

1 Dissociable neural circuits underlie the resolution of three discrete
2 sources of competition during task-switching.

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4 Kelly M. **Burke**^{1,2}, Sophie **Molholm**^{1,2,3},

5 John S. **Butler**^{2,4}, Lars A. **Ross**², John J. **Foxe**^{1,2,3,*}

6
7 ¹*The Dominick P. Purpura Department of Neuroscience*
8 *Albert Einstein College of Medicine*
9 *Bronx, NY 10461, USA.*

10
11 ²*The Cognitive Neurophysiology Laboratory,*
12 *Department of Pediatrics*
13 *Albert Einstein College of Medicine*
14 *Bronx, NY 10461, USA.*

15
16 ³*The Ernest J. Del Monte Institute for Neuroscience*
17 *Department of Neuroscience*
18 *University of Rochester School of Medicine and Dentistry*
19 *Rochester, NY 14642, USA.*

20
21 ⁴*School of Mathematical Sciences*
22 *Dublin Institute of Technology*
23 *Kevin Street, Dublin 8, Ireland.*

24
25
26
27 * **Correspondence:** John J. Foxe, PhD
28 The Ernest J. Del Monte Institute for Neuroscience
29 Department of Neuroscience, Box 603
30 University of Rochester School of Medicine
31 Rochester, NY 14642, USA.
32 Email: John_Foxe@URMC.Rochester.edu
33

35 **Abstract**

36 Humans perform sub-optimally when juggling more than one task, but are nonetheless required to
37 multitask during many daily activities. Rapidly and effectively switching attentional focus between tasks is
38 fundamental to navigating complex environments. Task-switching paradigms in conjunction with neuroimaging
39 have identified brain networks underpinning flexible reallocation of cognitive resources and a core network of
40 neural regions is repeatedly implicated (i.e., posterior parietal, inferior frontal, anterior cingulate, and middle
41 frontal cortex). Performance costs such as reduced accuracy and slowed responses accompany the first
42 execution of a task following a task-switch. These costs stem from three main sources of competition: 1) the
43 need to reconfigure task-rules, 2) the immediate history of motor responding, and 3) whether inputs to be acted
44 upon provide congruent or incongruent information regarding the appropriate motor response, relative to the
45 recently “switched-away-from” task. Here, we asked whether both common (domain-general) and non-
46 overlapping (dissociable) neural circuits were involved in resolving these three distinct sources of competition
47 under high-demand task-switching conditions. Dissociable neural circuits were active in resolving each of the
48 three sources of competition. No domain-general regions were implicated in all three. Rather, two regions were
49 common across rule-switching and stimulus incongruence, and five regions to incongruence and response-
50 switching. Each source of conflict elicited activation from many regions including the posterior cingulate,
51 thalamus, and cerebellum, regions not commonly implicated in the task-switching literature. These results
52 suggest that dissociable neural networks are principally responsible for resolving different sources of
53 competition, but with partial interaction of some overlapping domain-general circuitry.

54

55 **Keywords:** task-switching, neuroimaging, cognitive flexibility, cognitive control, fMRI, conflict

56

57 **Introduction**

58 The mechanisms by which cognitive control is exerted in the human brain are of fundamental interest to
59 neuroscientists. These neural processes are integral to our ability to flexibly change what we attend and respond
60 to from moment-to-moment. When these processes are dysfunctional, such as in Autism Spectrum Disorder (de
61 Vries & Geurts, 2012; Reed & McCarthy, 2012; Chmielewski & Beste, 2015) or schizophrenia (Lesh *et al.*,
62 2011; Dickson *et al.*, 2016), they can greatly impact an individual's ability to successfully navigate daily life.
63 One classic and highly effective way to study cognitive control is to ask experimental participants to switch
64 from one task to another and compare their performance during this switching to when they simply repeat either
65 of the assigned tasks alone. It is well-established that this switching incurs costs: response speeds are typically
66 slower and task accuracy poorer following a task-switch than following a task-repeat (Jersild, 1927; Spector &
67 Biederman, 1976; Rogers & Monsell, 1995; Wylie *et al.*, 2003a; Koch & Allport, 2006; Foxe *et al.*, 2014;
68 Weaver *et al.*, 2014). A considerable body of work has revealed a set of key contributing factors to these costs.
69 1) The first reason is the most intuitive: getting rid of the rules held in the brain for task A and loading up the
70 rules for task B likely incurs a time cost. We will refer to this here as the *rule-switch* cost. 2) Second, research
71 indicates that motor response history also matters. That is, if the previous task required response X but the
72 current one requires response Y, regardless of whether the task changed or not, this *response-switch* generally
73 incurs a cost. 3) Third, evidence shows that rules from the previous task cannot be completely inhibited, such
74 that if stimuli or a stimulus dimension from the previous task are still present, they interfere with performing the
75 current one. This stimulus-based interference will be referred to as a *stimulus incongruence* cost for our
76 purposes going forward. Thus, there are three known sources of “competition” that contribute to switch costs;
77 competition in the sense that competing task rules, competing response histories, and competing stimulus-
78 response mappings all play their part in slowing the task-switching process and in reducing the accuracy of
79 performance.

80 A key question is how each of these sources of competition is resolved in the brain: what are the
81 underlying neural circuits, and are each resolved through activation of common or partly dissociable neural
82 circuits? Although previous work has been done in this field, no single study has investigated the underlying
83 circuitry of all three sources of competition: *rule-switching*, *response-switching*, and *stimulus incongruence*.

84 Thus, a precise delineation of the subcomponents of the neural reconfiguration processes that regulate cognitive
85 control during task-switching has yet to be conducted. There is precedence in the behavioral literature that while
86 these three aspects of cognitive control interact with each other, they can be independently manipulated and thus
87 represent dissociable cognitive processes (Goschke, 2000; Meiran *et al.*, 2000; Wylie *et al.*, 2004b).

88 Most prior cognitive flexibility studies have focused on examining the rule-switching aspect of task-
89 switching, and have reliably demonstrated that regions in the frontal and parietal lobes are more active during a
90 switch of rule than during a task repetition (Dove *et al.*, 2000; Braver *et al.*, 2003; Wylie *et al.*, 2003b; 2004a;
91 Buchsbaum *et al.*, 2005; Liston *et al.*, 2006; Wylie *et al.*, 2009; Greenberg *et al.*, 2010). These commonly active
92 regions include the posterior parietal cortex (PPC; all acronyms used in this paper can be found in
93 Supplementary Table A), inferior frontal junction (IFJ), pre-supplementary motor area (pre-SMA), middle
94 frontal cortex, and anterior cingulate cortex (ACC). Nonetheless, not all rule-switching studies have found all of
95 these regions to be active. This is likely due to the variety of tasks that have been used across studies, which can
96 be addressed in part through meta-analysis to determine the regions consistently involved in cognitive
97 flexibility. One such meta-analysis of five types of switching (shifting between rules, objects, attributes of
98 objects, stimulus-response mappings, or locations) addressed which, if any, regions were involved in all five
99 types of switching, and thus could be interpreted as generalized cognitive control regions (Wager *et al.*, 2004).
100 They identified seven such regions - medial prefrontal cortex, right pre-SMA, left and right anterior and
101 posterior intraparietal sulcus, and left inferior temporal cortex – while a subsequent meta-analysis determined
102 that the left inferior frontal junction and left posterior parietal cortex were the common regions involved in three
103 types of rule-switching (switching between perceptual features, stimulus-response mappings, or between task
104 rules) (Kim *et al.*, 2012). Thus, across a variety of task-switching studies, the parietal lobe and frontal regions
105 such as the inferior frontal junction and medial prefrontal cortex were consistently engaged (Vallesi *et al.*,
106 2015).

107 Within a task-switching study, when the behavioral response on the current trial requires a response that
108 is different from the previous trial, there is typically a slowing down in response time due to this response-
109 switching (Meiran, 1996; Meiran *et al.*, 2000; Mayr, 2002; Wylie *et al.*, 2004b; Dreisbach *et al.*, 2006).
110 However, response-switching and rule-switching interact in an interesting way. When response-switch trials are

111 separated by whether they were a rule-switch trial or rule-repeat trial, participants are faster when there is a rule-
112 switch compared to a rule-repeat. On the other hand, separating out response-repeat trials in the same way
113 demonstrates that rule-repeating is faster than rule-switching (Wylie *et al.*, 2004b). Overall, it is easier when
114 both modalities switch or when both repeat, rather than when one switches and the other repeats. In Go/No-Go
115 paradigms, a response to a trial may even be necessary to elicit the rule-switch cost in the first place (Schuch &
116 Koch, 2003). However, we are aware of no study that explicitly investigated the neural sources of the response-
117 switch cost, despite a need to better understand which regions are active during these distinct sources of
118 competition during task-switching (Wylie *et al.*, 2004b).

119 Typical task-switching experiments require that the participant perform two different tasks on the same
120 kind of stimulus (e.g. a colored shape). One task may require the participant to respond based on the color of the
121 stimulus while the other task requires responding purely based on the shape of the stimulus. Responding
122 correctly, therefore, requires attending to the relevant stimulus parameter and ignoring the other. However, when
123 each stimulus dimension indicates a different response, this stimulus incongruence typically slows participants
124 compared to when each stimulus dimension indicates the same response (Meiran, 1996; Mecklinger *et al.*, 1999;
125 Meiran *et al.*, 2000; Mayr, 2002; Mayr *et al.*, 2003; Wylie *et al.*, 2004b; Dreisbach *et al.*, 2006; Wylie *et al.*,
126 2006). The stimulus incongruence cost can also be augmented when the current task is a rule-switch. (Rogers &
127 Monsell, 1995; Goschke, 2000; Meiran, 2000; Waszak *et al.*, 2005). On this kind of trial, the irrelevant stimulus
128 dimension was also the most recently relevant one and is now indicating a different response than the current
129 relevant dimension, possibly making the irrelevant stimulus dimension even more distracting. Studies
130 investigating the neural sources of stimulus incongruence costs generally implicate the ACC (Mayr *et al.*, 2003;
131 Swainson *et al.*, 2003; Fassbender *et al.*, 2004; Woodward *et al.*, 2006; Kim *et al.*, 2010). One theory about the
132 ACC's role in stimulus incongruence costs posits that the ACC is involved in resolving conflict of information-
133 processing, which subsequently activates the prefrontal cortex – a region commonly implicated in task-
134 switching studies - to reduce the conflict susceptibility (Botvinick *et al.*, 2001). More specifically, evidence
135 indicates that the ACC may register a change in conflict that needs to be resolved (Mayr *et al.*, 2003). In
136 addition to ACC, two specific regions likely to be engaged by manipulations of stimulus incongruence are PPC,
137 where activity has been shown to increase with the salience of the irrelevant stimulus (Liston *et al.*, 2006), and

138 the inferior frontal junction which appears to be involved in cognitive control, particularly in studies using
139 strongly incongruent stimuli that are difficult to ignore (Derrfuss *et al.*, 2004; Derrfuss *et al.*, 2005).

140 Given the dearth of studies on the neural sources of *response-switching* and *stimulus incongruence*
141 specifically, we can take advantage of the extensive task-switching literature and conflict monitoring literature
142 to predict a subset of frontal and parietal regions to be involved in each of the three sources of competition
143 involved in task-switching. Here, we utilized a multi-session approach to acquire at least four times as much
144 data per participant as is typical to gain intra-individual reliability and sensitivity with a repeated measures
145 analysis. We hypothesize that each source of competition will reveal engagement of unique, dissociable neural
146 circuits that are specific to that source of competition, as well as domain-general regions active in resolving
147 more than one source of competition. For example, rule-switching may necessitate activation of the pre-SMA
148 because of the changing association of abstract rules with appropriate motor responses (Bunge *et al.*, 2003;
149 Boettiger & D'Esposito, 2005), while response-switching may engage inferior frontal cortex, a region involved
150 in regulating response inhibition (Rubia *et al.*, 2001; Bell *et al.*, 2014a; Bell *et al.*, 2014b; Scalzo *et al.*, 2016).
151 Moreover, stimulus incongruence may increase activity in the ACC, a region involved in conflict detection
152 (Mayr *et al.*, 2003; Swainson *et al.*, 2003; Fassbender *et al.*, 2004; Woodward *et al.*, 2006; Kim *et al.*, 2010),
153 and IFJ which is active when salient, behaviorally-relevant stimuli are present (Corbetta & Shulman, 2002). At
154 the same time, we predict that all three sources of competition will involve activation of the generalized
155 cognitive control regions PPC and prefrontal cortex (e.g. IFJ).

156

157

158 **Methods**

159 General Approach: We employed a multi-session approach whereby participants performed a task-
160 switching paradigm over four separate functional magnetic resonance imaging (fMRI) scanning sessions (i.e.,
161 across four separate testing days), with the principle aim of this approach being to greatly enhance power at the
162 individual participant level. All neuroimaging analyses used a repeated measures approach to account for the
163 multi-session data. It should be noted that all participants also completed four additional sessions while high-
164 density electroencephalography (EEG) data were recorded. These data are not reported here and will be reported
165 separately. The Institutional Review Board of Albert Einstein College of Medicine approved all materials and
166 procedures, and all ethical guidelines were in accordance with the tenets of the Declaration of Helsinki.

167 Participants: Eleven adults with normal or corrected-to-normal vision participated. Individuals were
168 excluded from the study if they had metal in their bodies, a history of brain injury, or a psychiatric diagnosis
169 (see *Table 1*). One participant was not able to attend the fourth fMRI session, and one session from another
170 participant needed to be excluded due to movement artifact; therefore, there were 42 experimental sessions
171 (days) from eleven participants included in all analyses. Participants provided informed, written consent and
172 were modestly compensated for their time.

173 Stimuli and Task: A cued, speeded, task-switching paradigm was presented using Presentation software
174 (NeuroBehavioral Systems) which was based on a design to isolate rule-switching preparatory processes from
175 stimulus decoding and motor response processes (Spector & Biederman, 1976; Wylie *et al.*, 2004b; 2006).
176 Throughout the entirety of the experiment, the monitor displayed a gray background of [128 128 128]. Each
177 two-second long trial commenced with a colored rectangle subtending 4.25° vertically and 6.38° horizontally of
178 visual angle in the center of the screen for 200 ms, which was the task cue (i.e. yellow for the letter task, blue for
179 the number task; this color-task association was randomly assigned for each participant and remained constant
180 for all four sessions). This was followed by small central crosshairs for 500 ms and then the imperative stimuli
181 appeared for 200 ms, which were a letter and number randomly assigned to either side of the crosshairs each
182 subtending 1.18° vertically (see *Figure 1*). A screen with crosshairs was displayed for the remaining 1100 ms
183 while the participant responded or withheld a response with a button press on a response pad. When the cue
184 indicated the letter task the participants were instructed to “respond as quickly and accurately as possible to the

185 letter task by responding with a button press for a vowel and withholding for a consonant. For the number task,
186 respond as quickly and accurately as possible by responding with a button press for even numbers and
187 withholding for odd numbers.” Letters were randomly selected from the set [A E G I K M R U] and the numbers
188 were randomly selected from the set [2 3 4 5 6 7 8 9]. Each trial contained both a letter and number so the task
189 cue was integral to responding appropriately to the stimulus. The side of the crosshairs to which the letter and
190 number were displayed was random so that participants could not anticipate which side of the screen to attend
191 to. Given the random selection of stimuli, rule-switches were 50% probable; incongruent stimuli and congruent
192 stimuli were equally probable; and response-switches were equally likely as response-repeats. Four trials were
193 presented in a row followed by six seconds of rest to allow for BOLD signal decay. This trial sequence was
194 repeated 16 times within a block, after which participants could rest before starting the next block, and 16 blocks
195 were run per session. Four blocks were Pure blocks where only one task was cued. Overall this means that there
196 were 2304 trials included per participant for all analyses. This was important to ensure the participant’s ability to
197 perform each task on its own. If there were any changes in behavior throughout the session, we could determine
198 if this was due to the switching of tasks or a general fatigue. Whether a participant started the session with the
199 letter task or number task was counterbalanced between sessions and between participants. At the beginning of
200 the participant’s first session, they practiced ten trials of the letter task and ten trials of the number task to ensure
201 they understood the experiment and its timing.

202 Condition Definitions: The first trial from each four-trial series was excluded as it represented neither a
203 rule-switch nor rule-repeat. A rule-switch trial was where the cued task was different from the previous (e.g. the
204 letter task preceded by the number task or vice versa), and a rule-repeat trial was where the same task was cued
205 as in the previous trial. Response-switch trials required a different response (either withholding a response or
206 making a response) from the previous trial whereas response-repeat trials called for the same response as in the
207 preceding trial. Response time analysis was necessarily constrained to those response-switch or response-repeat
208 trials involving a motor response, but the fMRI analysis could take advantage of both successful withhold trials
209 and successful response trials. Stimulus incongruent trials were those in which one stimulus indicated to respond
210 and the other indicated to withhold a response (e.g. a vowel and odd number, or a consonant and even number).

211 Stimulus congruent trials had stimuli that both indicated the same response (e.g. a vowel and even number, or a
212 consonant and odd number).

213 Behavioral Analysis: Response times (RTs) were calculated for each session of a given participant
214 according to the three sources of “conflict” (i.e. rule-switching, stimulus incongruence, and response-switching).
215 Accuracy was determined as the percentage of correct responses (correct hits + correct rejections) to the total
216 number of trials (correct hits + correct rejections + omission errors + commission errors). Behavioral costs for
217 each participant were calculated according to each of the three conflicts (e.g. rule-switch cost = average rule-
218 switch RT – average rule-repeat RT). If two button press responses occurred within one trial, only the first
219 response was included in analysis; the second one was interpreted as an extraneous response. Minimum and
220 maximum response times were determined by excluding any responses that occurred within 200 ms of the
221 presentation of the stimulus (these responses are seen as either late responses to the previous trial or extraneous
222 mouse clicks), and excluding responses that occurred more than 2.5 standard deviations after the mean response
223 time for that session (Manzi *et al.*, 2011). An omnibus 4-way ANOVA on the three conditions of interest and
224 session (first, second, third, fourth) was conducted on the response times to determine whether the factors of
225 interest interacted, and to verify whether repeated sessions had any effect on the data as well.

226 fMRI Acquisition: Participants lay comfortably supine in a 3.0 T Philips TX Achieva MRI scanner
227 (Royal Philips, Amsterdam, Netherlands), with foam earplugs and heavy-duty headphones over them, and with
228 goggles laying gently over their eyes to display the computer screen (using Resonance Technology
229 VisuaStimDigital with funclab software). The scanner has a thirty-two channel head coil and acquired T2, EPI,
230 FLAIR, DTI, and T1-weighted structural MPRAGE (Magnetization Prepared Rapid Gradient Echo) scans.
231 Whole-brain functional scans were acquired through twelve blocks of 114 volumes. Each volume consisted of
232 forty-eight axial slices in an ascending interleaved order at 3 x 3 x 3 mm³ using a T2-weighted echo-planar
233 sequence (TR/TE: 2000/20 ms, flip angle = 90°, 240 mm FOV). The short TE was used because we were
234 specifically interested in ensuring good signal capture from anterior cognitive control regions where there are
235 usually field inhomogeneities (Weiskopf *et al.*, 2006; Weiskopf *et al.*, 2007). We fully expected that anterior
236 regions would be involved in task-switching and thus wanted to capture these regions well, and although we
237 were aware that the short TE sacrifices BOLD signal slightly, the long and repeated scan sessions (3.5-4 hours

238 per participant) was expected to compensate for this. The inter-stimulus interval was 2000 ms, as well as the TR,
239 so oversampling was not employed in the current study. fMRI sessions were a total of 1 hour and 20 minutes,
240 and the task was presented for 60 minutes of that time.

241 fMRI Preprocessing: fMRI processing was carried out using BrainVoyager QX v2.4 (Brain Innovation
242 BV, The Netherlands) (Goebel *et al.*, 2006). The T1-weighted anatomical scans for each participant were
243 normalized into Talairach space using the AC-PC landmark and fitting 6 parameters (the superior, inferior,
244 anterior, posterior, left, and right-most parts of the brain). Processing for all functional runs included: removal of
245 the first two volumes to allow for equilibrium effects, slice scan time correction, 3D motion correction using a
246 trilinear/sinc interpolation and 6 vectors (translation in the X, Y, and Z dimensions, 3 Euler angles of rotation),
247 temporal filtering (high-pass GLM-Fourier basis with 2 sines/cosine), normalization to Talairach space using the
248 AC-PC landmark and fitting 6 parameters), and spatial smoothing using an 8 mm isotropic full-width half-
249 maximum Gaussian filter kernel. Each functional run was precisely aligned and co-registered to the T1
250 anatomical scan. Any runs with excessive movement (greater than 3 mm of translation or 3° of rotation) were
251 excluded. This excluded one scan session of one participant, which had too much movement. In addition, only
252 3.9% of all remaining runs from all participants were excluded due to excessive motion.

253 fMRI Activation Analyses: An event-related design was used to examine the three sources of conflict
254 present in this experiment: rule-switching (rule-switch > rule-repeat), response-switching (response-switch >
255 response-repeat), and stimulus incongruency (incongruent stimuli > congruent stimuli). Each condition of
256 interest (rule-switch, rule-repeat, response-switch, response-repeat, incongruent stimuli, congruent stimuli) was
257 modeled with a boxcar function that was convolved with a standard two-gamma hemodynamic response
258 function (with an event length assumed to be 2000 ms, 5 seconds until response peak, 15 seconds until the
259 undershoot peak, and a response undershoot ratio of 6). Volume time-courses for each run of each participant
260 were entered into a random-effects general linear model (RFX-GLM) in BrainVoyager, which was used in an
261 ANCOVA Random Effects Analysis. The ANCOVA was set up with two within-subjects factors: 2 conditions x
262 4 sessions. This approach followed done separately and independently for each of the three sources of conflict
263 (rule-switching vs rule-repeating, incongruency vs congruency, and response-switching vs response-repeating).
264 The ANCOVA tested for the Condition factor, resulting in a map where each voxel had an F-stat and its

265 associated p-value. fMRI analysis inherently has multiple statistical comparisons and so thresholding of some
266 kind is required to statistically compensate for increased false positives. For each of the three contrasts of
267 interest (rule-switching, incongruency, and response-switching) we applied p-value- and cluster-thresholding.
268 The map's p-value threshold was decreased to below 0.01 and then the Cluster-Level Statistical Threshold
269 Estimator in BrainVoyager was used. In order to correct for multiple statistical comparisons, this estimator is
270 based on a Monte Carlo simulation of random image generation, with added spatial correlations between
271 neighboring voxels, voxel intensity thresholding, and cluster identification. After 1,000 simulations, a minimum
272 cluster size was determined for that statistical map that yields a false positive detection rate of 5% or less
273 (Forman *et al.*, 1995). The cluster threshold estimator determined that cluster minimum should be 30 voxels for
274 the rule-switching data, 18 voxels for the incongruency data, and 24 voxels for the response-switching data.
275 These thresholds were used for each of the maps. The average beta-weight for the voxels within each contiguous
276 region for each condition was calculated and plotted to show the absolute difference in activation or
277 deactivation. The centers of mass in Talairach coordinates were used to determine the brain region that best
278 represented the region of activation, according to the Talairach Daemon (<http://www.talairach.org/>).

279 Overlapping Regions: To determine which regions were involved in more than one source of conflict,
280 we applied conjunction analysis in BrainVoyager to map voxels that were significant in more than one analysis
281 and whether any voxels were significantly involved in all three analyses.

282 Effects of Time: Participants coming in for multiple sessions allows an investigation of whether there
283 are changes in behavior or network activity across time. To determine if there were any effects of session on the
284 response time data, we used RFX-GLM in the ANCOVA Random Effects Analysis with two within-subjects
285 factors but instead tested for the Session factor. To anticipate the results, there were no significant effects of
286 session in the data.

287

288 **Results**

289 *Behavioral Performance:* The three-way ANOVA demonstrated an interaction between the three
290 sources of conflict of interest ($F(1,10) = 9.866$, $p = 0.010$) and a 2-way interaction between rule-switch and
291 response-switch ($F(1,10) = 9.342$, $p = 0.012$). Post-hoc t-tests revealed that response-repeating was faster with a
292 rule-repeat than a rule-switch ($t(21) = 2.83$, $p = 0.010$) and response-switching was faster with a rule-switch than
293 with a rule-repeat but this was not significant ($t(21) = -1.55$, $p = 0.136$). Interestingly, the expected 2-way
294 interaction between rule-switch and stimulus incongruence was not significant ($F(1,10) = 3.818$, $p = 0.079$). In
295 addition, although the average response times indicated trends toward rule-switch costs, stimulus incongruence
296 costs, and response-switch costs, these were not strong enough to emerge as main effects (see *Figure 2A*). Table
297 3 lists the average response times and standard deviations for each participant. In a study design such as this,
298 one concern is that response times may slow to the benefit of accuracy. But in fact, the data demonstrated a
299 correlation where slower participants were less accurate ($r = -0.62$, $p = 0.0412$; see *Figure 2C*). However, with a
300 cohort of 11 participants, any correlational observations should be interpreted with caution.

301 *fMRI Data:* The three contrasts revealed a variety of distinct regions and overlapping regions of
302 involved in resolving the three sources of conflict (see *Table 4*). The contrast examining rule-switching effects
303 revealed five regions that were significantly differentially active for rule-switch versus rule-repeat trials, that
304 included left inferior frontal junction, left precuneus, left thalamus, and a locus in posterior cingulate that was
305 more active for rule-switching than rule-repeating and a locus in posterior cingulate that had less deactivation to
306 rule-switching (see *Figure 3*). The contrast examining incongruency effects demonstrated activations in the
307 cingulate, superior frontal gyrus, medial frontal gyrus, middle frontal gyrus, precuneus, cerebellum, thalamus,
308 and insula (see *Figure 4*). Although our analysis does not allow for investigating statistical interactions, we can
309 still determine that two of these regions – precuneus and thalamus – were involved in both rule-switching and
310 incongruency. Investigating response-switching effects revealed ten regions significantly involved, which were
311 predominantly cerebellar and subcortical, along with the middle frontal gyrus, postcentral gyrus and medial
312 frontal gyrus (see *Figure 5*). Interestingly, some of these regions were common to both incongruency and
313 response-switching, with just the caudate, thalamus, postcentral gyrus, and anterior cingulate cortex unique to
314 the response-switching contrast and did not come out in the other analyses (see *Figure 6*). Also, the medial

315 frontal gyrus, right postcentral gyrus and anterior cingulate showed stronger deactivation patterns for response-
316 switching than response-repeating. The medial frontal gyrus which was involved in resolving incongruency as
317 well, was similarly more deactivated for the trials with incongruent stimuli compared to those with congruent
318 stimuli.

319

320 **Discussion**

321 We set out here to map the cortical circuitry underlying three known sources of competition that
322 contribute to response slowing during task-switching, examining the thesis that resolving these sources of
323 conflict likely involves both domain-general cognitive control regions as well as dissociable sub-circuitry. We
324 describe three distinct networks that were evident when the discrete sources of conflict were expressly isolated
325 in our analyses (i.e., for rule-switching, response-switching and stimulus incongruence). Somewhat surprisingly,
326 and contrary to our original hypothesis, there were no overlapping regions active during all three comparisons,
327 so the current results do not support the existence of one or more domain-general cognitive control regions that
328 subserved all three of these functions. Instead, we found that there were both frontal and subcortical regions
329 involved in resolving conflict across a given pair of conditions, so some degree of domain generality was also
330 observed (see Figure 7 for a schematic summary overview). The main outcome of the current study though, was
331 the observation that largely distinct networks of regions were required to resolve each source of conflict inherent
332 in this task-switching paradigm. Rule-switching on its own recruited the typically observed frontal and parietal
333 regions reported in the task-switching literature (Wager *et al.*, 2004; Kim *et al.*, 2012) along with the thalamus
334 and posterior cingulate cortex. Stimulus incongruence involved the cingulate as predicted but also the
335 cerebellum and frontal regions with a medial frontal gyrus deactivation. Response-switching involved sub-
336 cortical, anterior cingulate, and cerebellar involvement in addition to a frontal deactivation. Although all three of
337 these analyses revealed networks of regions significantly involved, it was surprising that the behavioral analysis
338 did not reveal main effects when each of the three sources of conflict were isolated individually. Based purely
339 on average reaction times, our results are within the range typically found in similar task-switching studies,
340 albeit towards the lower end. In the current cohort, response-switching elicited the largest change in reaction
341 times, and interacted significantly with the other two sources of competition. What is striking is that despite the
342 lack of significant rule-switch or incongruence costs, the neuroimaging data did demonstrate robust changes in
343 neural activity. In what follows, we describe each of these extended circuits in more detail and discuss the
344 possible roles of the various functional hubs in resolving each distinct source of competition.

345 ***Rule-switching***

346 Rule-switching (changing the rule from letter-based to number-based or vice versa) activated the
347 precuneus, a region consistently reported in task-switching studies. Activity in the precuneus has previously
348 been time-locked to attention shifting in a card-sorting task (Nagahama *et al.*, 1999), to attention shifting
349 between different targets in space (Selemon & Goldman-Rakic, 1988), and has been associated with a variety of
350 tasks compared to rest (Utevsky *et al.*, 2014), so its involvement here when participants were required to
351 reconfigure the task rule they should follow is not surprising. Similarly, the posterior parietal cortex is also
352 consistently implicated in task-switching (see meta-analyses by (Wager *et al.*, 2004; Liston *et al.*, 2006; Kim *et*
353 *al.*, 2012)) and the current study's finding of left posterior parietal cortex activation further confirms this
354 region's role in cognitive control. The clear laterality in our findings in the parietal lobe and frontal lobe are in
355 agreement with left-laterality sometimes reported in the literature (Dove *et al.*, 2000; Philipp *et al.*, 2013;
356 Muhle-Karbe *et al.*, 2014). However, there is no consensus as of yet regarding which regions are bilaterally or
357 unilaterally involved in task-switching and we will therefore discuss our findings in more general terms. Rule-
358 switching also activated a region on the border of both the precentral gyrus and inferior frontal cortex, which is
359 commonly referred to as the inferior frontal junction (IFJ) (Derrfuss *et al.*, 2004). This region is often found to
360 be involved in task-switching (Dove *et al.*, 2000; Braver *et al.*, 2003; Swainson *et al.*, 2003; Brass & von
361 Cramon, 2004). Meta-analysis has revealed the IFJ may be specifically involved in the updating of the task
362 representation (Derrfuss *et al.*, 2005). The thalamus has been shown to be involved in task-switching as well.
363 Nuclei in the thalamus were crucial for modulating synchrony between cortical areas during an attention task in
364 macaques (Saalman *et al.*, 2012), further indicating that the thalamus regulates information flow throughout
365 inter-regional cortico-cortical networks (Bell & Shine, 2016).

366 Rule-switching was also associated with differential activation within the posterior cingulate cortex
367 (PCC), which we had not specifically predicted. The posterior cingulate is believed to serve as a hub within the
368 so-called default mode network, and it is thought to show generally high levels of background activity during
369 so-called "resting states", activity that is then significantly decreased or suppressed during task performance
370 (Gusnard *et al.*, 2001; Raichle *et al.*, 2001; Hayden *et al.*, 2010; Spreng *et al.*, 2010; Leech *et al.*, 2011;
371 Korgaonkar *et al.*, 2014). Its functional role is not yet well understood, but based on its structural and functional
372 connections with the fronto-parietal network, it may well play a role in transitioning between network states

373 (Hagmann *et al.*, 2008; Agam *et al.*, 2013) and in dynamically controlling attention from the internal to the
374 external environment. Here, two distinct loci of activity in the posterior cingulate were significantly involved in
375 rule-switching. One locus, which spanned 27 mm³ and was located medially, but in the left hemisphere, was not
376 significantly activated for rule-repeating compared to baseline, but was for rule-switching. The other locus, with
377 a center of mass in the right hemisphere that spanned 127 mm³, was significantly engaged for both conditions
378 relative to baseline, but more so for rule-switches than repeats. These regional activations suggest a more active
379 role for PCC in resolving rule-switching. That is, we do not observe relative decreases in activation during
380 higher levels of task engagement. The current study is not the first to demonstrate greater PCC activity during
381 task-switching relative to task-repeating (Braem *et al.*, 2013) (Dreher *et al.*, 2002; Braem *et al.*, 2013).
382 Interestingly, in the study by Braem and colleagues, PCC activity during switching was impacted by the valence
383 of affective visual stimuli presented between trials (i.e. positive vs negative), suggesting a possible role for the
384 PCC in the affective modulation of cognitive control processes. Indeed, a number of other studies have reported
385 PCC involvement in evaluating the subjectivity or the salience of stimuli in general. For example, in a go/no-go
386 task with emotionally salient faces, PCC was active during successful task performance when the participant
387 was under conflicting emotional conditions. Participants were put under an emotional state of threat (e.g. the
388 possibility of hearing aversive sounds) or excitement (e.g. the possibility of winning money) and on each trial an
389 emotional cue, a happy, sad, or neutral face was presented. On trials where the emotion of the presented cue
390 conflicted with the emotion of the overall state (e.g. threat condition and a happy face), the PCC was more
391 active than when the emotional states did not conflict. (Cohen *et al.*, 2016). Studies have also correlated activity
392 of the PCC with the subjective value of a chosen option in studies on decision-making in both monkeys and
393 humans (Kable & Glimcher, 2007; Luhmann *et al.*, 2008; Levy *et al.*, 2011). The generalizability of these
394 affect- or salience- related findings to the current study is, of course, somewhat limited since there was no
395 affective or salience manipulation of the stimulus materials.

396 A recent study provides another interesting wrinkle on the potential role of the PCC in rule switches.
397 Manelis and colleagues presented participants with a series of objects with the task being to determine if a given
398 object was “old” (seen before within a given block) or “new” (never seen before) (Manelis *et al.*, 2017). In a
399 variant of this task, they then presented occasional reset signals such that previously “old” objects should now

400 be considered as “new” for the purposes of that task block – which they termed “pseudonew”. The PCC was the
401 sole area to show complete sensitivity to this task-resetting manipulation, with its activity reflecting an item’s
402 novelty (or not) according to the task instructions, regardless of whether the item had been seen during
403 preceding blocks. In other words, the posterior cingulate was sensitive to the rule-switch, much as we find here.

404 Overall, the current findings and much of the extant literature would suggest that the posterior cingulate
405 plays a more prominent role in task-switching than might have been previously appreciated, likely as a region
406 that detects conflicts of many types and reallocates resources of other networks to optimize further processing.
407 The PCC, with strong connections to parahippocampal areas, could also play a role in retrieving relevant
408 information from long-term memory (Kim *et al.*, 2010; Kim, 2011). We can only speculate at this point but
409 further studies into changes of rules under different contexts will likely better delineate its specific role, and we
410 will return to the potential role of the posterior cingulate below when we discuss its involvement in the
411 resolution of stimulus-stimulus incongruence.

412 In sum, the regions involved in the current rule-switching findings suggest a more detailed and elaborate
413 set of perceptual-cognitive processes during successful rule-switching than has been forwarded previously. One
414 possible way of thinking about how these regions could work together to resolve rule-switching (although we
415 would stress that this is but one possible sequence), could be: increased transition from internally-guided
416 thoughts to the external environment (posterior cingulate), increased information flow between networks
417 (thalamus), update of the task (IFJ), and increased attention to the visuospatial input (precuneus).

418 ***Response-switching***

419 The activations to response-switching were also revealing. A response-switch occurred when the correct
420 response to the current trial was different from the previous trial (e.g. a Go when the previous trial was a No-
421 Go), regardless of the task. Response-switching elicited differential activity in the left middle frontal and left
422 inferior temporal gyrus. In addition, sub-cortical (specifically the caudate and thalamus) and cerebellar
423 activations were also observed. A somewhat surprising finding was that the medial frontal cortex was more
424 active for response-repeating compared to response-switching. However, in both of these conditions, activity
425 levels were actually less than during rest (i.e. the beta-weights were negative for both conditions). Previous
426 studies suggest that the medial frontal cortex is integral to the medial frontal-subcortical circuit which has been

427 implicated as a mediator of motivation, engagement, and the maintenance of task-relevant processes (Stuss *et*
428 *al.*, 2005). As such, it is perhaps surprising that this region was not significantly active above baseline for
429 response-switches.

430 Middle frontal cortex was also significantly involved in response-switching. It is noteworthy that
431 activity levels in middle frontal cortex during response-repeating were similar to baseline, whereas they were
432 significantly increased above baseline for response-switching. This observation accords well with meta-analysis
433 findings, where bilateral middle frontal cortex was found to be involved in response suppression during
434 Go/NoGo tasks, and during Wisconsin Card Sorting Tasks (WCST), but not specifically in task-switching
435 studies (Buchsbaum *et al.*, 2005). Here, we find no evidence for its involvement in rule switching, but clear
436 involvement during response switching.

437 The posterior lobe of the cerebellum was also implicated in the response-switching analysis (and during
438 analysis of stimulus-stimulus incongruence effects – see below). While little is known about the role of the
439 cerebellum in task-switching, this is certainly not the first study to find that it is significantly involved (De
440 Bartolo *et al.*, 2009; Dickson *et al.*, 2016). It is perhaps not surprising that the brain structure most associated
441 with motor control would be active during the resolution of motor conflict in a paradigm like the current one
442 (Peterburs & Desmond, 2016). That it was not activated during isolated rule-switches (above) suggests that
443 previous observations of cerebellar involvement in task-switch may have been confounding what might be
444 thought of as “conceptual” rule-switches with motoric switches, an issue certainly worth pursuing more deeply
445 in future studies.

446 We had predicted that the anterior cingulate cortex (ACC) would likely be involved in resolving the
447 conflict created by incongruent stimuli, based on prior literature (Botvinick *et al.*, 2001; Mayr, 2002; Kim *et al.*,
448 2010). Here, however, it was for response-switching that we observed its involvement. It is important to note
449 that the identified region here, while primarily situated in anterior cingulate, also extended somewhat anteriorly
450 into medial frontal gyrus. Studies have consistently found the ACC involved in resolving incongruency of visual
451 stimuli (Bush *et al.*, 2000; Swainson *et al.*, 2003; Fassbender *et al.*, 2004; Woodward *et al.*, 2006). One study
452 also found anterior ACC involvement when there was incongruency in response mapping (i.e. response conflict)

453 (van Veen & Carter, 2005), but it is difficult to interpret how this relates to our finding of deactivation of the
454 ACC for a switch of response.

455 The postcentral gyrus also showed relative deactivation for response-switching compared to baseline,
456 but it was more deactivated compared to response-repeating. And it is worth noting that although the identified
457 region was primarily in postcentral gyrus, it did also extend anteriorly into precentral gyrus and posteriorly into
458 inferior parietal cortex. The postcentral gyrus is known to receive and process somatosensory input (Iwamura,
459 1998; Iwamura *et al.*, 2001; Staudt, 2010), but this cannot explain these findings because participants had their
460 hand on the response pad for the duration of the study, and pressed the button equally in response-switch and
461 response-repeat trials. However, another task-switching study, designed to limit working memory demands and
462 isolate only switching processes, found postcentral gyrus involvement in task-switching, with the caveat that
463 every task-switch also required a motor switch and thus this activation could be related to motor switch demands
464 (Smith *et al.*, 2004). Regarding the functional role that the postcentral gyrus may play during these switches, a
465 study on motor reach errors found the postcentral gyrus to be involved in errors resulting in behavioral goal
466 changes and not errors that lead to adaptation of limb dynamics (Diedrichsen *et al.*, 2005). These findings
467 suggest that the postcentral region is an area that performs and learns new visuo-motor transformations, which is
468 relevant during switching of responses. However, it is important to understand why the current study found
469 deactivation during response-switches instead of activation, as the above studies would suggest. While
470 deactivation in functional neuroimaging studies is poorly understood overall, recently more studies have focused
471 on deactivation, with a few specifically on motor deactivation (Allison *et al.*, 2000; Kudo *et al.*, 2004).
472 Deactivation in motor cortices in response to motor activity has been shown, on the supposition that
473 interhemispheric control of motor action also involves deactivation of the opposite hemisphere to prevent
474 interference (Marchand *et al.*, 2007). This fits well with our findings of response-switch deactivation only in the
475 right hemisphere. All participants in this study used their right hand to respond to the task. Therefore, there
476 could be right-hemisphere deactivation to allow for better left-hemisphere control, especially during the
477 response-switch condition which requires altering the motor response and could therefore require increased
478 processing.

479 The inferior temporal gyrus is part of the visual system's 'what' pathway, such that lesions to this region
480 result in impairments in object recognition (Creem & Proffitt, 2001). Response-switching may require more
481 activation of the inferior temporal gyrus because there is increased need to interpret and categorize the stimulus
482 before initiating a change in behavior. Cognitive flexibility has traditionally been thought of as a cortical
483 process, occurring through frontal and parietal regions; however evidence indicates that subcortical regions are
484 involved and even necessary (van Schouwenburg *et al.*, 2010). The basal ganglia are thought to encode novel
485 actions (Redgrave *et al.*, 2013) and to help regulate response selection during cognitive flexibility tasks
486 (Verstynen *et al.*, 2012). Although there is little to go on from previous neuroimaging studies regarding
487 response-switching, it would certainly be reasonable to expect activation in the striatum. In the context of task-
488 switching, the striatum has been demonstrated to be active regardless of how the switch was cued (Liu *et al.*,
489 2015). Patients with traumatic brain injury show a negative correlation between caudate body volume and task-
490 switch accuracy, and a negative association between caudate head size and task-switch response times
491 (Leunissen *et al.*, 2014). As further evidence of the role of the basal ganglia, stroke patients with lesions
492 focalized to the striatum had impaired task-switching performance (Cools *et al.*, 2006). Alongside the striatum,
493 the thalamus has also been shown to be engaged during cognitive flexibility (Liu *et al.*, 2015). In a meta-
494 analysis of cognitive control studies, the thalamus was significantly associated with inferior frontal junction
495 (IFJ) activations, which is believed to be involved in the updating of the representation of the task. Since there is
496 relatively little work on response-switching, a simple model of the respective roles of the identified regions
497 might be useful. Based on our current findings and on the extensive related literature, the following processing
498 sequence represents one plausible scenario: response-switching engages the inferior temporal gyrus for further
499 visual processing of the stimulus, the middle frontal gyrus aids in decision-making based on the stimuli (Hare *et*
500 *al.*, 2009), the cerebellum detects a need to modulate the response (De Bartolo *et al.*, 2009; Dickson *et al.*,
501 2016), the striatum allows the conscious awareness of the new response requirement (Graybiel, 1998; Squire &
502 Dede, 2015), and the thalamus relays that information back to the cortex to elicit the correct response (Saalman
503 *et al.*, 2012; Bell & Shine, 2016).

504 ***Stimulus incongruence***

505 Examination of the effects of stimulus congruence (i.e. when the letter and number indicated the same
506 motor response versus when they indicated conflicting motor responses) also revealed a network of regions that
507 was more active during incongruent trials compared to congruent trials. Unique activations of the superior
508 frontal gyrus, medial frontal gyrus, posterior cingulate, insula, and cerebellar regions were observed. Stimulus
509 incongruence also activated a subset of regions that were recruited during the resolution of response-switching:
510 middle frontal gyrus, inferior temporal gyrus, putamen, and two cerebellar loci. As mentioned above, posterior
511 lobe cerebellar involvement was observed during the resolution of response-switches, as it was here during the
512 resolution of stimulus-incongruence, but it was not observed when rule-switches were isolated. Again, it is
513 perhaps unsurprising that the cerebellum might be specifically involved in situations where the conflict in the
514 system is due to competing motor responses. In the case of response switches, this is likely because the currently
515 indicated response does not match the previously executed one, and in the case of stimulus congruence, this may
516 be because the currently indicated response does not match the contemporaneously cued response in the to-be-
517 ignored stimulus dimension (e.g. what the letter is telling the participant to do while she or he is actively
518 engaged in the number task).

519 Medial frontal gyrus is typically implicated in sustaining task-set representations (Cummings, 1995;
520 Stuss *et al.*, 2005), so it is perhaps surprising that this study revealed its involvement in resolving stimulus
521 incongruence. This story is further complicated by the observation that one locus within the medial frontal gyrus
522 showed more deactivation for incongruent stimuli compared to congruent stimuli, while another locus within
523 medial frontal cortex showed increased activation for incongruent stimuli. The common observation here is that
524 trials with incongruent stimuli elicited greater differential activity relative to baseline than did trials containing
525 congruent stimuli; but perhaps the medial frontal gyrus has two distinct roles in resolving this conflict. It
526 remains a puzzle, however, that we did not observe rule-switching related activation in this region, given its
527 presumed role in task-set representation.

528 Insular cortex has been variously implicated in emotion regulation and the limbic system (Wager *et al.*,
529 2004) as well as in multisensory processing (Bushara *et al.*, 2003; Chen *et al.*, 2015), but also during many
530 studies that have investigated cognitive control processes (Fassbender *et al.*, 2006; Simoes-Franklin *et al.*, 2010;
531 Droutman *et al.*, 2015). Here, we observed insular involvement during processing of incongruent stimuli. One of

532 the inherent qualities of incongruent stimuli is that one of the stimulus dimensions indicates a “go” response,
533 whereas the other indicates a “stop” response (i.e. withhold or arrest your response). It is interesting therefore
534 that in a previous study from our group, we observed clear insular activation for both cued and uncued STOPS in
535 a variant of a response-inhibition task (Fassbender *et al.*, 2009), and the current findings are also entirely
536 consistent with a recent “activation likelihood estimation (ALE)” study that evaluated 111 neuroimaging studies
537 that assessed neural activations in conflict-related paradigms (Li *et al.*, 2017). These authors showed clear
538 activation in bilateral insula in response to “stimulus-stimulus” conflicts; that is, tasks where the response
539 demanded by the task-relevant feature of a stimulus was incompatible with the response associated with the
540 task-irrelevant feature of the same stimulus, very much as was the case in the current study. Thus, it seems
541 reasonable to propose that the insular activations we observe here are related to the need for motor suppression
542 to the incompatible “instruction” provided by the irrelevant stimulus dimension (see Wessel and Aron, 2017 for
543 a similar interpretation (Wessel & Aron, 2017)).

544 The posterior cingulate cortex was significantly involved in resolving trials with incongruent stimuli
545 compared to congruent stimuli. The reader will recall that the PCC was also involved in rule-switches, but it is
546 important to point out that the PCC region found active here for incongruent stimuli does not overlap with the
547 regions identified during rule-switching. Studies have demonstrated distinct functional roles for different loci
548 within the PCC, and the current findings clearly further support this multi-role interpretation (Leech *et al.*, 2012;
549 Liang *et al.*, 2016). As with rule-switches, increased PCC activation during the resolution of stimulus-stimulus
550 incongruence does not fit well with the notion that PCC should be less active during higher-load task
551 performance (Gusnard *et al.*, 2001; Raichle *et al.*, 2001). Indeed, a recent study demonstrated greater PCC
552 deactivation during a condition with incongruent stimulus-response mappings compared to congruent mappings
553 (Li *et al.*, 2015). This finding was interpreted as the need for suppression of task-irrelevant activity to allow for
554 better external cognitive function, as might be expected during more taxing conditions (see (Anticevic *et al.*,
555 2012)), and work has also shown that the strength of anti-correlation between the so-called default mode
556 network (comprising PCC) and the fronto-parietal attentional control network is linked to better task
557 performance in the form of less variable reaction times (Kelly *et al.*, 2008). However, as with the current study,
558 other studies have demonstrated a more “active” role for the posterior cingulate during taxing cognitive control

559 operations, as we discussed above. What then is the role of the PCC in resolving the stimulus-stimulus
560 incongruence inherent in the current task? One plausible explanation might lie in our use of orthographic
561 stimuli. For example, in one recent study employing sentence stimuli, sentences were constructed such that they
562 could either end with a word that was contextually congruent or one that wasn't (e.g. "The pen leaked ink," or
563 "The pen leaked chocolate"). Increased PCC activation was observed for incongruent relative to congruent
564 endings (Catarino *et al.*, 2011), and other studies have also implicated the PCC in semantic processing
565 (Frishkoff *et al.*, 2004; Binder *et al.*, 2009). Although our stimuli were considerably more basic letter-number
566 combinations than the stimulus materials used in these studies, it is possible that the semantic decoding of them
567 may have driven the increased PCC activation in the case of incongruent pairings.

568 We found the left thalamus involved in both rule-switching and incongruency, while the right thalamus
569 was involved in response-switching. The thalamus has previously been implicated in task-switching (Liu *et al.*,
570 2015), although its precise role is not clear. The thalamus is traditionally understood as a processing hub for
571 sensory information (Nakajima & Halassa, 2017) and connecting subcortical regions to the cortex (Bell &
572 Shine, 2016). It may also regulate cortical connectivity between networks for task completion (Nakashima *et al.*,
573 2018), which fits well with the current study's finding that there was thalamic involvement in all three sources
574 of cognitive conflict. The thalamus is likely an important source for network control aiding changes in task sets
575 or response sets.

576 The middle frontal gyrus, on the other hand, has been shown to be involved in reorienting attention and
577 to be generally involved in attentional networks (Japee *et al.*, 2015). Its involvement in resolving stimulus
578 incongruence is consistent with the additional attentional demands that are likely required to discern the relevant
579 stimulus dimension. Stimulus incongruence (and response-switching, as discussed above) also activated the
580 putamen in the current study. The putamen has been shown to aid in rule-based learning (Ell *et al.*, 2006), and so
581 this finding further supports its role in category learning and decision-making tasks. Another necessary process
582 during task-switching studies is to appropriately process and interpret the visual stimuli. The inferior temporal
583 gyrus is integral to this process (Denys *et al.*, 2004) and was clearly observed in the current study for trials with
584 incongruent stimuli, which can be reasonably expected to require increased visual processing compared to trials
585 with congruent stimuli. Many studies have demonstrated that the ACC plays a role in the error monitoring and

586 detection necessary to reallocate attention (Botvinick *et al.*, 2001; Mayr *et al.*, 2003; Swainson *et al.*, 2003;
587 Fassbender *et al.*, 2004; Derrfuss *et al.*, 2005; Liston *et al.*, 2006; O'Connell *et al.*, 2007; Kim *et al.*, 2010).
588 Although the current study's cingulate activation was not as anterior as seen in many of these prior studies, it
589 likely reflects a similar functional role. Studies that have tried to determine whether ACC is involved in
590 stimulus-only conflict or response conflict have found that ACC is involved when there is a conflict in the
591 response (Milham *et al.*, 2001; Liu *et al.*, 2006). This is in line with our results because the irrelevant stimulus in
592 a given trial was incongruent because it elicited a different behavioral response than the relevant stimulus. ACC
593 activation can be modulated by top-down motivation or awareness. Greater ACC activation has been linked to
594 awareness of errors, compared to unaware errors (Orr & Hester, 2012), and motivation through incentives can
595 differentially activate rostral ACC compared to caudal ACC (Simoës-Franklin *et al.*, 2010). The current
596 findings of ACC activation further cement its role as a monitor of potential conflict and need for regulation in
597 task-switching studies, but likely in other domains as well. The superior frontal gyrus is often found as an
598 integral region during task-switching (Nagahama *et al.*, 1999; Cutini *et al.*, 2008). Because of its role in
599 resolving stimulus incongruence in the current study, we surmise that it may have a more general role in
600 resolving cognitive conflict that allows for the filtering of irrelevant stimuli and engagement of the appropriate
601 task.

602 ***Study Limitations***

603 A limitation of this study is the relatively modest number of participants in our cohort, raising issues of
604 power and generalizability. Although 11 participants were studied, it merits re-emphasizing that this study
605 comprised a total of 42 scan sessions, with the express purpose of this design being to take advantage of a
606 repeated measures statistical approach in analyzing both the neuroimaging and behavioral data. It also bears
607 emphasizing that within each of the 42 scanning sessions, the density of data was considerably greater than is
608 typical of the great majority of studies in this field, where task-related data for each participant are typically
609 derived from sessions on the order of 10-20 minutes each. Here, each participant provided upwards of 3.5-to-4
610 hours of data for the task-based analysis, more than an order of magnitude more data than is typical. When
611 considering how well a study is powered, the density of data available for each subject is a key consideration. In
612 all experimental designs, the goal is to optimize the investigator's ability to observe possible signal relative to

613 background noise. While increasing sample size is one way to do this, another equally effective way is to
614 increase the number of repeated measures made of any given item/participant, as was done here.
615 Generalizability is a concern with any study that does not adequately sample a representative group of
616 individuals and this is certainly also the case with this study where the participants represent a convenience
617 sample, specifically recruited because they were easily accessible and could be relied upon to return for repeated
618 experimental sessions.

619 Another potential limitation pertains to the relatively rapid and regular stimulus presentation rates
620 utilized here and how these might affect the ability of the applied linear model to effectively extract processes
621 that were exclusively related to the condition of interest without other collinearities. Of course, in testing task-
622 switching processes, it is key that relatively fast and consistent cue-to-target intervals are used so that the
623 processes of interest are appropriately taxed. This is because the use of larger inter-trial-intervals introduces
624 entirely new factors, such as differential time-based task-set decay, while varying the length of inter-trial-
625 intervals has been shown to introduce sequential dependencies, such that switch costs on a current trial are
626 affected not only by the inter-trial-interval leading into that trial, but also by the one preceding it (Grange &
627 Cross, 2015). Therefore, the temporal structure of the current paradigm was designed to eliminate these other
628 confounds and was a necessary compromise. Returning to the original concern regarding the potential for
629 collinearities, it is also key to point out that while the alternation between trials was rapid and consistent in the
630 current study, the occurrence of the each of the conditions of interest was in fact random. As such, the timing
631 between instances of a given condition of interest (e.g. rule-switches) varied from 2 seconds to 60 seconds (see
632 Supplementary Figure E), a temporal structure that lends itself very well to the event-related fMRI approach.

633 As with any study, there are some limitations of interpretation based on our study design. One important
634 aspect to note is that every time there was a rule-switch, there was also a cue-switch (i.e. going from a blue
635 rectangle to a yellow rectangle). This can be a possible confound in that we have not isolated rule-switch effects
636 *independent* of cue-switch effects. Part of this issue is addressed because rule-switch trials included both those
637 that had blue cues preceded by yellow cues and trials that had yellow cues preceded by blue cues. However, one
638 study that did explicitly investigate cue-switch processes alone found that lateral premotor cortex, inferior
639 temporal gyrus, and fusiform gyrus were involved in encoding the cue information (Brass & von Cramon,

640 2004). We did not find these regions in our rule-switch analysis and therefore feel that it is unlikely that we are
641 capturing activity purely due to cue-switch effects.

642 Lastly, in the conjunction analyses presented herein, some of the overlapping voxels are limited to a
643 relatively small area. Unfortunately, this study does not allow us to determine whether such instances might
644 represent two distinct but overlapping loci of activity within the same region or whether these represent simple
645 activations of the same region. Here, we have chosen to discuss these findings as brain regional activations, and
646 it will fall to future work to more precisely investigate specific overlap patterns within a given functional region.

647 ***Conclusion***

648 This study demonstrates substantial differences in network activation for three distinct aspects of
649 cognitive flexibility within a single task-switching paradigm, pointing to largely dissociable sources of
650 competition (i.e., mostly non-overlapping neural circuits) as the primary modus by which separable sources of
651 competition are resolved. We did not find evidence for any one set of regions that was common to all three
652 sources of competition, although some regions were found to participate in conflict resolution across two of the
653 sources. Thus, while the study does not point to a set of domain-general processes, it does suggest shared
654 circuitry for some aspects of conflict resolution, with regions such as the precuneus, middle frontal cortex, and
655 inferior temporal gyrus implicated in resolving more than one source of conflict during task performance.

656 **Acknowledgments**

657 The authors thank Ms. Sarah Fendrich of Ossining High School who provided valuable assistance
658 during a summer internship with KMB at the Einstein Cognitive Neurophysiology Laboratory.

659

660 **Funding**

661 This work was supported by a grant from the National Science Foundation Division of Behavioral and
662 Cognitive Sciences (BCS1228595) to JJF.

663

664 **Data Sharing Statement**

665 At the time of publication, the authors will make all relevant data from this project available on a
666 publicly accessible data repository (e.g. Figshare).

667

668 **Disclosure of Potential Conflicts of Interest**

669 All authors declare that they have no affiliations with or involvement in any organization or entity with
670 any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

671

672 **Research involving Human Participants and/or Animals**

673 This research involved the participation of human subjects. The Institutional Review Board of Albert
674 Einstein College of Medicine approved all materials and procedures, and all ethical guidelines were in
675 accordance with the tenets of the Declaration of Helsinki.

676

677 **Informed Consent**

678 Informed, written consent was obtained from all participants included in this study.

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1118

Table 1. Demographics of Sample (N=11)

Characteristic	Mean	SD	Range
Age (years)	26.73	4.76	22-33
Education*	4	2	1-7
Ethnicity	N	%	
Hispanic/Latino	6	55	
Non-Hispanic/Latino	4	36	
Unknown	1	9	
Handedness	N	%	
Right	9	82	
Left	1	9	
Both	1	9	
Sex	N	%	
Male	9	82	
Female	2	18	

*Education = Highest degree earned: 1 = professional certificate; 2 = some college, no degree; 3 = associate degree; 4 = bachelors degree; 5 = masters degree; 6 = some graduate school; 7 = MD/PhD/JD/PharmD

Block Progression	
1	Pure - task A
2	Pure - task B
3	Mixed
4	Mixed
5	Mixed
6	Mixed
7	Pure - task A
8	Mixed
9	Mixed
10	Mixed
11	Mixed
12	Pure - task B
13	Mixed
14	Mixed
15	Mixed
16	Mixed

Table 2. Sequence of blocks throughout one scan session. Participants started with a pure block of one task, either the letter or number task, which was counterbalanced between participants and scans. This was followed by a pure block of the other task to counterbalance experience. Systematically throughout the scan, they had two more pure blocks. In the event participants' performance decayed over time, it would be possible to determine if it was an overall effect possible due to fatigue or a switch-specific effect.

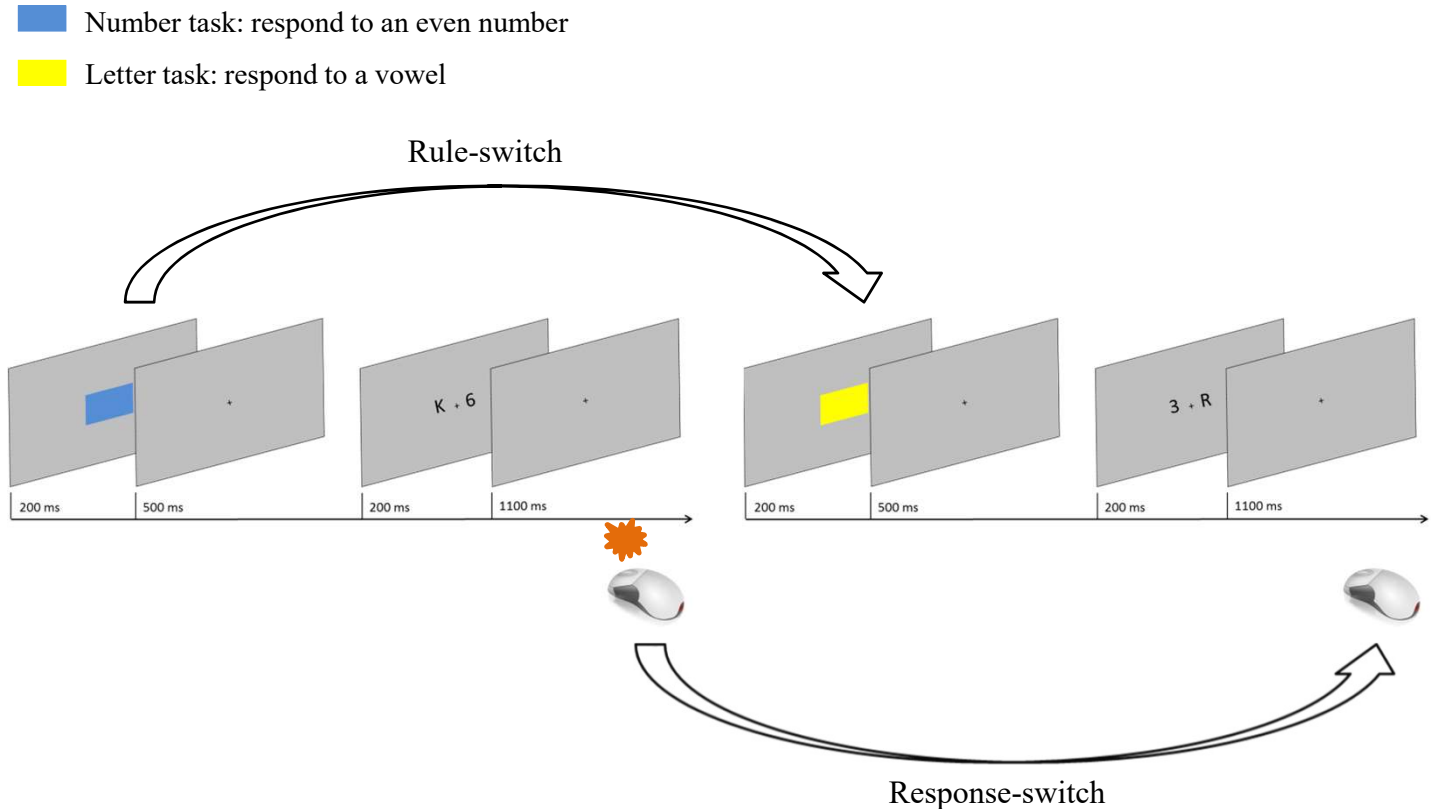


Figure 1. Example stimuli for two trials: a color cue was presented to indicate the task, 700 ms later the stimuli appeared and the participant responded within 1300 ms. The next color cue appeared, which could switch or repeat rules, thus creating a rule-switch or rule-repeat trial. Trials could have stimuli which were congruent with each other (i.e. indicating the same response for the letter task and number task) or incongruent with each other (i.e. the letter and number indicating different responses). In addition, each trial could be categorized by whether the motor response changed from the previous trial (e.g. a No-Go trial followed by a Go trial) or whether it repeated (e.g. a No-Go trial followed by a No-Go trial).

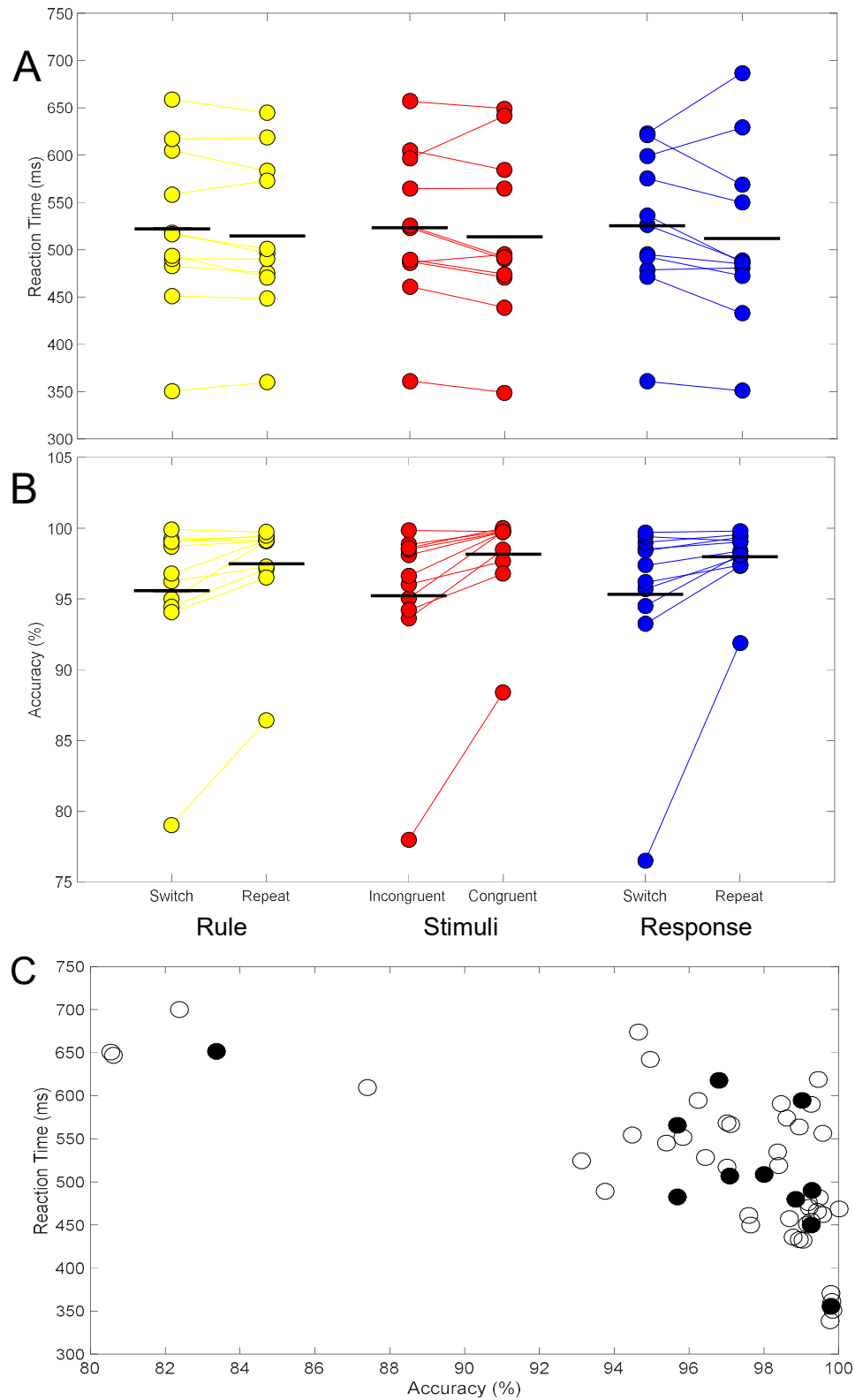


Figure 2.A) The average reaction times were slower for each of the three sources of conflict; B) the average accuracy was also slower; and C) reaction time and accuracy were negatively correlated based on both the averages of the participants (filled circles), or averages from each session (open circles).

	Response Times (ms)	
	Average	Standard Deviation
Subject 1	651.74	179.72
Subject 2	479.27	108.71
Subject 3	507.16	125.59
Subject 4	565.76	179.25
Subject 5	617.67	164.14
Subject 6	490.34	93.04
Subject 7	508.50	111.66
Subject 8	449.80	90.10
Subject 9	355.14	45.80

Table 3. Overall average response times for each participant and their standard deviations.

Contrast	Region	Center of Mass			Volume		Contrast	Region	Center of Mass			Volume	
		X	Y	Z	(voxels)	(cm ³)			X	Y	Z	(voxels)	(cm ³)
Rule-switch > Rule-repeat													
	R Posterior cingulate	27	-64	15	4702	126.95							
	L Posterior cingulate	-4	-39	18	986	26.62							
	L Inferior frontal junction	-41	7	32	1689	45.60							
						Overlap (Rule-switch \cap Incongruency)							
						L Precuneus							
						L Thalamus							
Incongruent > Congruent													
	R Cerebellum - posterior lobe tuber	40	-60	-24	897	24.22							
	R Insula	33	15	9	1373	37.07							
	R Posterior cingulate	4	-27	19	4505	121.64							
	R Superior frontal gyrus	21	52	3	560	15.12							
	L Medial frontal	-3	-1	48	2379	64.23							
	L Cerebellum - anterior lobe culmen	-2	-41	1	1234	33.32							
						Overlap (Incongruency \cap Response-switch)							
						R Medial frontal gyrus							
						L Middle frontal gyrus							
						L Claustrum/Putamen							
						L Inferior temporal gyrus							
						R Cerebellum - posterior lobe pyramis							
						R Cerebellum - posterior lobe tonsil							
Response-switch > Response-repeat													
	R Caudate	15	22	11	1198	32.35							
	R Thalamus	13	-7	8	822	22.19							
	R Postcentral Gyrus	55	-25	38	1593	43.01							
	L Anterior cingulate	-4	43	0	1993	53.81							

Table 4. Regions that came out significant in our repeated measures ANOVA of the imaging data for task-switching, incongruency, response-switching. The left-hand side of the table shows which regions came out only for each of the three analyses. On the right-hand side of the table are the clusters of voxels that were significant in more than one analysis. Centers of mass are in Talairach coordinates. The overall average beta-weights for each contrast are shown next to each ROI.

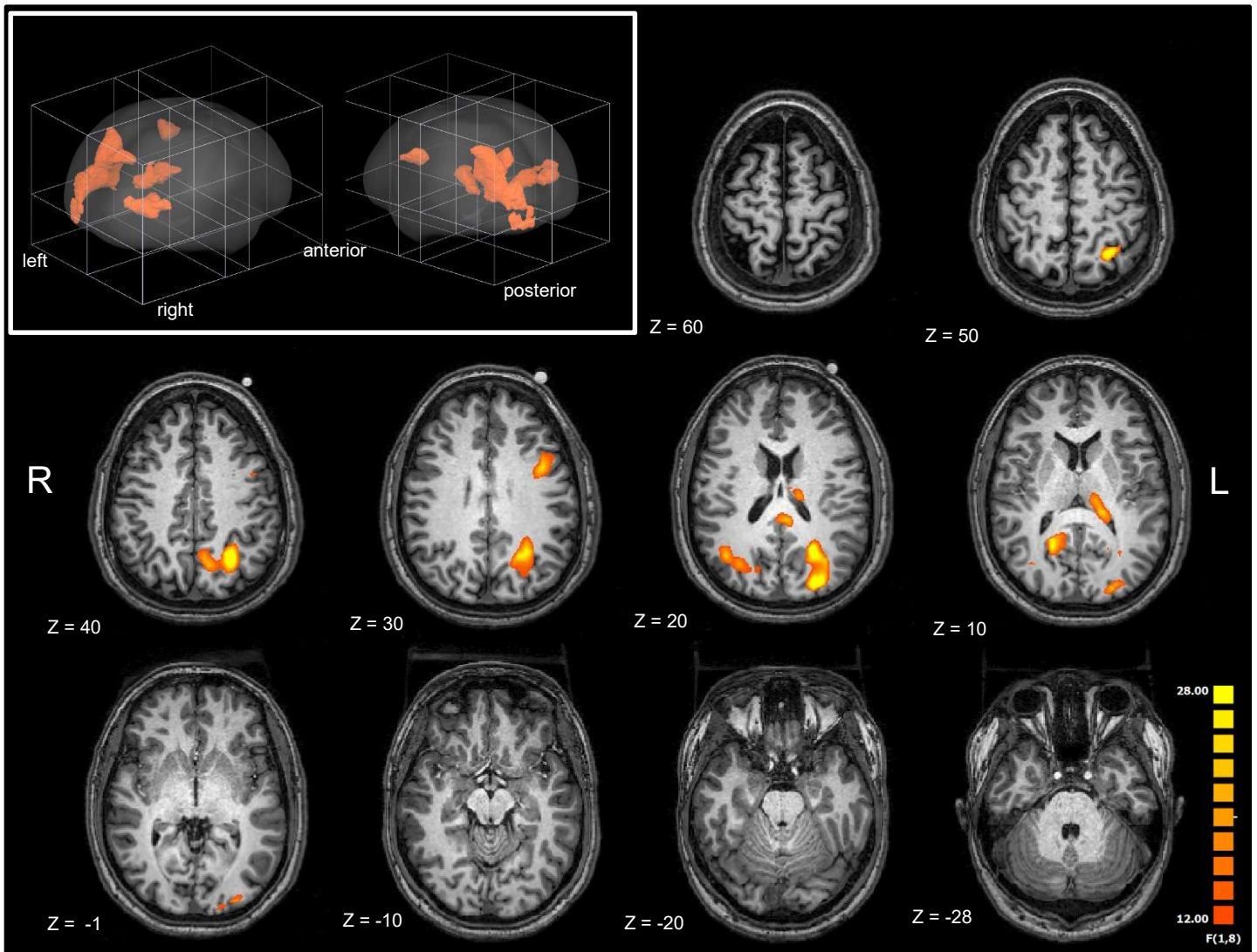


Figure 3. Map of regions significantly involved in rule-switching. The upper left panel shows all the significant regions in orange in a 3D rendering. In the horizontal slices, the color range is according to the F-stat for each voxel, ranging from 12 to 28. Images are in radiological format (right is left), and z coordinates are in Talairach space.

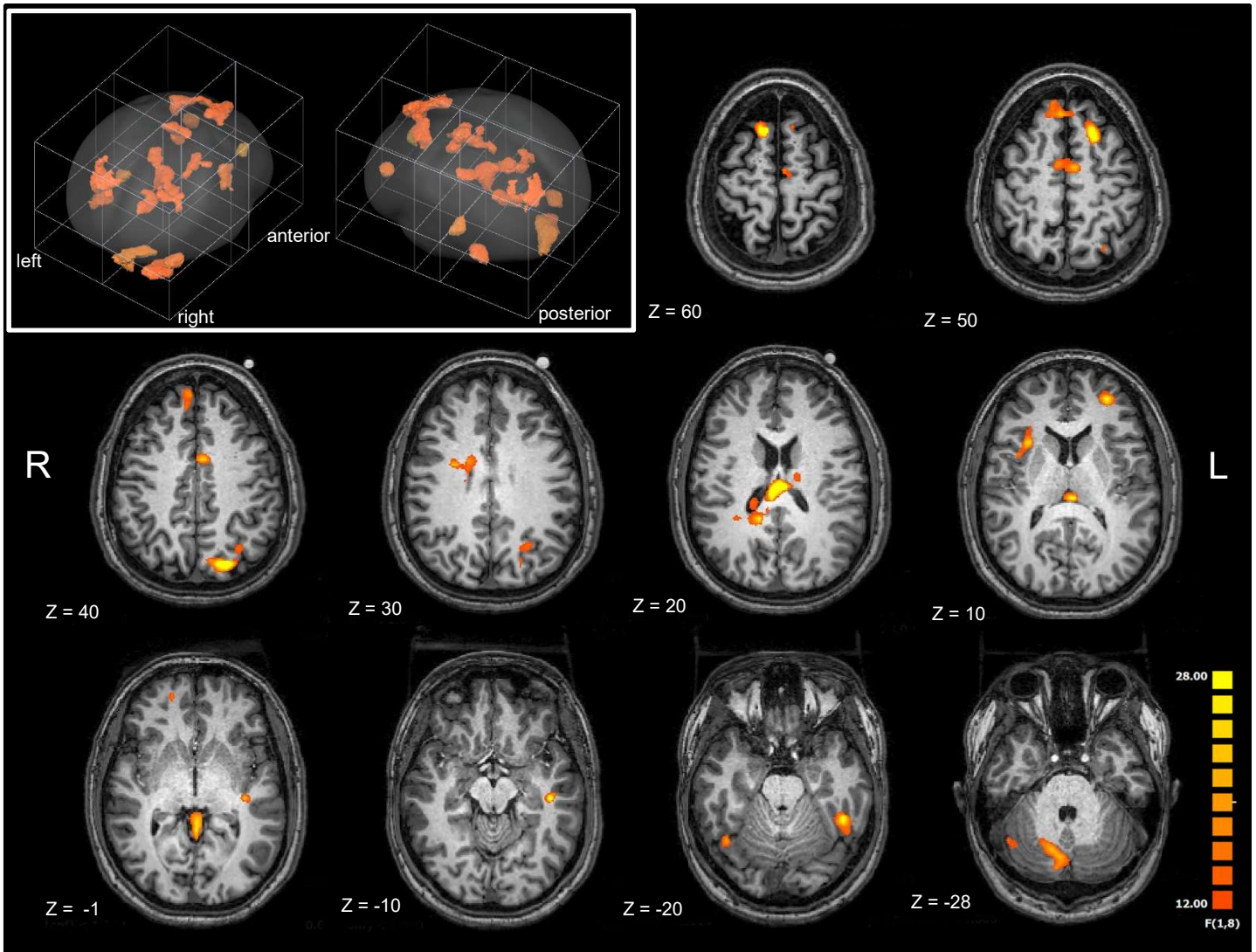


Figure 4. Map of regions significantly involved in incongruity. The upper left panel shows all the significant regions in orange in a 3D rendering. In the horizontal slices, the color range is according to the F-stat for each voxel, ranging from 12 to 28. Images are in radiological format (right is left), and z coordinates are in Talairach space.

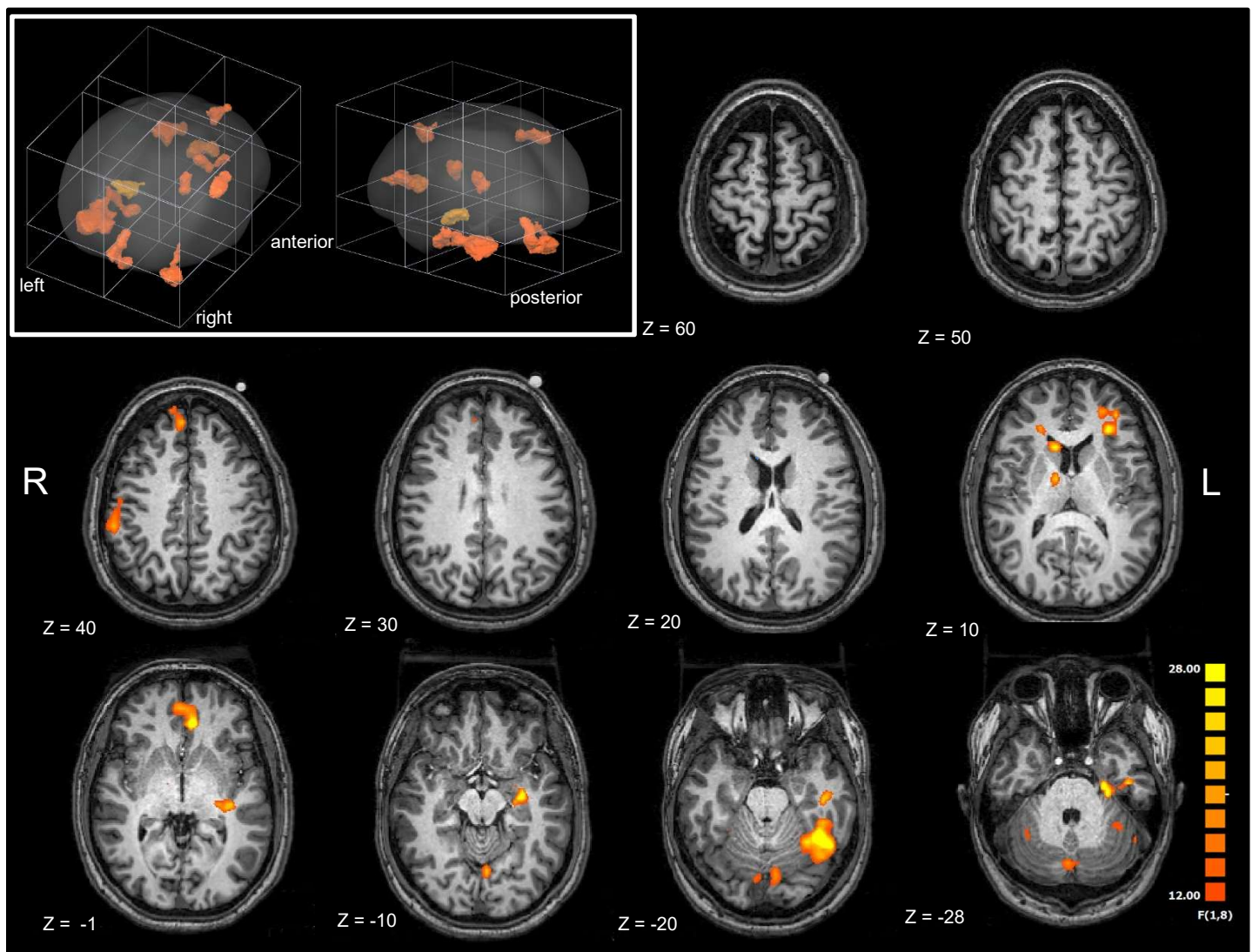


Figure 5. Map of regions significantly involved in response-switching. The upper left panel shows all the significant regions in orange in a 3D rendering. In the horizontal slices, the color range is according to the F-stat for each voxel, ranging from 12 to 28. Images are in radiological format (right is left), and z coordinates are in Talairach space.

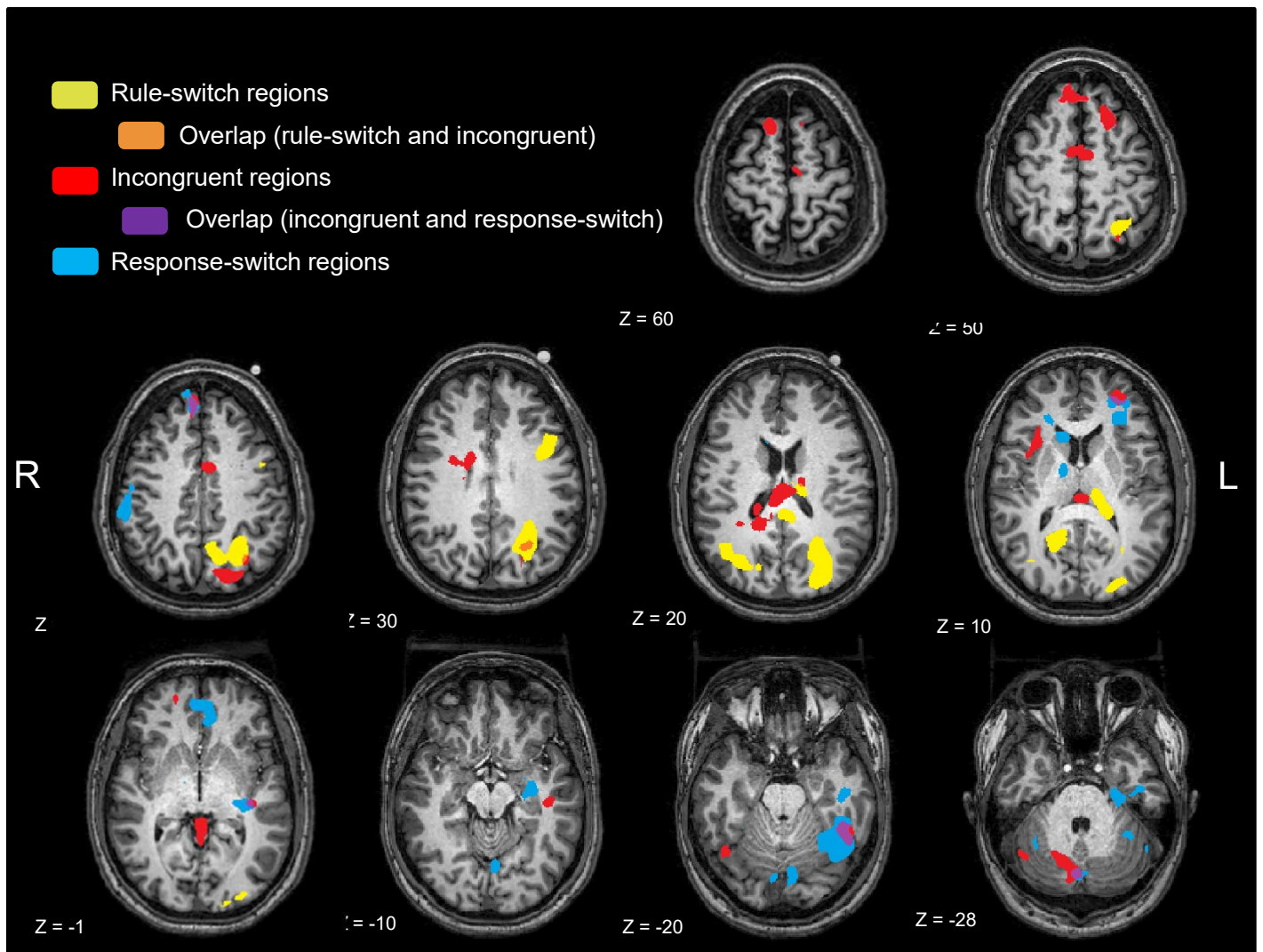


Figure 6. Map of all areas involved in all three sources of conflict, including where they overlap. For simplicity, solid colors are used to represent each condition or overlap of conditions. Images are in radiological format (right is left), and z coordinates are in Talairach space.

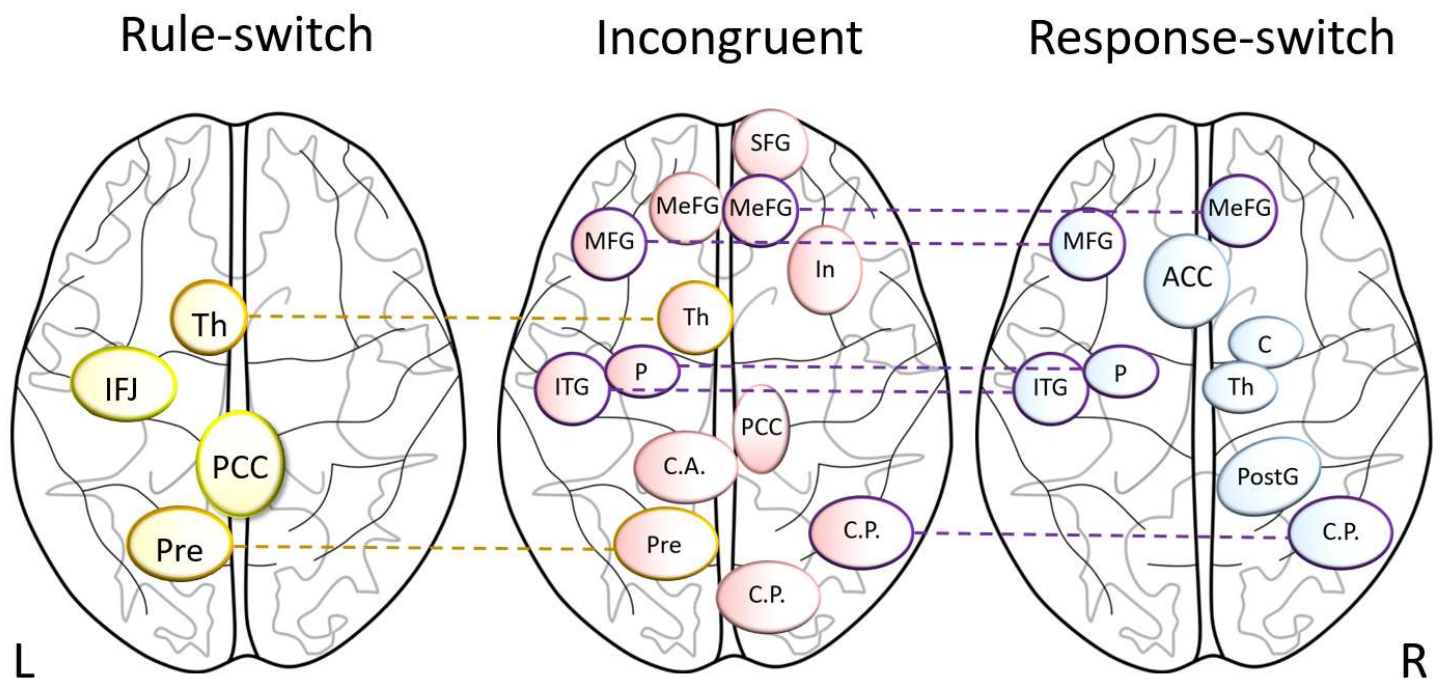
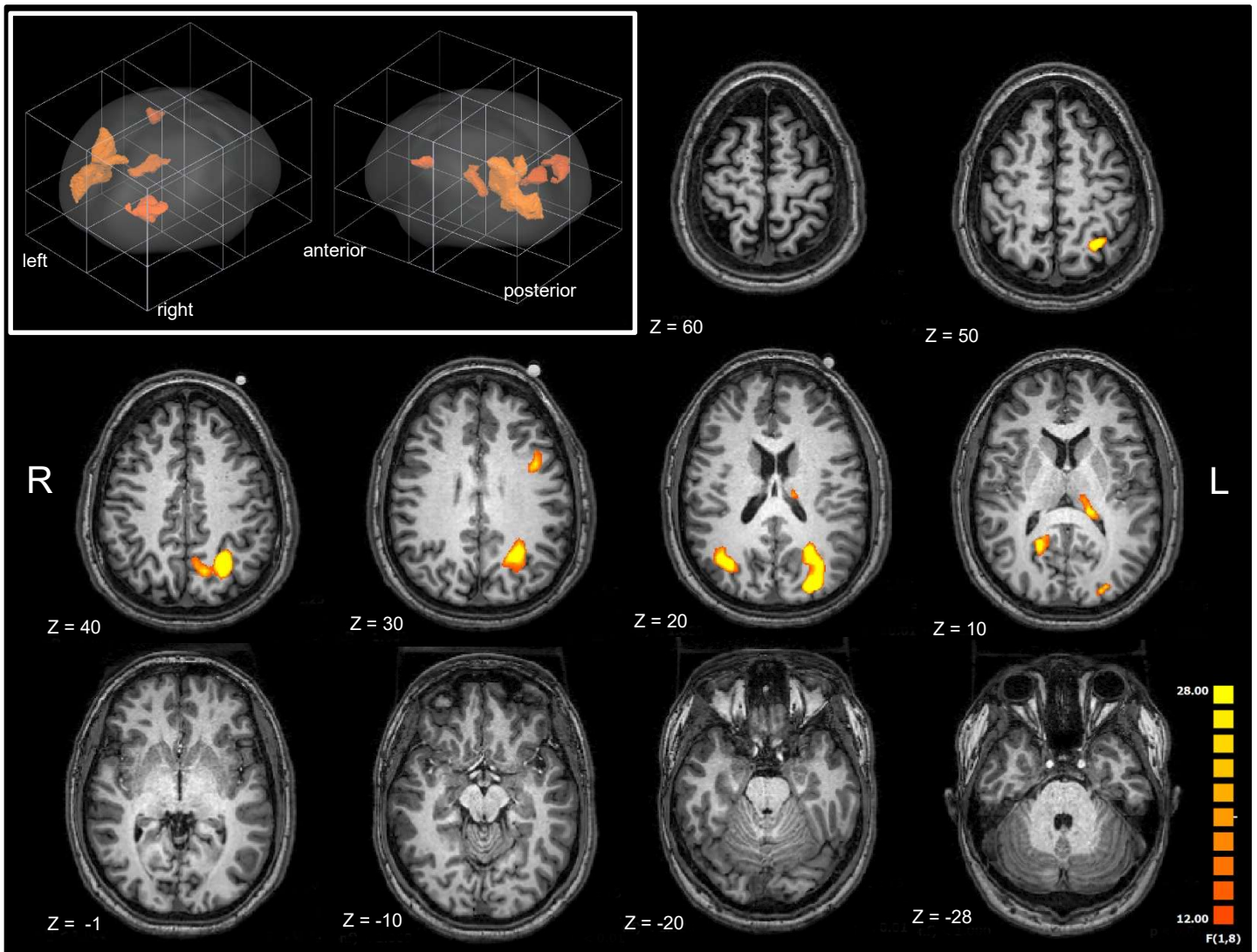


Figure 7. Schematic representation of the regions involved in the three sources of conflict investigated in this study. While some regions were involved in more than one source of conflict (dotted lines), there were no domain-general regions involved in all three.

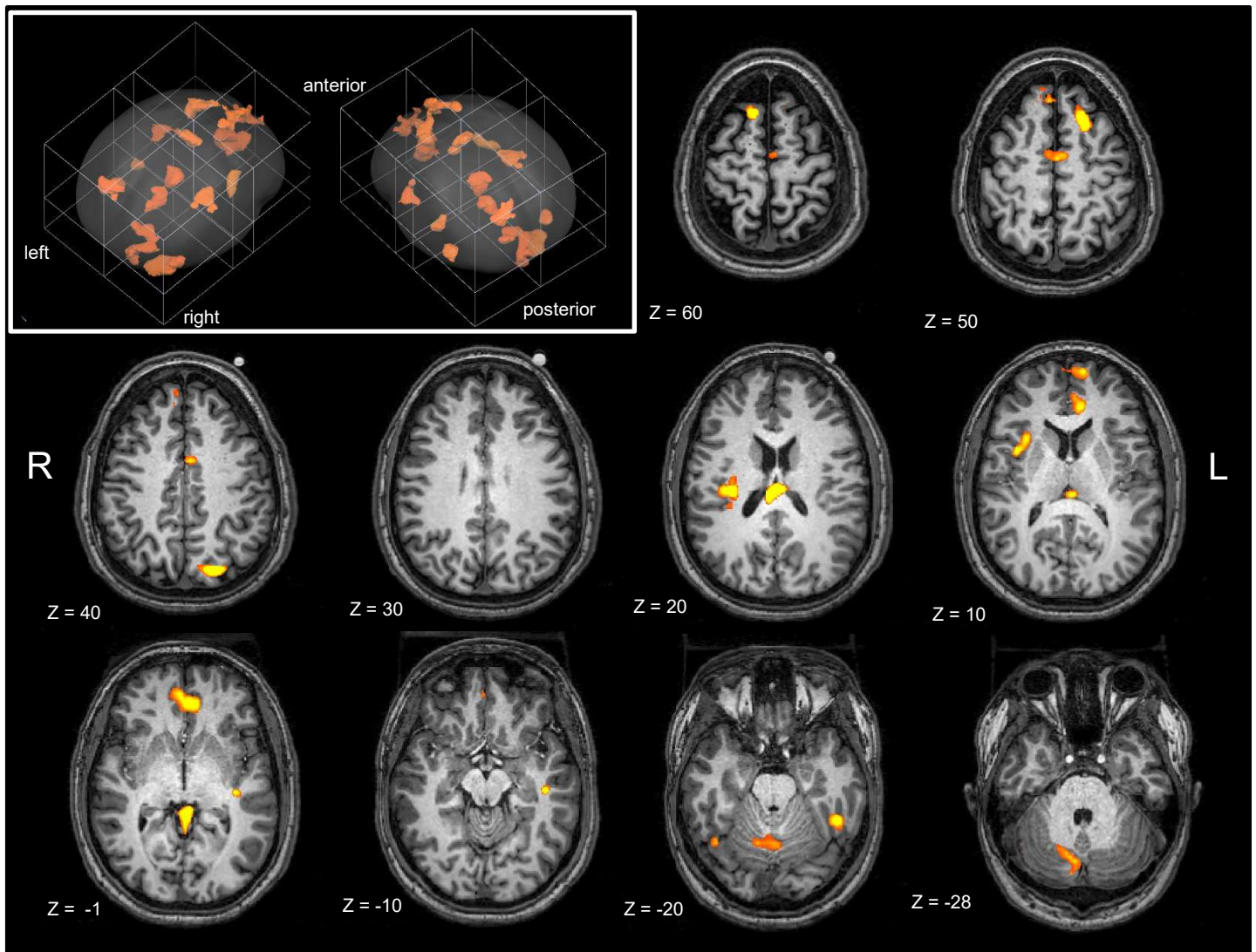
Legend: ACC = anterior cingulate cortex, C = caudate, C.A. = cerebellum anterior lobe, C.P. = cerebellum posterior lobe, In = insula, IFJ = inferior frontal junction, ITG = inferior temporal gyrus, MeFG = medial frontal gyrus, MFG = middle frontal gyrus, P = putamen, PCC = posterior cingulate cortex, PostG = postcentral gyrus, Pre = precuneus, SFG = superior frontal gyrus, Th = thalamus.

Supplementary Table A. Acronyms Used in This Paper

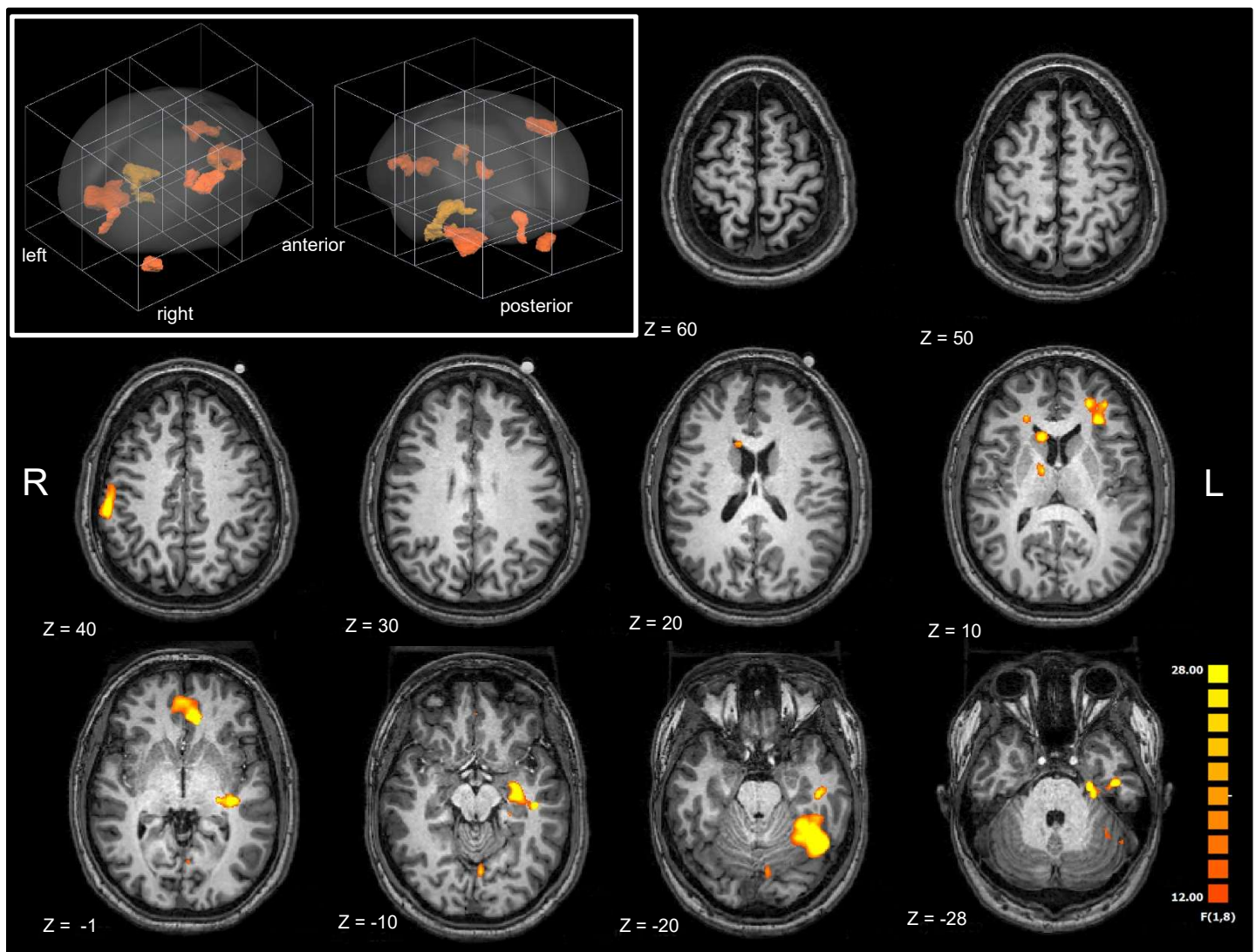
ACC	anterior cingulate cortex
ASD	autism spectrum disorders
DLPFC	dorsolateral prefrontal cortex
EEG	electroencephalography
fdr	false discovery rate
fMRI	functional magnetic resonance imaging
IFJ	inferior frontal junction
PPC	posterior parietal cortex
pre-SMA	pre-supplementary motor area
RFX-GLM	random-effects general linear model
RT	reaction time
TE	echo time
TR	repetition time



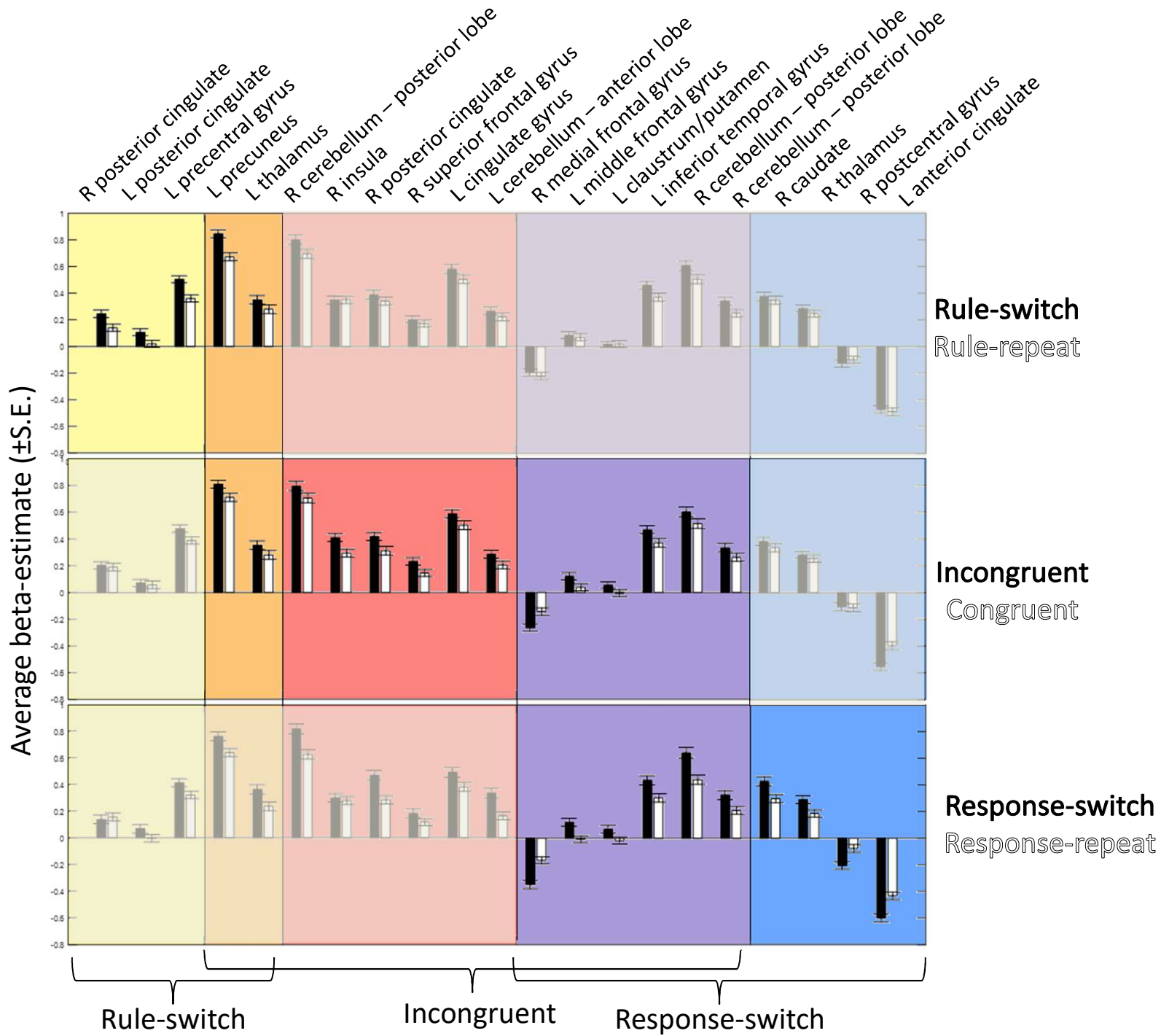
Supplementary Figure A. Map of regions significantly involved in rule-switching excluding the one potential outlier participant. The upper left panel shows all the significant regions in orange in a 3D rendering. In the horizontal slices, the color range is according to the F-stat for each voxel, ranging from 12 to 28. Images are in radiological format (right is left), and z coordinates are in Talairach space. This map shows a strong resemblance with Figure 3 with all participants.



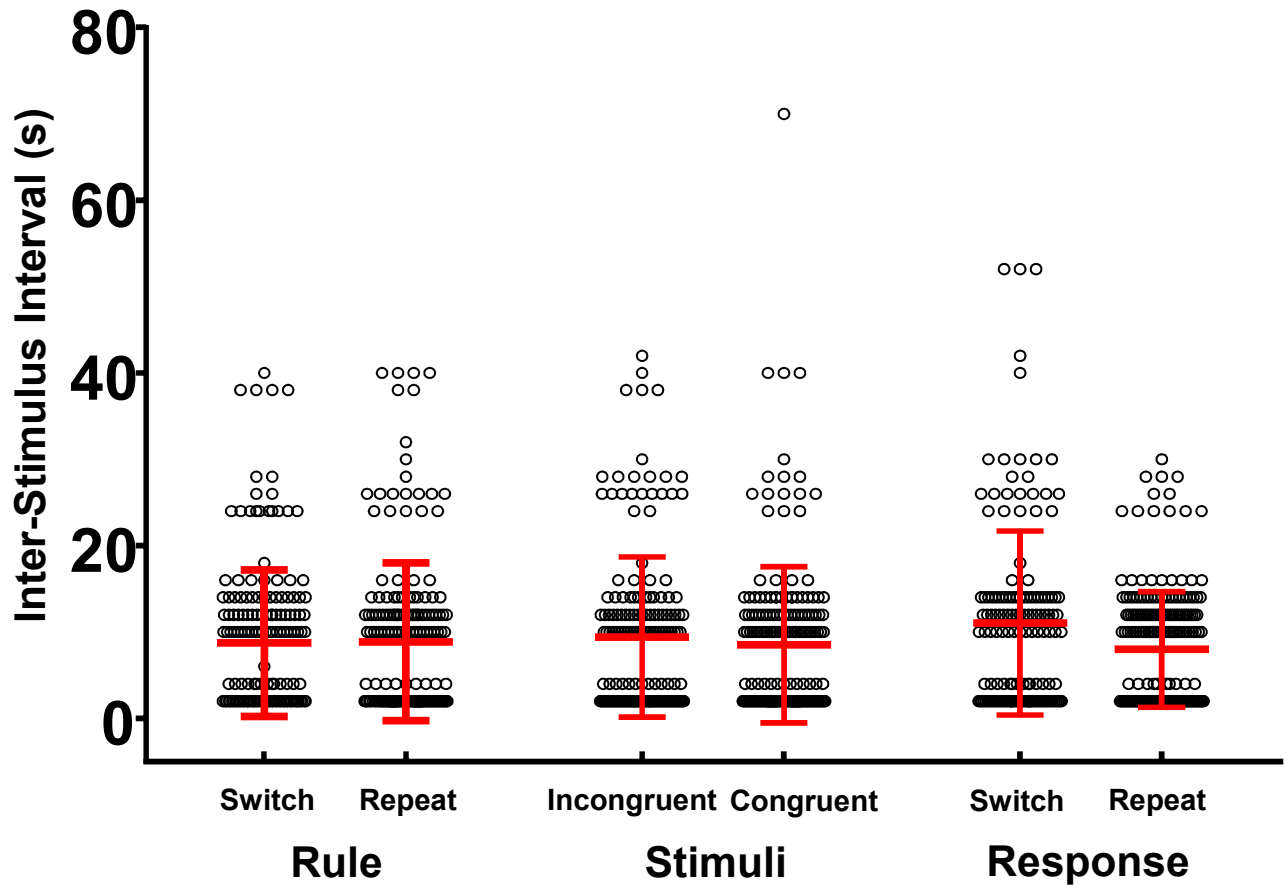
Supplementary Figure B. Map of regions significantly involved in incongruity, excluding one potential outlier participant. The upper left panel shows all the significant regions in orange in a 3D rendering. In the horizontal slices, the color range is according to the F-stat for each voxel, ranging from 12 to 28. Images are in radiological format (right is left), and z coordinates are in Talairach space. This map is very similar to Figure 4 which contained all participants together.



Supplementary Figure C. Map of regions significantly involved in response-switching, excluding one potential outlier participant. The upper left panel shows all the significant regions in orange in a 3D rendering. In the horizontal slices, the color range is according to the F-stat for each voxel, ranging from 12 to 28. Images are in radiological format (right is left), and z coordinates are in Talairach space.



Supplementary Figure D. Beta-estimates for each significant cluster found in our analyses under each condition. They are sorted by which analyses they came out significant for. The top row shows beta-estimates for rule-switching and rule-repeating, the middle row is for incongruent and congruent trials, and the bottom row shows estimates for response-switching and response-repeating. Averages and standard errors are computed with the beta-estimates from each run from each participant.



Supplementary Figure E. Event-related fMRI studies can succumb to an issue where the conditions occur at the same time throughout runs or scan sessions and confound the general linear model. Here we demonstrate that the conditions in our study were randomly placed through each run and session so that, although the average inter-stimulus interval is 9 seconds, the standard deviation and variability is similarly around 10 ms.