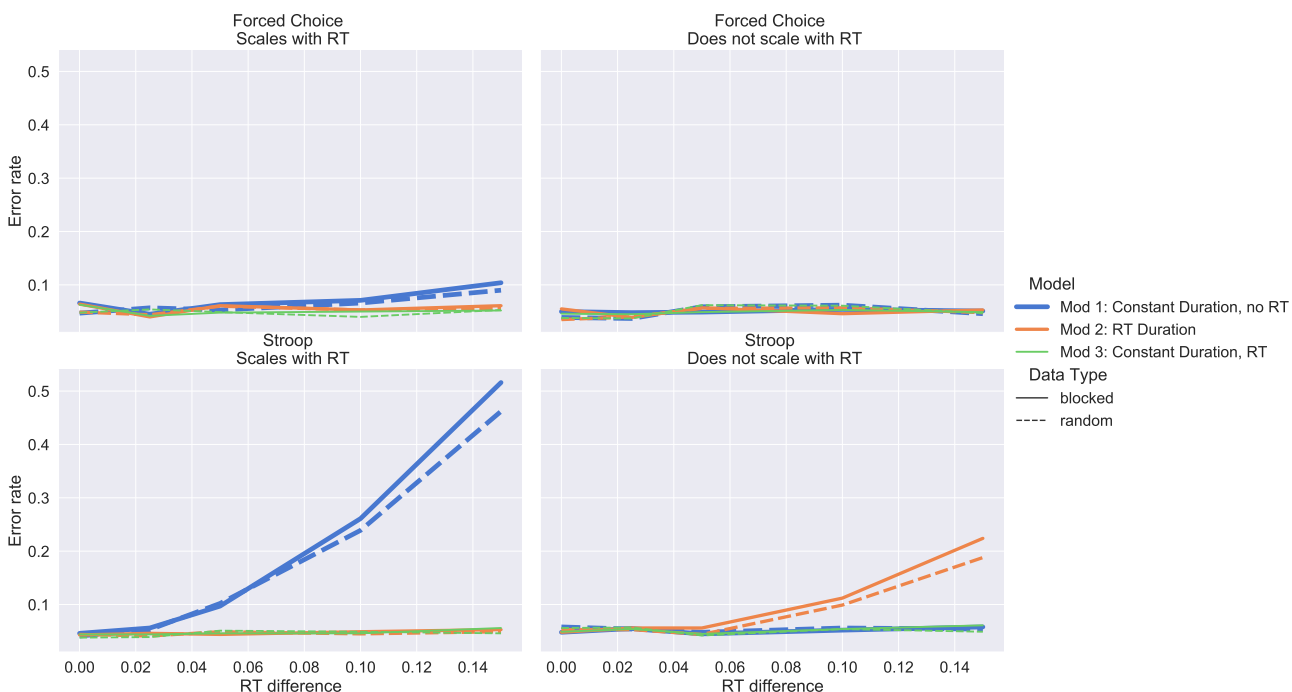
601

## Supplement

602

### The response time paradox in functional magnetic resonance imaging analyses

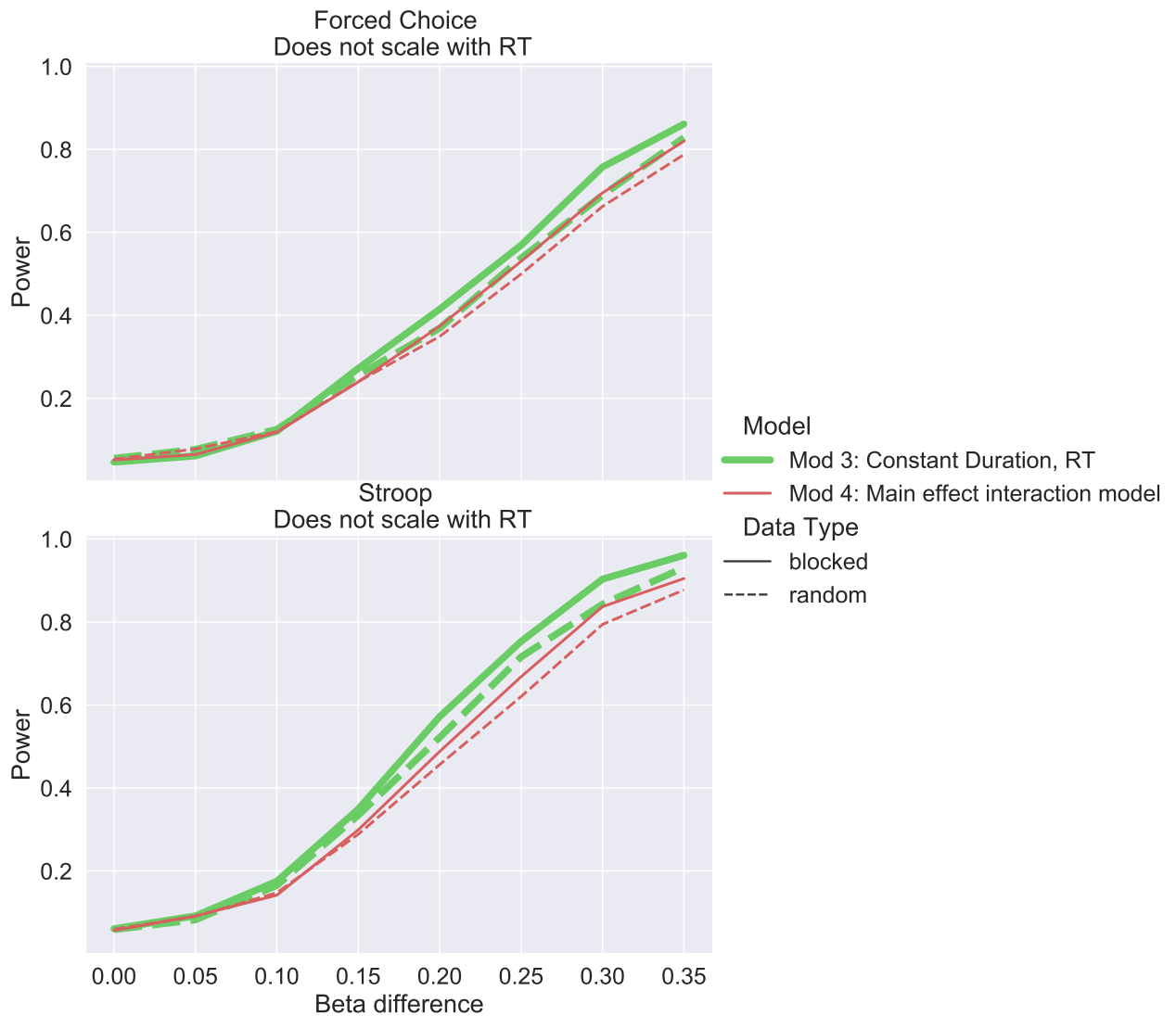
#### 603 Error rate when ISI ranges between 3-6s



**Figure S1.** Type I error as RT difference between conditions increases. This illustrates that results are similar to when the ISI ranged between 2-4s (result in main manuscript). The Forced Choice Task RT distribution was used in the top panels, while Stroop RT distribution was used in the bottom panels, both with an ISI between 3-6s was used and inference of interest was the 1-sample t-test of the condition effect with 100 subjects. 2500 simulations were used to calculate the error rate.

#### 604 Power differences when studying condition differences after testing for interaction

605 Here we study the power for a condition effect after testing for a potential condition by RT interaction. The interaction  
606 model contained two condition regressors and two RT regressors, split by condition. RTs were centered by the theoret-  
607 ical RT based on the distribution used to simulate RTs. Although the slopes of the interaction model were not found to  
608 significantly differ, their magnitudes will not be exactly equal and this introduces variance into the condition difference  
609 estimate from this model. This is reflected in the reduced power compared to the ConsDurRT model (Figure S2).



**Figure S2.** Power for testing main condition difference effect after an interaction was found to be not significant. Power is lost if the main effect of condition is studied in the interaction model, directly, due to the estimated sloped not being equal, which introduces variability into the estimate. Power is improved if the condition difference is then studied using the ConsDurRT model. Note, the p-value cutoff for testing the interaction and main effect of condition were set to .025 to preserve the overall error rate at 5%.

## 610 Details about tasks involved in real data analysis

611 The Attention Network Test (ANT) is a task designed to test three attentional networks: (1) alerting, (2) orienting, and  
612 (3) executive control. The ANT combines attentional and spatial cues with a flanker task (a central imperative stimulus  
613 is flanked by distractors that can indicate the same or opposite response to the imperative stimulus). On each trial a  
614 spatial cue is presented, followed by an array of five arrows presented at either the top or the bottom of the computer  
615 screen. The subject must indicate the direction of the central arrow in the array of five. The cue that precedes the  
616 arrows can be non-existent, a center cue, a double cue (one presented at each of the two possible target locations), or  
617 a spatial cue that deterministically indicates the upcoming target location. Each network is assessed via reaction times  
618 (RTs). The alerting network contrasts performance with and without cues, the orienting network contrasts performance  
619 on the task with or without a reliable spatial cue, and executive control (conflict) is measured by assessing interference

620 from flankers.

621 The Dot Pattern Expectancy (DPX) task measures individual differences in cognitive control. Participants are pre-  
622 sented with a cue made up of dots. This cue can be a valid cue – referred to as A (e.g., ":") – or an invalid cue – referred  
623 to as B (e.g., ".."). Next a probe is presented, also made up of a simple dot formation. This probe can be valid (X) or  
624 invalid (Y). Participants are instructed to respond to valid probe and cue combinations (targets – AX combinations) with  
625 a key press (e.g., "x") and all others (non-targets) with a different key press (e.g., "m").

626 The Delay-Discounting Task (DDT) is a measure of temporal discounting, the tendency for people to prefer smaller,  
627 immediate monetary rewards over larger, delayed rewards. Participants complete a series of 27 questions that each  
628 require choosing between a smaller, immediate reward (e.g., \$25 today) versus a larger, later reward (e.g., \$35 in 25  
629 days). The 27 items are divided into three groups according to the size of the larger amount (small, medium, or large).  
630 Modeling techniques are used to fit the function that relates time to discounting. The main dependent measure of  
631 interest is the steepness of the discounting curve such that a more steeply declining curve represents a tendency to  
632 devalue rewards as they become more temporally remote.

633 The cued task-switching task indexes the control processes involved in reconfiguring the cognitive system to support  
634 a new stimulus-response mapping. In this task, subjects are presented with a task cue followed by a colored number  
635 (between 1-4 or 6-9). The cue indicates whether to respond based on parity (odd/even), magnitude (greater/less than  
636 5), or color (orange/blue). Trials can present the same cue and task, or can switch the cue or the task. Responses are  
637 slower and less accurate when the cue or task differs across trials (i.e., a switch) compared to when the current cue or  
638 task remains the same (i.e., a repeat).

639 The Stop-Signal Task is designed to measure motor response inhibition, one aspect of cognitive control. On each trial  
640 of this task participants are instructed to make a speeded response to an imperative "go" stimulus except on a subset  
641 of trials when an additional "stop signal" occurs, in which case participants are instructed that they should make no  
642 response. The Independent Race Model describes performance in the Stop-Signal Task as a race between a go process  
643 that begins when the go stimulus occurs and a stop process that begins when the stop signal occurs. According to this  
644 model, whichever independent process reaches completion first determines the resulting behavior; earlier completion  
645 of the go process results in an overt response (i.e., stop-failure), whereas earlier completion of the stop process results  
646 in successful inhibition. The main dependent measure, stop-signal reaction time (SSRT), can be computed such that  
647 lower SSRT indicates greater response inhibition. One variant of the task measures proactive slowing, the tendency  
648 for participants to respond more slowly in anticipation of a potential stopping signal. This variant often uses multiple  
649 probabilities of a stop signal (e.g., 20% and 40%) to manipulate participants' expectancies about the likelihood of a stop  
650 signal occurring. The extent of slowing in the higher compared to the lower stop probability conditions is an index of  
651 proactive slowing/control.

652 The motor selective stop-signal task measures the ability to engage response inhibition selectively to specific re-  
653 sponses. In this task, cues are presented to elicit motor responses (e.g., right hand responses, left hand responses).  
654 A stop-signal is presented on some trials, and subjects must stop if certain responses are required on that trial (e.g.,  
655 right hand responses) but not others (e.g., left hand responses) if a signal occurs. In contrast to a simple stop-signal  
656 task in which all actions are stopped when a stop-signal is presented, this task aims to be more like stopping in "the  
657 real world" in that certain motor actions must be stopped (e.g., stop pressing the accelerator at a red light) but others  
658 should proceed (e.g., steering the car and/or conversing with a passenger). Commonly, stop-signal reaction time (SSRT),  
659 the main dependent measure for response inhibition in stopping tasks, is prolonged in the motor selective stopping  
660 task when compared to the more canonical simple stopping task. This prolongation of SSRT is taken as evidence of the



661 cost of engaging inhibition that is selective to specific effectors or responses.

662 The Stroop task is a seminal measure of cognitive control. Successful performance of the task requires the ability  
663 to overcome automatic tendencies to respond in accordance with current goals. On each trial of the task, a color word  
664 (e.g., “red”, “blue”) is presented in one of multiple ink colors (e.g., blue, red). Participants are instructed to respond  
665 based upon the ink color of the word, not the identity of the word itself. When the color and the word are congruent  
666 (e.g., “red” in red ink), the natural tendency to read the word facilitates performance, resulting in fast and accurate  
667 responding. When the color and the word are incongruent (e.g., “red” in blue ink), the strong, natural tendency to read  
668 must be overcome to respond to the ink color. The main dependent measure in the Stroop task is the “Stroop Effect”,  
669 which is the degree of slowing and the reduction in accuracy for incongruent relative to congruent trials.

670 **Exclusion information by task for real data analysis**

**Table S1.** Exclusion information for Attention Network task.

<b>Incomplete data</b>	<b>Subject omitted (issues with behav. &gt; 50% of tasks)</b>	<b>High motion &gt;20% total volumes</b>	<b>No response on &gt;45% of trials</b>	<b>Stopped performing task at end of scan</b>	<b>Poor performance (subjective)</b>
1	1	0	0	0	0
1	1	0	0	0	0
1	1	0	0	0	0
1	1	0	0	0	0
1	0	0	0	0	0
1	0	0	0	0	0
1	0	0	0	0	0
1	0	0	0	0	0
0	1	0	0	0	1
0	1	0	0	0	0
0	1	0	0	0	0
0	1	0	0	0	0
0	1	0	0	0	0
0	1	0	0	0	0
0	1	0	0	0	0
0	1	0	0	0	0
0	0	1	0	0	0
0	0	1	0	0	0
0	0	1	1	0	0

**Table S2.** Exclusion information for Delay-Discount task.

<b>Incomplete data</b>	<b>Subject omitted (issues with behav. &gt; 50% of tasks)</b>	<b>High motion &gt;20% total volumes</b>	<b>No response on &gt;45% of trials</b>	<b>Stopped performing task at end of scan</b>	<b>Poor performance (subjective)</b>	<b>Made same choice on all trials</b>
1	1	0	0	0	0	0
1	1	0	0	0	0	0
1	1	0	0	0	0	0
1	1	0	0	0	0	0
1	1	0	0	0	0	0
1	1	0	0	0	0	0
1	1	0	0	0	0	0
1	1	0	0	0	0	0
1	0	0	0	0	0	0
1	0	0	0	0	0	0
1	0	0	0	0	0	0
1	0	0	0	0	0	0
0	1	0	1	0	0	0
0	1	0	0	0	0	0
0	1	0	0	0	0	0
0	1	0	0	0	0	0
0	0	0	0	0	0	1
0	0	0	0	0	0	1
0	0	0	0	0	0	1
0	0	0	0	0	0	1
0	0	0	0	0	0	1
0	0	0	0	0	0	1
0	0	0	0	0	0	1
0	0	0	0	0	0	1
0	0	0	0	0	0	1
0	0	0	0	0	0	1

**Table S3.** Exclusion information for Dot Pattern Expectancy task.

<b>Incomplete data</b>	<b>Subject omitted (issues with behav. &gt; 50% of tasks)</b>	<b>High motion &gt;20% total volumes</b>	<b>No response on &gt;45% of trials</b>	<b>Stopped performing task at end of scan</b>	<b>Poor performance (subjective)</b>
1	1	0	0	0	0
1	1	0	0	0	0
1	1	0	0	0	0
1	1	0	0	0	0
1	1	0	0	0	0
1	1	0	0	0	0
1	1	0	0	0	0
1	1	0	0	0	0
1	0	0	0	0	0
0	1	0	0	0	1
0	1	0	0	0	1
0	1	0	0	0	0
0	1	0	0	0	0
0	0	1	0	0	0
0	0	1	0	0	0
0	0	1	0	0	0
0	0	0	0	1	0
0	0	0	0	0	1
0	0	0	0	0	1

**Table S4.** Exclusion information for Motor Selective Stop Signal task.

<b>Incomplete data</b>	<b>Subject omitted (issues with behav. &gt; 50% of tasks)</b>	<b>High motion &gt;20% total volumes</b>	<b>No response on &gt;45% of trials</b>	<b>Stopped performing task at end of scan</b>	<b>Poor performance (subjective)</b>	<b>&gt;75% stop success rate</b>	<b>&lt;25% stop success rate</b>
1	1	0	0	0	0	0	0
1	1	0	0	0	0	0	0
1	1	0	0	0	0	0	0
1	1	0	0	0	0	0	0
1	1	0	0	0	0	0	0
1	1	0	0	0	0	0	0
1	1	0	0	0	0	0	0
1	1	0	0	0	0	0	0
1	1	0	0	0	0	0	0
1	0	0	0	0	0	0	0
0	1	0	1	0	0	1	0
0	1	0	0	0	0	0	0
0	1	0	0	0	0	0	0
0	1	0	0	0	0	0	0
0	0	0	0	0	1	0	0
0	0	0	0	0	0	1	0
0	0	0	0	0	0	1	0
0	0	0	0	0	0	0	1
0	0	0	0	0	0	0	1

**Table S5.** Exclusion information for Stop Signal task.

<b>Incomplete data</b>	<b>Subject omitted (issues with behav. &gt; 50% of tasks)</b>	<b>High motion &gt;20% total volumes</b>	<b>No response on &gt;45% of trials</b>	<b>Stopped performing task at end of scan</b>	<b>Poor performance (subjective)</b>	<b>&gt;75% stop success rate</b>	<b>&lt;25% stop success rate</b>
1	1	0	0	0	0	0	0
1	1	0	0	0	0	0	0
1	1	0	0	0	0	0	0
1	1	0	0	0	0	0	0
1	1	0	0	0	0	0	0
1	0	0	0	0	0	0	0
0	1	0	0	0	0	0	0
0	1	0	0	0	0	0	0
0	1	0	0	0	0	0	0
0	1	0	0	0	0	0	0
0	1	0	0	0	0	0	0
0	1	0	0	0	0	0	0
0	0	1	0	0	0	0	0
0	0	1	0	0	0	0	0
0	0	1	0	0	0	0	0
0	0	0	1	0	0	1	0
0	0	0	0	0	0	1	0
0	0	0	0	0	0	1	0

**Table S6.** Exclusion information for Stroop task.

<b>Incomplete data</b>	<b>Subject omitted (issues with behav. &gt; 50% of tasks)</b>	<b>High motion &gt;20% total volumes</b>	<b>No response on &gt;45% of trials</b>	<b>Stopped performing task at end of scan</b>	<b>Poor performance (subjective)</b>
1	1	0	0	0	0
1	1	0	0	0	0
1	1	0	0	0	0
1	1	0	0	0	0
1	1	0	0	0	0
1	1	0	0	0	0
1	1	0	0	0	0
1	1	0	0	0	0
1	1	0	0	0	0
1	0	0	0	0	0
0	1	0	0	0	1
0	1	0	0	0	0
0	1	0	0	0	0
0	1	0	0	0	0
0	0	1	0	0	0
0	0	1	0	0	0
0	0	0	1	0	1

**Table S7.** Exclusion information for Cued Task Switching task.

<b>Incomplete data</b>	<b>Subject omitted (issues with behav. &gt; 50% of tasks)</b>	<b>High motion &gt;20% total volumes</b>	<b>No response on &gt;45% of trials</b>	<b>Stopped performing task at end of scan</b>	<b>Poor performance (subjective)</b>
1	1	0	0	0	0
1	1	0	0	0	0
1	1	0	0	0	0
1	1	0	0	0	0
1	0	0	0	0	0
0	1	0	1	0	0
0	1	0	0	0	1
0	1	0	0	0	0
0	1	0	0	0	0
0	1	0	0	0	0
0	1	0	0	0	0
0	1	0	0	0	0
0	1	0	0	0	0
0	1	0	0	0	0
0	0	1	0	0	0
0	0	1	0	0	0
0	0	0	1	0	0