

# Complexity in Relational Processing Predicts Changes in Functional Brain Network Dynamics

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**The ability to link variables is critical to many high-order cognitive functions, including reasoning. It has been proposed that limits in relating variables depend critically on relational complexity, defined formally as the number of variables to be related in solving a problem. In humans, the prefrontal cortex is known to be important for reasoning, but recent studies have suggested that such processes are likely to involve widespread functional brain networks. To test this hypothesis, we used functional magnetic resonance imaging and a classic measure of deductive reasoning to examine changes in brain networks as a function of relational complexity. As expected, behavioral performance declined as the number of variables to be related increased. Likewise, increments in relational complexity were associated with proportional enhancements in brain activity and task-based connectivity within and between 2 cognitive control networks: A cingulo-opercular network for maintaining task set, and a fronto-parietal network for implementing trial-by-trial control. Changes in effective connectivity as a function of increased relational complexity suggested a key role for the left dorsolateral prefrontal cortex in integrating and implementing task set in a trial-by-trial manner. Our findings show that limits in relational processing are manifested in the brain as complexity-dependent modulations of large-scale networks.**

**Keywords:** cognitive control, reasoning, connectivity, fMRI, prefrontal cortex

## Introduction

In humans, higher order cognition such as deductive reasoning is crucial for adaptive and rational goal-directed behavior (Johnson-Laird 2010). Given increasingly complex task demands, cognitive abilities typically become more effortful and can eventually break down, suggesting that task complexity places limits on higher order cognition and the regulation of adaptive behavior (Halford et al. 2005). Investigations of the brain underpinnings of such limits in processing complex information are crucial for understanding the biological processes that underlie higher cognitive capacities in humans.

A critical component of cognitive reasoning is the ability to ascertain relationships between contextual variables, and to act in accordance with these relations to produce appropriate responses (Bunge, Wallis et al. 2005). This concept has been formalized in the “relational complexity metric,” which postulates that the cognitive load of deductive reasoning is related to the number of variables that need to be linked into a representation of the problem’s solution (Halford, Wilson et al. 1998; Halford et al. 2007).

Several studies have shown that the prefrontal cortex plays a central role in regulating the formation, maintenance, and use of relations between variables (Christoff et al. 2001; Kroger et al. 2002; Bunge, Wendelken et al. 2005; Badre et al. 2010; Golde et al. 2010; Crescentini et al. 2011; Krawczyk et al. 2011; Watson and Chatterjee 2011). Evidence supports a rostral-caudal gradient of function within the prefrontal cortex, with more abstract and complex relations processed by progressively more rostral regions (Koechlin and Summerfield 2007; Badre and D’Esposito 2009; Badre et al. 2010). Results from functional magnetic resonance imaging (fMRI) studies further suggest that these prefrontal regions may interact with posterior brain regions, including the superior parietal lobule and the occipital cortex, to integrate, maintain, and implement relations during reasoning (Goel and Dolan 2001; Kroger et al. 2002; Goel 2007; Golde et al. 2010; Wendelken et al. 2011; Reverberi et al. 2012; Knowlton et al. 2012). More broadly, the evidence for such segregated brain activity during the processing of relations is consistent with recent studies suggesting that trial-by-trial cognitive control engages a large-scale functional brain network encompassing frontal and parietal cortices (Dosenbach et al. 2006, 2007, 2008).

Here, we used a classic deductive reasoning paradigm, the Wason Selection Task (Wason 1968), and novel fMRI analyses to examine the influence of relational complexity on network-based neural dynamics. In its general form, the Wason task requires participants to determine whether a given rule can be disconfirmed by a small subset of propositions. As it is known that even highly educated individuals make characteristic errors of logic in this task (Wason 1971; Evans and Ball 2010), we initially trained our participants to help them avoid these misconceptions and to minimize individual differences in strategies. We manipulated relational complexity by parametrically varying the number of variables that needed to be integrated to solve a given problem. Using this design, we aimed to characterize any complexity-induced changes in brain activity and modulatory coupling (i.e., connectivity) among frontal and prefrontal regions (Christoff et al. 2001; Kroger et al. 2002; Bunge, Wallis et al. 2005; Badre et al. 2010; Crescentini et al. 2011; Krawczyk et al. 2011). We examined complexity-induced changes in frontal dynamics in the context of broader functional changes in a large-scale cognitive control network operating on a rapid (trial-by-trial) timescale, and encompassing fronto-parietal cortices. We also examined whether functional changes in the fronto-parietal network are dynamically related to changes in a cognitive control system operating at a slower timescale (determined by task set; Dosenbach et al. 2007, 2008). We predicted that

functional interactions within and between these 2 major control systems should play a central role in limiting the integration of complex relations during reasoning.

## Materials and Methods

### Participants

Twenty-three right-handed, adult participants (12 females) were recruited. One female participant was excluded from the analyses due to excessive head motion (>2 mm) during the functional acquisition, and 1 male participant was discarded due to technical failure in acquiring behavioral data. Thus, data from 21 participants, aged from 21 to 39 years (mean  $\pm$  SD = 28.6  $\pm$  5.0 years), were included in the analyses. All participants provided informed written consent to participate in the study, the procedures of which were approved by The University of Queensland Human Research Ethics Committee. The study was conducted in accordance with the Declaration of Helsinki.

### Paradigm and Procedures

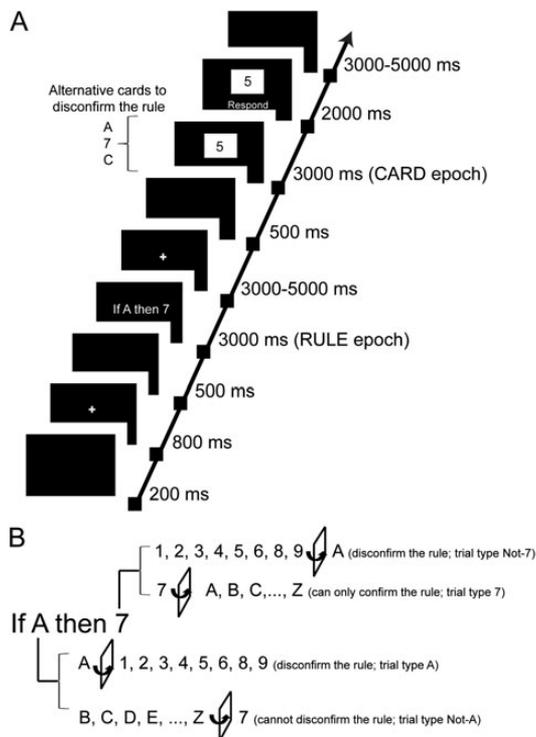
We optimized the conventional version of the Wason Selection Task (WST) for functional magnetic resonance imaging (fMRI), and programmed the task using Presentation software (<http://www.neurobs.com/>). The design of this modified reasoning task is depicted in Figure 1A.

Each trial commenced with a central fixation cross (800 ms) followed by a short-blank interval (500 ms), before a logical rule establishing a relation between 2 alphanumeric variables (e.g., “If A then 7”) was presented for 3000 ms. Rules always consisted of a single letter and a single digit (1–9), with letters and digits presented with equal frequency as the first and second elements of the rule across runs. A total of 180 different rules were presented throughout the experiment. Following a randomly varied time period of 3000–5000 ms, a single digit (50% of the trials) or letter was displayed for 3000 ms. Participants were instructed to consider this character as one side of a card and to indicate, as quickly and as accurately as possible, if the card was potentially able to “disconfirm” the rule, assuming the other side of the card could contain any possible letter (if the face side contained a number) or digit (if the face side contained a letter; see Fig. 1B). Critically, participants were instructed that the rule was not bidirectional. Thus, for example, the rule “If A then 7” does not imply “If 7 then A.”

Five unique task conditions were created by presenting card elements that were 1) the same as the first element of the rule (e.g., A, assuming the rule “If A then 7”); 2) different to the first element of the rule (e.g., C); 3) the same as the second element of the rule (e.g., 7); 4) different to the second element of the rule (e.g., 5); and 5) a nonalphanumeric element that was completely unrelated to the rule, serving as an active control condition (e.g., %). A null trial, in which a white fixation cross was presented for the whole duration of the trial, was also included as a passive control condition. These 6 trial types were presented with equal frequency in pseudo-random order across 5, 10-min runs, each consisting of 36 task trials (6 per condition). The order of trials in each run was generated using the fMRI sequence-optimizing algorithm *optseq2* (<http://surfer.nmr.mgh.harvard.edu/optseq/>).

Stimuli were projected onto a semitransparent viewing screen located at the head end of the MR scanner using an LCD projector. Participants viewed the projected stimuli via a mirror mounted on the head coil. Participants were instructed to respond as quickly and as accurately as possible within a 2000-ms window after the word “Respond” appeared on the screen (Fig. 1A), so that no motor activity was present during the card period. Responses were registered using an MR-compatible optical fiber response box.

Prior to entering the MRI scanner, participants engaged in a training and practice session that lasted ~30 min, to ensure that the logic of the task was clearly understood and to minimize individual differences in strategy. Given our example rule (If A then 7), if the first element of the rule (A) appeared on the card, any element other than



**Figure 1.** Schematic representation of the experimental paradigm. We developed a modified version of the Wason Selection Task, in which participants engage in a card-turning game with the goal of disconfirming a given rule (e.g., “If there is an A on one side of the card, there is a 7 on the other”). Cards always had a digit on one side and a letter on the other. (A) On each trial, participants were first shown a rule, followed by a single card (e.g., 5) that might or might not be able to disconfirm the rule. (B) Before starting the experiment, participants practiced the task with feedback to ensure they understood the rules and to reduce errors and individual differences in cognitive strategies. For the example shown here, if the face side contains any digit but the one mentioned in the rule (i.e., a 7), then the rule is disconfirmed if A appears on the reverse side. By contrast, if there is a 7 on the face, no letter on the reverse side can disconfirm the rule. If there is an A on the face, any digit on the reverse other than 7 can disconfirm the rule. If any letter but A appears on the face no digit on the reverse side can disconfirm the rule.

7 on the reverse side of the card disconfirms the rule (e.g., a 5 on the other side of the card would disconfirm the rule). Therefore, the answer would be “yes.” This is trial type “A” in Figure 1B). By contrast, if a card shows an element that differs from the rule’s first element (e.g., “C,” trial type “Not-A,” Fig. 1B), this cannot inform on the validity of the rule because “C” and “5” do not disconfirm “If A then 7.” Therefore, the answer is “no.” If a card shows an element that matches the second element of the rule (trial type 7 in Fig. 1B), this card can only “confirm” the rule (if the reverse side contains “A”) but cannot disconfirm it (if the reverse side contains a letter other than “A”). Therefore, the answer is “no.” Finally, a card showing an element that is different from the rule’s second element (“Not-7” in Fig. 1B) can disconfirm the rule (e.g., if the card shows a 5, then an A on the other side would disconfirm the rule “If A then 7”). Therefore, the answer would be “yes.” Participants practiced the task, with feedback, on a desktop computer. Results from the practice session confirmed that all participants performed the task above what would generally be expected in such WST paradigms (Canessa et al. 2005).

Critically, a “different rule” was displayed prior to every card, so that it was not possible for participants to reduce the task to a mere matching of elements. For every problem, therefore, elements had to be identified by mapping between card elements and rule elements, based on the relation in the rule. Thus, for the new rule, “If 3 then Z,” a “2” is a “Not-3” card, a “P” becomes a “Not-Z” card, and so on. The relation between “3” and “Z” is mapped to the relation between (say) “2” and “P,” and the status of card elements is defined by this relation

in at least some cases, as outlined below. To summarize, therefore, while our training regime reduced errors and encouraged a consistent cognitive strategy across participants, it did not obviate or circumvent the relational processes that the task is designed to measure.

According to the relational complexity metric, the relative complexity of deductive reasoning elicited by each card can be quantified by the number of variables that need to be linked in order to determine whether the card can disconfirm the rule (Halford, Wilson et al. 1998; Halford et al. 2007; Halford et al. 2010). The rule “If *A* then 7” relates 2 variables, the “antecedent” (*A*) and “consequent” (7). Each card also contains 2 variables, corresponding to the element on the “face” side (*A*, *C*, 5, 7 in this example) and the possible element on the “reverse” side (with any alphanumeric character).

Alphanumeric characters on the card that match either element of the rule (e.g., *A* or 7) provide an aid that reduces the cognitive load of the reasoning required. The *A* card matches the antecedent of the rule, and if the reverse side is Not-7 (e.g., 5), the rule is disconfirmed. This is a binary relation, *A* and Not-7, which is of low complexity. The 7 card matches the consequent of the rule, and if the face side is Not-*A*, the rule is not disconfirmed. This also is a binary relation, Not-*A* and 7, though the match to the consequent (7) would be less accessible than the direct match between the *A* and the antecedent. Consequently, the 7 card should be somewhat more difficult than the *A* card. In contrast, the *C* card (also referred to as the Not-*A* card) requires not only consideration of the 2 rule variables, but also identification of the face variable as a negative instance of the antecedent variable. Processing the negation of the antecedent increases the complexity and is equivalent to the ternary relation (*C*, not-antecedent, consequent). Finally, the 5 card (or Not-7) requires participants to consider that the “reverse” element could be *A*, then to construct a representation of the relation *A* and Not-7 negates “*A* implies 7.” The 5 does not match the *A* component of the rule, and the Not-7 does not match the 7 component of the rule, so both internal representations must be generated, and then related to the antecedent and consequent of the rule. This relation requires the internal representation of all 4 variables, which is at the limit of human relational processing capacity (Halford et al. 2005). Thus, according to the relational complexity metric, the *A* and the 7 cards represent the lowest level of relational complexity, the Not-*A* (*C*) card represents the next highest level of complexity, and the Not-7 card represents the highest complexity of all cards.

### Magnetic Resonance Imaging

Acquisitions were conducted on a 3T Siemens Magnetom Trio magnetic resonance scanner (Erlangen, Germany) using a 32-channel head coil. Functional sequences consisted of gradient-echo echo-planar images (GE-EPI; time to repetition, 2550 ms; time to echo, 32 ms; flip angle, 90°) within a field of view of 210 × 210 mm, an in-plane resolution of 3.3 × 3.3 mm, and with a slice thickness of 3 mm (no gap). Thirty-seven interleaved axial slices were acquired to cover the entire brain for all functional sequences. The first 2 images were discarded to allow tissue magnetization to reach a steady state.

### Data Analysis

#### Behavioral Analysis

Task accuracy and reaction time (RT) data did not follow a normal distribution and were therefore analyzed using univariate nonparametric statistics (Friedman test) implemented in SPSS 19 (Chicago, IL, USA).

#### fMRI

**Preprocessing.** Image preprocessing and analysis was performed in SPM8 (Wellcome Department of Cognitive Neurology, London, UK). Functional images were corrected for acquisition time (slice timing), spatially realigned to the middle volume and spatially normalized to a standard neuroanatomical space defined by the Montreal Neurological Institute (MNI) EPI template. The normalized images were resampled to 3-mm isotropic voxels and then smoothed with FWHM Gaussian

kernel of 8 mm. Time-series were high-pass filtered with a 128-s cut off period to remove low-frequency noise and signal drifts, and were additionally corrected for first-order (AR1) serial autocorrelations.

**Statistics.** Statistical analyses were performed by adopting the general linear model (GLM) as implemented by SPM8 running in Matlab (Natick, Massachusetts, USA). At the first level (within-subject analysis), conditions of interest were modeled as boxcar functions convolved with a canonical hemodynamic response function and its temporal derivative. The model comprised regressors for the rule presentation epochs (3 s), the card epoch (3 s) for each card type, and null epochs of 3 s overlapping in time with the rule and card presentation epochs. Given that errors were one of our predictors for changes in brain activity and connectivity as a function of complexity, the card regressors included both correct and incorrect trials. The inclusion of all trials also guaranteed balanced within-subjects contrasts between the different card conditions. Note that activity associated with the rule period was not modeled separately for the different card conditions, as rules were always of the same format and complexity. Estimated motion parameters were also included in the model as nuisance regressors. The resulting first-level contrast images were carried over to second-level random-effects analyses.

**Brain activity during the rule period.** We first examined patterns of brain activity associated with the formation and encoding of trial-specific relations by comparing blood oxygen-level-dependent (BOLD) changes during the null epochs with BOLD changes during the rule epochs. For this analysis, the threshold for significance was set to  $P < 0.05$  corrected for multiple comparisons at the cluster level [Familywise error (FWE) correction, cluster sizes estimated at  $P = 0.001$  uncorrected].

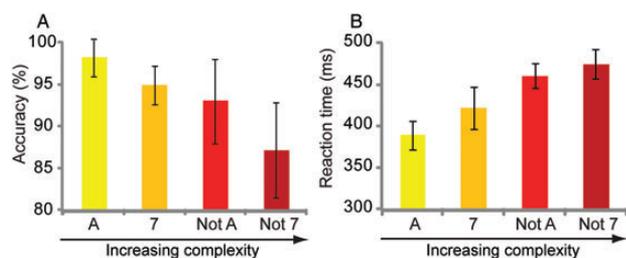
**Brain activity during the card period.** We next isolated the average BOLD responses related to processing of the different card conditions ( $P < 0.05$  FWE corrected at cluster level, cluster size estimated at  $P = 0.001$  uncorrected). Neural activity during the null epochs was compared with the average activity from the card epochs. Post hoc analyses were undertaken to interrogate significant activations arising from the different card conditions. Specifically, task-related  $\beta$ -regression values were extracted from spheres having a diameter of 5 mm and centered on the average local maxima of each region of interest. Differences across card conditions were tested using standard univariate statistics. To further explore changes in brain activity in the regions of interest, we analyzed the evolution of the BOLD signal as a function of time in each card condition (i.e., event-related BOLD time course). This latter analysis was performed using algorithms implemented in the software rfxplot (Gläscher, 2009).

**Effective connectivity changes associated with card processing.** Functional interactions supporting card processing were investigated with psychophysiological interaction (PPI) modeling (Friston et al. 1997; O'Reilly et al, 2012). PPI is a well-established technique that can be used to determine whether the connectivity between a pair of regions increases during a given context or task. Here, we used PPI to examine such connectivity during the processing of each card type. PPI analyses have typically been implemented to assess which voxels in the brain show an increase in context-specific connectivity with respect to a single predefined seed region. Pairwise correlation is not a desirable connectivity measure in this case because it does not disambiguate context-specific connectivity from resting-state connectivity or connectivity associated with a common neuromodulatory input. We implemented a multiregional PPI to assess how the influence of each brain region on all others was modulated during the processing of each card type. Multiregional PPI is a simple generalization of the PPI approach; rather than assessing the connectivity between a single-seed region and all brain voxels, we defined multiple regions and assessed the connectivity between each pair of regions. The 18 regions considered corresponded to the main clusters isolated by the GLM analysis (i.e., the average card effect, FWE corrected at the voxel

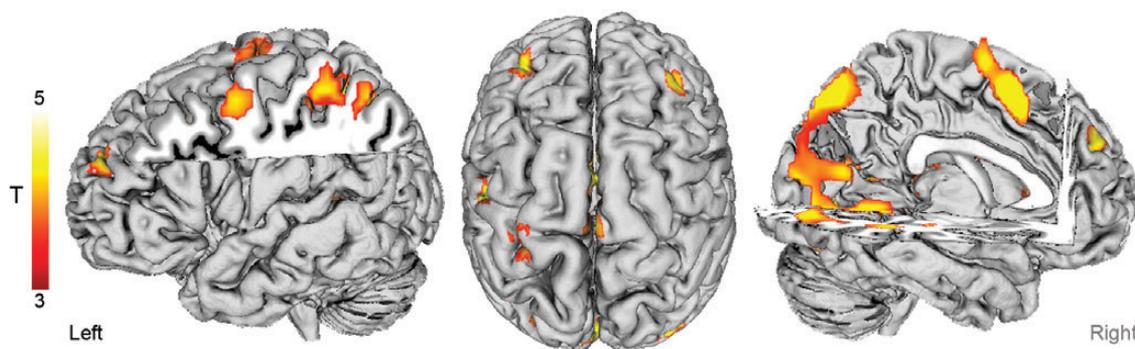
level). For each participant and region, brain activity (first eigenvariate) was extracted from a spherical seed region having a diameter of 5 mm around the peak activation voxel, defined by a positive average card effect minus the temporally corresponding baseline (null trials).

The PPI signal was determined for each region by elementwise multiplication of the region's activity with the card versus baseline regressor. This PPI signal is therefore equal to the region's activity during times associated with processing of a specific card, but zero for all other card processing conditions and  $-1$  for the baseline. Note that the hemodynamic response function (HRF) was first deconvolved from the region's activity before multiplication, and the final PPI term was convolved with the HRF. These steps were performed using SPM (spm\_peb\_ppi.m) for each region, card type, and participant. A GLM was used to model card-dependent influences of any given region upon another. The activity of the region being influenced (i.e., the target, or afferent region) was the dependent variable, while the explanatory variable was the PPI term corresponding to the region exerting the influence (i.e., the source, or efferent region). In this way, a region for which the PPI signal is a good predictor of its activity indicates a stronger influence on that region (by the region used to determine the PPI signal) during card processing but not at other times during the acquisition. As is standard in PPI analyses, the card versus baseline regressor, and the activity of the region used to determine the PPI term (i.e., the main effects of the psychological and physiological factors), were included as nuisance covariates. This step was taken to alleviate correlations due to shared task input.

Repeating this procedure for every pair of regions resulted in an  $18 \times 18$  connectivity matrix for each individual and card type, where each element ( $i, j$ ) of the connectivity matrix stored the parameter estimate ( $\beta$ ) for the corresponding PPI term and quantified the card-dependent influence that region  $i$  exerts on region  $j$  (i.e., effective connectivity; see Friston 2011 for details on this specific measure of effective connectivity).



**Figure 2.** Behavioral data obtained during scanning for the 4 card types of the modified WST. The A condition trials were the least complex and thus the easiest, and the “Not-7” trials were most difficult. (A) Accuracy. (B) Reaction time (error bars represent the within-subjects standard error of the mean).



**Figure 3.** Brain activity during rule processing. Processing of the rule was associated with significant activity in a diffuse set of regions encompassing the lateral prefrontal, lateral frontal, parietal and occipital cortices, and the dorsal cingulate cortex ( $P < 0.05$  FWE corrected at cluster level).

We tested whether the extent of any card-dependent influence of one region on another significantly differed across the 5 active card conditions. A within-subjects analysis of variance (ANOVA) was used to test this hypothesis for each of the  $18 \times 17 = 308$  connections. The network-based statistic (NBS; Zalesky et al. 2010; Cocchi et al. 2012a; Zalesky et al. 2012) was used to correct for multiple comparisons. The NBS ascribed a corrected  $P$ -value to each network of regions for which inter-regional interactions differed across the 5 card conditions. A primary  $F$ -statistic threshold of 3 was used for the NBS.

## Results

### Behavioral Measures

RTs were measured from the onset of the Respond display, which followed the “Card” display (Fig. 1A). As depicted in Figure 2, although overall accuracy levels were high, due to the training and feedback provided prior to testing, participants showed a linear performance deterioration across the 5 conditions ( $X^2 = 25.85$ ,  $df = 4$ ,  $P < 0.01$ ). Reduced performance as a function of increased relational complexity was also confirmed by analyses of the RTs ( $X^2 = 21.96$ ,  $df = 4$ ,  $P < 0.01$ ). Thus, as predicted by the relational complexity hypothesis, participants' accuracy was reduced and RTs were prolonged with increases in the relational complexity (i.e., number of variables to consider in order to solve the problem) of the card condition.

### fMRI

#### Brain Activity During the Rule Period

During presentation of the rule in each trial, participants had to form and encode a new set of trial-specific relations. Analyses of the fMRI data indicated that this ability involves a diffuse set of brain regions encompassing dorsal cingulate cortex, lateral frontal and prefrontal cortices, posterior parietal cortices, anterior insula, and the striatum (Fig. 3 and Table 1).

#### Brain Activity During the Card Period

A significant effect of the different card conditions was shown in a set of brain regions encompassing the superior parietal cortex, the dorsal cingulate and supplementary motor cortices, the frontal cortex, the rostralateral prefrontal cortex (RLPFC), and the dorsolateral prefrontal cortex (DLPFC). In addition, card processing engaged a large cluster encompassing the anterior insula, the striatum, and the thalamus (Fig. 4 and Table 2). The analysis of brain activity induced by each

**Table 1.**  
Brain activity during the rule period

	Anatomy <sup>a</sup>			Statistics <sup>b</sup>				
	x	y	z	$K_E$	Z	$P_{corr}$		
<b>Rule minus null trials</b>								
Occipital cortex	36	-70	-20	5618	5.15	<0.001		
	18	-88	-2		5.80			
	-18	-82	-14		5.71			
	-15	-91	1		5.08			
Parietal cortex	33	-61	46	314	5.05	<0.001		
	-27	-55	43		4.85			
	-27	-51	40		4.77			
	3	-85	37		4.72			
Temporal cortex	-45	-40	1	107	4.73	0.02		
	3	-85	37		4.72			
	-3	8	52		4.95			
	-3	-4	64		5.28			
Dorsal cingulate and supplementary motor cortices	9	20	37	294	3.56	<0.001		
	-21	26	4		4.64			
	-12	23	10		3.82			
	-51	-1	46		4.59			
Anterior insula and caudate nucleus	-30	-4	52	101	3.99	0.02		
	-33	47	37		4.59			
	-33	50	25		83		4.34	0.04
	-33	50	25		83		4.34	0.04

<sup>a</sup>Activity coordinates (x, y, z) are given in Montreal Neurological Institute (MNI) atlas space.

<sup>b</sup>P-values are familywise error (FWE) corrected for multiple comparisons at cluster level.

card (minus the corresponding null trials) indicates that similar clusters were activated in each card condition, with the exception of rostralateral prefrontal clusters that were not significantly engaged by the control card (Table 2). As depicted in Figure 4, card complexity was associated with an increase in the BOLD signal in most of the clusters (representative regions shown). These observations were statistically validated by within-subjects ANOVA on  $\beta$ -regression values ( $P < 0.05$  for all comparisons shown in Fig. 4, except for a trend level for the left parietal cortex  $P = 0.07$ ).

Note that comparable results were obtained from exploratory analyses that excluded data from incorrect trials.

#### Effective Connectivity Changes Associated with Card Processing

Changes in (PPI) effective connectivity during card processing were assessed among the cortical clusters isolated by the GLM analysis described above (see Table 3 for details).

Results showed a significant change in connectivity as a function of card complexity in a large-scale functional brain network encompassing the RLPFC, DLPFC, lateral frontal cortex, anterior cingulate cortex, the parietal and occipital cortices, and the anterior insular cortices (Fig. 5A). Connectivity was generally lower during the processing of the control card (active baseline) and the cards characterized by lower relational complexity (A and 7). In contrast, cards requiring complex manipulation of relations (Not-A and Not-7) induced consistently high functional coupling between connected regions (see the histogram in Fig. 5A).

Changes in effective connectivity as a function of relational complexity overlapped with the functional architecture of both the fronto-parietal network (trial-by-trial control) and the cingulo-opercular network (task set; Dosenbach et al. 2007, 2008; Dosenbach et al. 2010; also Power et al. 2011 and Fair et al. 2009; see Supplementary Table S1 for a comparison of the coordinates) (Fig. 5B). The requirement to consider progressively larger numbers of variables was related to

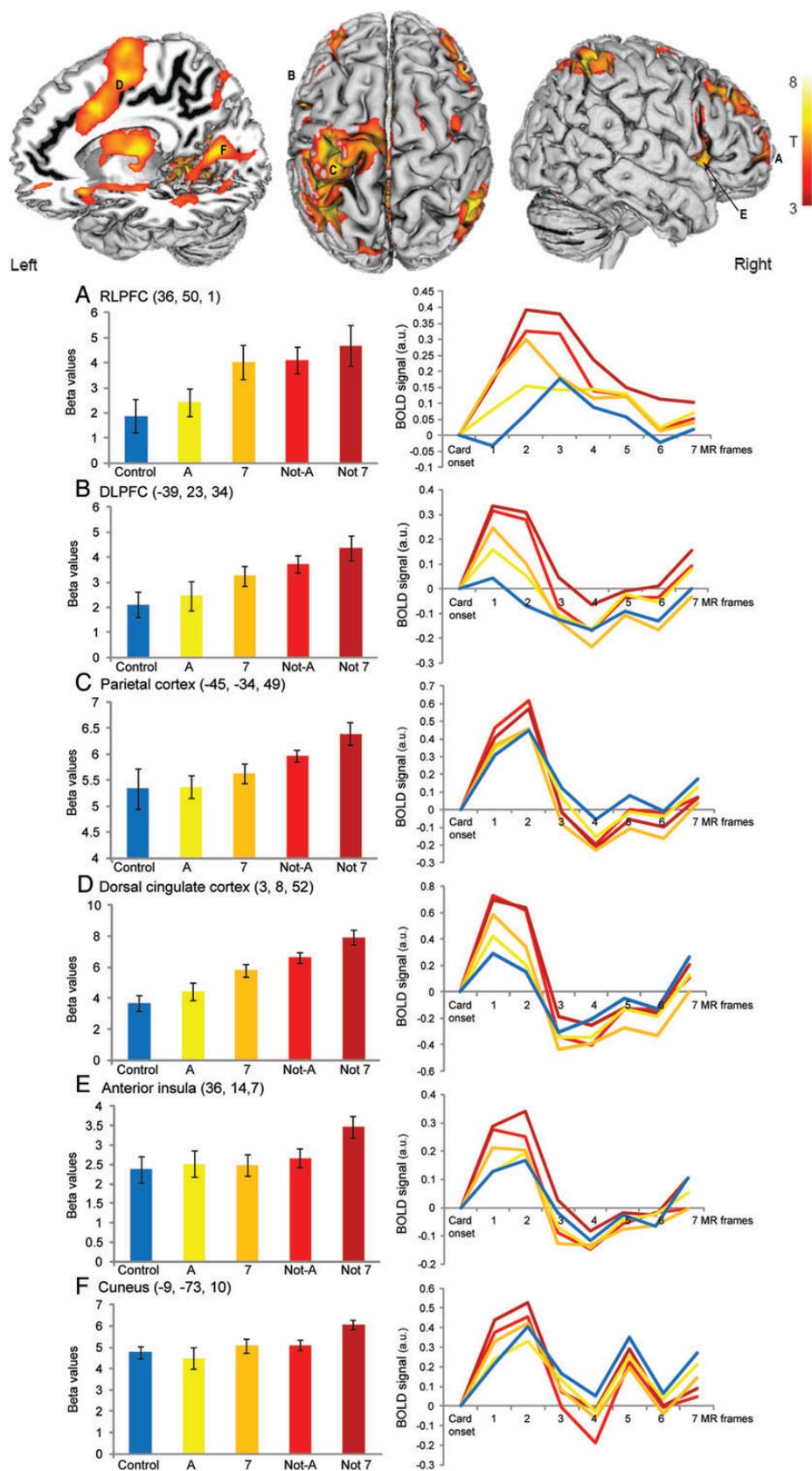
increased connectivity within and between brain regions encompassing these 2 cognitive control systems. Taken together, the findings suggest that the left DLPFC represents a key hub for integrating information from the contralateral DLPFC, the left frontolateral, as well as the occipital and parietal cortices (Fig. 5B). Also, the left DLPFC appears a target region for cingulo-opercular inputs from the dorsal anterior cingulate cortex, the anterior insula and the right RLPFC. The right RLPFC also showed complexity-induced changes in connectivity with the cuneus. Note that although the RLPFC is often associated with the fronto-parietal network (e.g., Dosenbach et al. 2010; Power et al. 2011; Sadaghiani et al. 2012), previous findings have shown that this region supports the maintenance and trial-by-trial implementation of subgoals (Koechlin et al. 1999; Sakai and Passingham 2003; Gilbert 2011). Because of its hybrid functional role, the RLPFC is likely to be a key hub for mediating fronto-parietal and cingulo-opercular control functions. This proposition is highlighted in Figure 5B, which shows that the right RLPFC is associated with both fronto-parietal and cingulo-opercular networks. Finally, results showed that the left lateral prefrontal cortex and regions within the visual network strengthened their modulation of the striatum as a function of increases in card complexity.

A comparable functional brain network and effective connectivity pattern were found when we included only correct trials in the analyses.

#### Discussion

Our objective in the current study was to characterize changes in whole-brain network dynamics as a function of relational complexity. Here we defined complexity as the number of variables that need to be linked with an existing set of relations (task rules) to solve a deductive problem, as exemplified in the Wason Selection Task (Halford, Bain et al. 1998; Halford et al. 2007). Before commencing the experiment, training was provided to ensure that all participants understood the logic of the task and to minimize individual differences in cognitive strategies. Thus, changes in task performance were specifically related to the number of variables that needed to be considered to access the problems' solution and not to individual differences in the way that variables were manipulated (i.e., cognitive strategies).

We used fMRI and a novel analysis approach that permitted quantification of changes in activity and (PPI) effective connectivity among spatially segregated brain regions. Results demonstrated that limits in processing relational complexity are associated with increased regional activity within, and functional interactions between, regions encompassing the rapid (trial-by-trial) fronto-parietal and slower (task set) cingulo-opercular control networks (Dosenbach et al. 2006, 2007, 2008, 2010). These findings provide a first comprehensive characterization of the dynamic brain processes that impose functional limits on the human capacity to process complex relations. More broadly, our results are consistent with mounting evidence that intellectual performance is related to dynamic reorganization of the functional interplay within and between large-scale brain systems (van den Heuvel et al. 2009; Leech et al. 2011; Fornito et al. 2012; Stevens et al. 2012).



**Figure 4.** Brain activity during card processing. After isolating the average effect of card processing on brain activity ( $P < 0.05$  FWE corrected at cluster level), post hoc analyses were performed on the card-specific beta series. Overall, results from the post hoc analyses showed that brain activity increased as a function of card complexity. Statistically, this observation was confirmed for the majority of the regions. The BOLD time-series (scaled to zero at stimulus onset) shown in the right panels support this conclusion (blue = control; yellow = A; orange = 7; red = Not-A; dark red = Not-7).

**Table 2.**  
Brain activity during the card period

	Anatomy <sup>a</sup>			Statistics <sup>b</sup>		
	x	y	z	K <sub>E</sub>	Z	P <sub>corr</sub>
<b>Average card activity minus null trials</b>						
Parietal cortex	-45	-34	49	12 636	6.84	<0.001
	42	-55	46		5.25	
	-30	-52	40		5.83	
	-57	-43	31		5.68	
Insula	-39	8	1		5.80	
	36	14	7		5.87	
	-30	17	7		5.79	
Dorsal anterior cingulate cortex	3	8	52		5.58	
Motor and supplementary motor cortices	-33	-10	64		5.32	
	-30	-16	58		5.96	
Striatum and thalamus	-18	-10	1		5.83	
	-21	-1	16		6.65	
	-15	-19	10		5.68	
	21	5	16		5.19	
Cerebellum	3	-52	-14		6.16	
Cuneus	-9	-73	10		5.51	
	12	-70	13		4.95	
Dorsolateral prefrontal cortex	42	26	31		4.82	
	-39	23	31		4.32	
Rostralateral prefrontal cortex	36	50	1		4.22	
Rostralateral prefrontal cortex	-24	44	-11	62	4.41	0.07 (<0.05 FDR)
	-30	56	-8		4.08	
Dorsal frontal cortex	33	-7	64	61	3.83	0.07 (<0.05 FDR)
<b>Card Control minus null trials</b>						
Cerebellum	30	-46	-26	4105	6.65	<0.001
Occipital cortex	-9	-73	10		5.35	
	15	-67	10		4.87	
Insula	39	11	10		5.35	
Striatum	21	-1	10		4.68	
Parietal cortex	-45	-37	52	4970	6.40	<0.001
	-39	-31	52		5.83	
	-33	-55	43		5.59	
	-54	-46	34		5.34	
Insula	-42	-4	13		5.04	
	-39	8	4		5.83	
Dorsal cingulate and supplementary motor cortices	3	2	58		5.81	
	5	-1	61		5.68	
Thalamus	-24	-22	-2		5.76	
	-18	-10	7		5.23	
Somatosensory cortex	-33	-25	73		5.50	
Parietal cortex	42	-55	46	671	6.06	<0.001
Lateral prefrontal cortex	33	47	34	356	5.23	<0.001
	-30	35	25	228	4.69	0.001
Lateral frontal cortex	-60	2	25	85	4.48	0.04
	-54	-1	43			
Temporal lobe	54	-22	-11	136	4.02	0.007
<b>Card A minus null trials</b>						
Insula	-39	8	1	5659	6.15	< 0.001
Parietal cortex	-45	-34	49		6.09	
	-39	-37	52		5.79	
	-48	-46	34		5.50	
	-24	-52	37		5.28	
Striatum	-24	-7	13		5.74	
	-30	-4	-5		5.58	
Motor cortex	-30	-16	58		5.58	
Dorsal cingulate and supplementary motor cortices	-3	-4	58		5.54	
	0	5	49		5.49	
	9	11	43		5.34	
	-12	-10	73		5.11	
Somatosensory cortex	-51	-19	19		5.52	
Striatum/Thalamus	-24	-16	1		5.18	
	-24	-22	-2		5.12	
Lateral prefrontal cortex	39	35	31		5.03	
Striatum and anterior insular cortex	21	-1	16	1154	5.85	<0.001
	39	11	-2		5.30	
Occipital cortex and cerebellum	30	-49	-26	2267	5.82	<0.001
	-36	-49	-26		5.62	
Parietal cortex	42	-52	43	427	5.39	<0.001
	54	-40	49		4.31	
Rostralateral prefrontal cortex	-24	44	-11	42	4.86	0.06 (FDR)
	36	50	-2	33	4.13	0.09 (FDR)
Lateral prefrontal cortex	-39	47	28	289	4.78	<0.001
	-35	26	28		4.58	
Medial temporal cortex	-45	-43	-2	103	4.28	0.01

(continued)

Table 2. Continued

	Anatomy <sup>a</sup>			Statistics <sup>b</sup>		
	x	y	z	K <sub>E</sub>	Z	P <sub>corr</sub>
<b>Card 7 minus null trials</b>						
Insula	-39	5	4	12 498	6.58	<0.001
	-39	-4	10		5.86	
Parietal cortex	-45	-34	49		6.54	
	-36	-31	52		6.18	
	42	-55	49		5.51	
Striatum	-24	14	4		6.43	
	-21	-1	13		6.19	
	-21	-7	16		6.14	
	18	2	13		5.65	
Dorsal cingulate and supplementary motor cortices	-3	-16	55		6.32	
	-3	2	52		5.87	
	-12	-7	55		5.76	
Motor and somatosensory cortices	-30	-16	55		6.32	
	-33	-10	67		5.09	
	-27	-16	73		5.67	
	-12	-10	76		5.49	
Cerebellum	12	-46	-23		6.60	
	3	-55	-5		5.94	
	3	-52	-11		5.88	
Thalamus	-25	-19	10		6.28	
	-18	-16	7		6.25	
	-24	-22	-2		5.76	
Occipital cortex	-9	-73	10		5.54	
Lateral prefrontal cortex	-47	8	19		5.52	
	-45	29	37		2.8	
Rostrolateral prefrontal cortex	33	56	-5		3.44	
	-36	56	-2		2.35	
Lateral frontal cortex	36	-7	64	82	4.13	0.02
<b>Card Not-A minus null trials</b>						
Parietal and occipital cortices	-45	-34	49	9307	6.77	<0.001
	-30	-52	40		5.86	
	12	-70	43		5.52	
	9	-73	46		5.27	
Motor cortex	-33	-10	64		6.55	
Dorsal cingulate and supplementary motor cortices	0	5	55		6.54	
	-3	-14	40		6.11	
Cerebellum	3	-52	-11		6.14	
Insula	-39	11	10		5.94	
	-39	8	4		5.94	
	-42	5	7		5.92	
	39	14	7		5.64	
	33	17	4		5.33	
	-42	-4	10		5.16	
Striatum and thalamus	-18	-4	16		5.85	
	-21	-10	16		5.72	
	18	2	19		5.72	
	-18	-10	10		5.67	
	18	-4	19		5.62	
	-15	-10	-2		5.49	
	-15	-19	10		5.45	
Dorsolateral prefrontal cortex	45	23	31		5.21	
	-39	23	31		4.07	
Parietal cortex	42	-52	43	619	6.11	<0.001
Rostrolateral prefrontal cortex	33	50	1	183	4.65	0.001
	30	59	1		4.48	
Inferior temporal cortex	-39	-46	-8	92	4.09	0.01
<b>Card Not-7 minus null trials</b>						
Dorsal cingulate and supplementary motor cortices	3	8	52	11 634	6.63	<0.001
	-3	14	43		6.31	
	9	20	37		6.03	
	-9	-7	73		5.31	
Parietal cortex	-45	-34	46		6.46	
	-57	-43	31		5.58	
	-27	-55	40		5.58	
Striatum	-21	-1	16		6.24	
	21	5	16		5.79	
	18	-1	13		5.52	
Insula	-42	5	10		6.23	
	-27	14	7		6.06	
	-39	8	1		6.01	
	30	14	7		5.92	
	30	17	4		5.82	
	-27	20	-8		5.78	
Cerebellum	5	-52	-14		5.01	
Motor cortex	-33	-10	64		5.79	

(continued)

Table 2. Continued

	Anatomy <sup>a</sup>			Statistics <sup>b</sup>		
	x	y	z	$K_E$	Z	$P_{corr}$
Dorsolateral prefrontal cortex	42	26	31		5.50	
	45	23	34		5.34	
	-42	20	31		4.08	
Thalamus	-18	-10	1		5.48	
	-15	-19	10		5.31	
Occipital cortex	-12	-73	10		5.40	
Rostrolateral prefrontal cortex	36	50	-2		2.73	
Parietal cortex	42	-52	43	589	5.66	<0.001

<sup>a</sup>Activity coordinates (x, y, z) are given in Montreal Neurological Institute (MNI) atlas space.

<sup>b</sup>P-values are familywise error (FWE) corrected for multiple comparisons at cluster level. FDR, false discovery rate.

Table 3.

Brain regions included to isolate changes in effective connectivity as a function of card complexity

	Anatomy <sup>a</sup>		
	x	y	z
Parietal cortex	-45	-34	46
	42	-55	46
Anterior insula	-30	17	7
	36	14	7
Dorsal anterior cingulate cortex	3	8	52
Striatum	21	5	16
Thalamus	-15	-19	10
Cuneus	-9	-73	10
	12	-70	13
Lateral frontal cortex	-57	8	22
Lateral prefrontal cortex	-36	47	28
	36	47	34
Dorsolateral prefrontal cortex	-39	23	31
	42	26	31
Rostrolateral prefrontal cortex	36	50	1
	-28	50	-8
Motor cortex	-30	-16	58
Cerebellum	3	-52	-14

<sup>a</sup>Coordinates (x, y, z) are given in Montreal Neurological Institute (MNI) atlas space.

### Behavioral Performance

The participants performed well in all card conditions (>86% correct overall), indicating that the training and heuristics provided prior to scanning were effective in helping to avoid the high error rates typically reported for the conventional WST (Wason and Shapiro 1971). Despite the relatively low number of errors, however, the overall pattern of performance across the 4 card conditions, in terms of error rates and RTs, mirrored the pattern yielded in typical versions of the WST. Hence, when seeking to disconfirm the rule “If A then 7,” participants often correctly classified the A and 7 cards but did not respond appropriately to the Not-A and Not-7 cards (Canessa et al. 2005; Evans and Ball 2010). Taken with previous results on classic versions of the WST, our findings suggest that the observed decline in performance as a function of card complexity is related to intrinsic limits in the brain’s capacity to process relations among increasing numbers of variables.

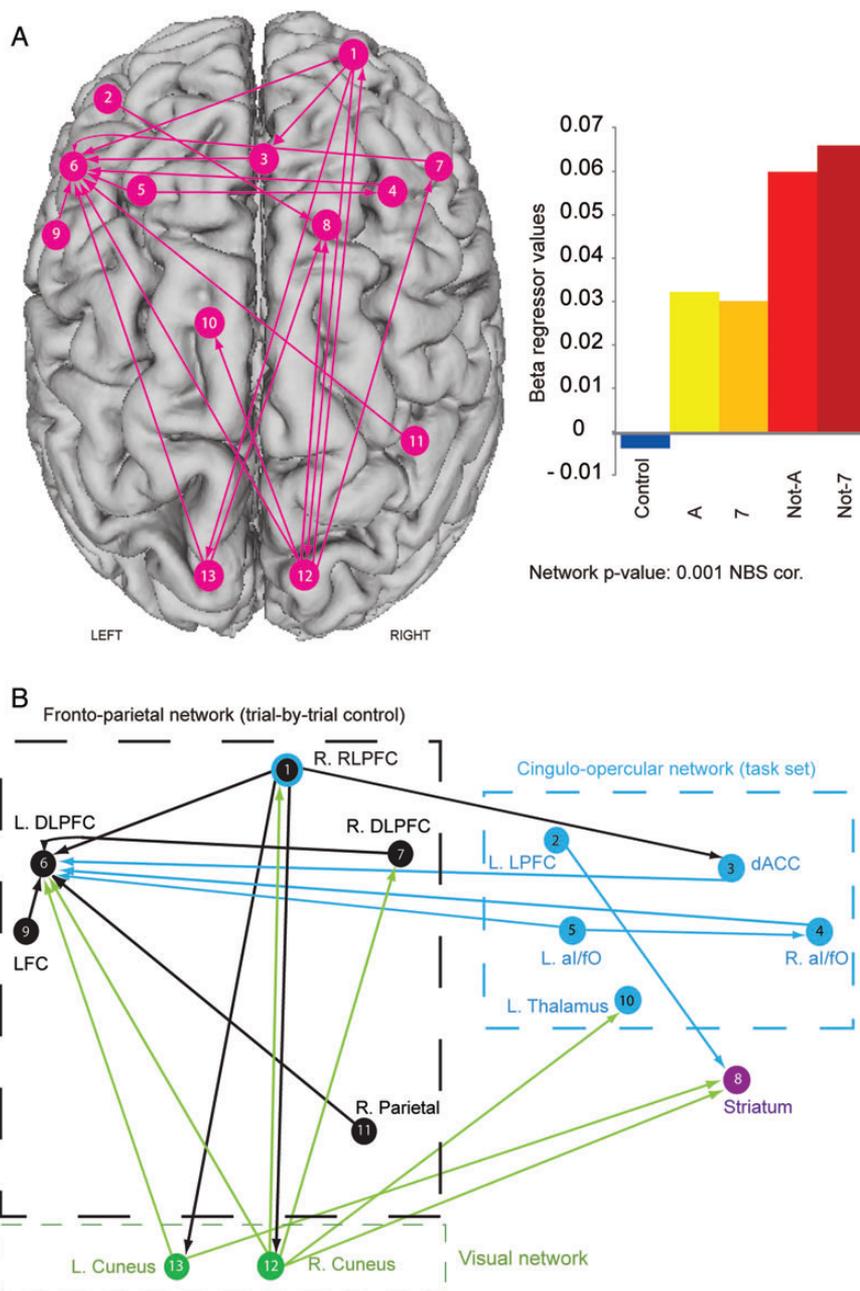
In our study, the cognitive processes entailed in selecting each card were assessed separately. This approach yielded a number of insights that are not possible with the classic version of the Wason task, in which all 4 cards are considered simultaneously (Wason 1968). Frequent selection of the 7

card (given the rule “If A then 7”) might reflect a tendency to favor confirming over disconfirming evidence, because 7 can only confirm, and cannot disconfirm, the rule. Alternatively, selection of the 7 might reflect ambiguity in interpretation of the rule, because it is a valid response according to a 2D (biconditional) interpretation of the rule. In our study, the frequency with which participants selected the 7 card was around 6% (see Fig. 2), much lower than has been found previously (Evans and Ball 2010). This suggests that participants typically interpret the rule as a biconditional, and that we effectively suppressed this response through preliminary training. Pragmatic reasoning schemas (i.e., generalized sets of rules defined in relation to classes of goals; Cheng and Holyoak 1985) such as permission might also suppress this response because permission more closely matches a conditional (Halford 1993). Ambiguity of the rule is implied by selection of the 7 card, and is related to training and knowledge, whereas relational complexity effects are indicated by failures to select the Not-7 card.

### Brain Activity Supporting Rule Processing

Rule processing involved the generation of an internal relational representation using the elements presented in the rule (e.g., A and 7). In line with existing knowledge on the cortical regions that integrate and maintain abstract rules, rule encoding in the WST engaged a widespread set of brain areas encompassing prefrontal, frontolateral, and cingulate cortices (Christoff et al. 2001, 2011 Kroger et al. 2002; Koehlin and Summerfield 2007; Badre 2008, 2010). This diffuse set of regional co-activations overlaps with 2 of the principal networks involved in cognitive control, namely the fronto-parietal and cingulo-opercular systems (Dosenbach et al. 2006, 2008). The fronto-parietal network supports dynamic (trial-by-trial) cognitive control and in our task is likely to be engaged to update internal relational representations in accordance with trial-specific rule elements. In contrast, the cingulo-opercular system is thought to underpin awareness of salient stimuli and the stable maintenance of task set (here the given logic) throughout task execution (Dosenbach et al. 2006, 2007; Seeley et al. 2007).

In addition to widespread cortical activity, rule processing was associated with significant striatal activity. The contribution of the striatum to the acquisition of abstract rules is consistent with previous studies showing that fronto-striatal networks are central to the establishment of new relational representations



**Figure 5.** Changes in effective brain connectivity as a function of card complexity. (A) Large-scale brain network showing global changes in connectivity for the different card conditions. The network was isolated by conducting a psychophysiological interaction analysis (PPI) for every pair of regions of interest, resulting in an  $18 \times 18$  connectivity matrix for each individual and card type. The 18 regions represent the main clusters involved in card processing isolated using the general linear model framework (see Table 3 for details). In these matrices, elements  $(i, j)$  stored the parameter estimate ( $\beta$ ) for the PPI term and quantified the card-dependent influence that region  $i$  exerts on region  $j$  (PPI effective connectivity, see Materials and Methods). Matrices were used to test whether the extent of card-dependent influence from one region to another significantly differed across card conditions. A within-subjects ANOVA was used to test this hypothesis. The NBS was used to correct for multiple comparisons. The  $x$ -axis in the bar chart depicts the 5 card conditions, and the  $y$ -axis indicates the absolute median value of connectivity between each pairwise connection. (B) Schematic representation of large-scale brain networks involved in limiting the processing of relational complexity: fronto-parietal (black), cingulo-opercular (light blue), and visual (green). DLPFC: dorsolateral prefrontal cortex; dACC: dorsal anterior cingulate cortex; RLPFC: rostralateral prefrontal cortex (note that this region is associated with both the fronto-parietal and cingulo-opercular networks; see text for details); LFC, lateral frontal cortex; LPFC, lateral prefrontal cortex; al/fo, anterior insula/frontal operculum.

in the prefrontal cortex (Asaad et al. 1998; Bunge, Wallis et al. 2005; Badre 2010; Badre et al. 2010). Taken together, our results are in agreement with existing neurophysiological data from human and nonhuman primates suggesting that the acquisition of task-related relational knowledge is supported by functional coupling between the striatum and the frontal cortex.

Critically, the rules used were always of the same general form (e.g., “If  $A$  then  $7$ ”), and thus were identical in their complexity. As a result, the observed differences in behavior and brain activity arising from the different card conditions cannot be attributed to differential processing of the rules, but must instead be due to the unique integration of each card element with trial-specific relational knowledge.

### **Brain Dynamics Related to Limits in Integrating Relational Complexity**

Processing card elements characterized by different levels of relational complexity modulated the dynamics of a large-scale brain network that encompasses the fronto-parietal and cingulo-opercular systems. Both segregated neural activity and effective connectivity across the diffuse brain network scaled as a function of card complexity, with higher values elicited by cards characterized as having greater complexity (i.e., Not-*A* and Not-7).

The relevance of frontal and prefrontal regions for relational mechanisms supporting the implementation of defined cognitive strategies has been shown by a number of previous fMRI studies. In particular, the DLPFC and the lateral frontal cortices have been associated with the online generation, evaluation, and active maintenance of task-relevant relational representations (Diwadkar et al. 2000; Bunge, Wallis et al. 2005; Crescentini et al. 2011, 2012; Wendelken et al. 2011). On the other hand, the RLPFC is thought to be critical for implementing trial-based goals (Rowe et al. 2007; Bengtsson et al. 2009; Reverberi et al. 2011) and plays a key role in applying rules while simultaneously maintaining alternative rules in an active state (Koechlin et al. 1999; Braver and Bongiolatti 2002; Kroger et al. 2002). Similarly, this anterior prefrontal region seems to support the simultaneous consideration, comparison, and integration of multiple relations (Christoff et al. 2001; Kroger et al. 2002; Fangmeier et al. 2006; Bunge and Wendelken 2009; Rodriguez-Moreno and Hirsch 2009; Green et al. 2010). Taken together, our findings point toward a central role for the RLPFC in generating appropriate delayed responses according to task sets (Sakai and Passingham 2003; Gilbert 2011). Not only are our results in agreement with current views on the role of prefrontal regions in relational processing, they also extend this understanding by suggesting that the pattern of effective connectivity from the left frontal, right DLPFC, and right rostrolateral prefrontal cortices to the left DLPFC is directly associated with limits in the efficient processing of relations to achieve behavioral goals.

In addition to characterizing the impact of frontal dynamics on limits in relational processing, our results highlight that such dynamics alone occur in the context of broader systemic changes. Specifically, our findings showed that the implementation of cognitive control strategies to solve complex relational problems involve the coordinated action of both the fronto-parietal and cingulo-opercular control systems (Dosenbach et al. 2006, 2007, 2008). Our analysis of effective connectivity also suggests that relational complexity modulates afferent connections between visual regions involved in integrating card stimuli and the DLPFC and right RLPFC. Overall, these changes in large-scale brain network dynamics are likely to reflect the increased effort in actively linking and maintaining online an increased number of variables according to the given logic.

Inputs to the left DLPFC from the right RLPFC, anterior insula, and dorsal anterior cingulate cortex were low in cards characterized by low complexity (i.e., *A* and 7) and high in cards characterized by higher complexity (i.e., Not-*A* and Not-7). The dorsal anterior cingulate and anterior insular cortices represent key neural hubs of the cingulo-opercular network, which is implicated in maintaining and implementing

task set (Dosenbach et al. 2006, 2007). Similarly, as mentioned above, the RLPFC has been implicated in the maintenance and trial-by-trial implementation of subgoals (Koechlin et al. 1999; Gilbert 2011). As such, increased effective connectivity between regions of this network and the left DLPFC in response to higher complexity cards is likely to reflect the greater demand for implementing the acquired logic when evaluating these cards, as compared to the easier implementation of only some of the steps of the logic when evaluating the lower complexity cards (e.g., *A* directly matches *A* in the rule and does not involve the implementation of all strategy steps). This suggestion is in line with the recent proposition that the anterior insula, along with the RLPFC, may represent a critical hub for the active generation of appropriate responses according to task goals (Bressler and Menon 2010; Menon and Uddin 2010; Nelson et al. 2010). The anterior insula is also thought to be critical in linking sympathetic arousal states with cognitive control functions (Craig 2009; Bressler and Menon 2010; Cocchi et al. 2012b; Critchley and Harrison, 2013). Thus, increased effective connectivity from the anterior insular cortices to the left DLPFC as a function of increased card complexity may be, at least to some extent, also related to increased arousal.

Numerous hypotheses have been advanced to explain the difficulty of the WST (Evans 2008). These include difficulty with disconfirmation of hypotheses, pragmatic reasoning schemas (Cheng and Holyoak 1985), Bayesian accounts based on optimization of information gain (Oaksford and Chater 2007) and social contract theories based on modules such as cheater-detection (Cosmides and Tooby 1992). Our finding that the different card types in the WST entail specific local activations and distinct levels of network connectivity has important implications for these hypotheses. For example, a strategy of matching elements (e.g., selecting the *A* and 7 cards for the rule “If *A* then 7”) might be chosen because it reduces the complexity and the related metabolic cost to achieve a goal (Bullmore and Sporns 2012). Indeed, matching elements may be regarded as a default strategy to avoid the higher metabolic demands of recognizing that Not-7 disconfirms the rule “If *A* then 7.” Pragmatic reasoning schemas, such as permission (Cheng and Holyoak 1985), might also reduce cognitive complexity by providing previously known confirming and disconfirming instances. For example, most adults know that driving without permission in the form of a license violates the traffic laws, and that accepting a benefit without fulfilling preconditions violates a social contract. Previous investigations of the WST have shown relatively high levels of correct responses when participants must decide on a rule such as “a person must be 18 years of age to consume alcohol” (Cheng and Holyoak 1985). This reduces cognitive complexity because the disconfirming instance, drinking while <18 years, is already known and does not need to be computed. Finally, relational complexity has also been considered a viable alternative to optimization of information in deductive reasoning (Halford 2009; Zielinski et al. 2010).

While the current study provides novel insights into the brain networks that support, and possibly even limit, the processing of relational complexity, it is important to acknowledge potential methodological limitations. Recent studies have shown that “micro” head movements may cause systematic changes in functional connectivity (Satterthwaite et al.

2012; Van Dijk et al. 2012; Yan et al. Forthcoming; Power et al. 2012a, 2012b). Although the effect of micro-head movements on task-based connectivity needs further investigation, we took the precaution of measuring frame-by-frame movements during card epochs (Power et al. 2012a, 2012b). Results showed that <8% of frames occurring during the card epochs contained head movement exceeding the selected threshold (0.2 mm; the 2 preceding and following frames were also excluded). Moreover, the distribution of the affected frames did not change as a function of relational complexity (see Supplementary Fig. S1). Taken together, results from this head-movement analysis argue against the possibility that the observed increase in effective connectivity as a function of complexity is merely an effect of micro-head movements. On the other hand, we acknowledge that the adopted measure of effective connectivity has limited causal interpretability in neural terms. Future studies adopting more direct and sophisticated measures of information flow between brain regions and systems (e.g., dynamic causal modelling, possibly using different techniques such as magnetoencephalography; Friston 2011) are required to confirm and extend the current findings.

### Concluding Remarks

We have shown that the number of variables that need to be linked into a representation to solve a problem predict performance in a complex-reasoning task. Limits in efficiently relating variables according to task goals are reflected in complexity-dependent network dynamics within and between 2 main control systems, namely, the fronto-parietal and cingulo-opercular networks. Overall, our study highlights the need to consider limits in high-order cognitive processes that require the manipulation of relations as complexity-induced changes in large-scale brain network dynamics beyond the frontal cortex.

### Supplementary Material

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

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