Recruitment of Anterior Dorsolateral Prefrontal Cortex in Human Reasoning: a Parametric Study of Relational Complexity

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Reasoning and problem solving depend on the ability to represent and integrate complex relationships among stimuli. For example, deciding whether an animal is dangerous requires integrating information about the type of animal, its size, its distance from oneself, and one's proximity to shelter. Relational complexity increases with the number of such interdependent elements that must be simultaneously considered to solve a problem. We used functional magnetic resonance imaging to identify brain regions that respond selectively in processing high levels of relational complexity. Performance on nonverbal reasoning problems in which relational complexity was varied parametrically was compared with performance on control problems in which relational complexity was held constant while difficulty was manipulated by adding distractor forms to the problems. Increasing complexity and adding distractors both led to increased activation in parietal and in dorsolateral prefrontal cortex, with high levels of relational complexity selectively activating anterior left prefrontal cortex. Our data provide evidence that brain regions specific to integrating complex relations among stimuli are distinct from those involved in coping with general task difficulty and with working-memory demands.

Introduction

Neuropsychological and neuroimaging studies have established that the dorsolateral prefrontal cortex (DLPFC) plays a major role in problem solving (Luria, 1973; Duncan *et al.*, 1995, 2000; Prabhakaran *et al.*, 1997; Waltz *et al.*, 1999) and working memory (Cohen *et al.*, 1994; Smith *et al.*, 1996; D'Esposito *et al.*, 1998). Fractionating this broad region into functional components has proven difficult. Specialization for processing different information modalities has been proposed to exist in the inferior-to-superior anatomical dimension, with superior frontal cortex specialized for spatial working memory and more inferior regions subserving non-spatial working memory (Courtney *et al.*, 1996; Goldman-Rakic, 1996). Other evidence has suggested hemispheric specializations for spatial and non-spatial working memory (Smith *et al.*, 1995; Belger *et al.*, 1998). Another approach focuses on division of prefrontal cortex into inferior and superior subregions that respectively specialize for maintenance and monitoring of information in all modalities (Owen *et al.*, 1996, 1998; D'Esposito *et al.*, 1998). Most of this research has focused on the middle and posterior portions of DLPFC.

Recent studies have characterized activation of more anterior DLPFC, from the border of Brodmann's area (BA) 46 into BA 10, extending towards the frontal pole (Christoff and Gabrieli, 2000). Anterior DLPFC tends to be activated by particularly difficult reasoning and problem-solving tasks (Nichelli *et al.*, 1994; Petrides, 1994; Berman *et al.*, 1995; Baker *et al.*, 1996; Goel *et al.*, 1997; Prabhakaran *et al.*, 1997; Goldberg *et al.*, 1998; Osherson *et al.*, 1998), especially those requiring branching between multiple goals (Gold *et al.*, 1996; Koechlin *et al.*, 1999), exploiting analogous relationships (Wharton *et al.*, 2000; Boroojerdi *et al.*, 2001), or integration of multiple constraints (Prabhakaran *et al.*, 2000).

In the present study, we tested the hypothesis that anterior DLPFC is selectively engaged by tasks that require explicit representation and manipulation of relational knowledge (Holyoak and Kroger, 1995; Robin and Holyoak, 1995). The basic unit of knowledge required for problem solving is a relation interconnecting the current problem state, a goal state, and some action that might transform the current state to bring it closer to the goal (Newell and Simon, 1972). The relational complexity of a reasoning task, and hence the load imposed on DLPFC, will be expected to increase with the number of relations that must be jointly considered to infer the required conclusion (Hummel and Holyoak, 1997; Halford *et al.*, 1998). For example, complexity would increase with the number of subgoals that must be jointly satisfied to achieve a superordinate goal. As an example in the domain of reasoning, in a transitive inference task the reasoner must integrate two binary relations (e.g. Bob is taller than Charles, Abe is taller than Bob) in order to derive a valid inference (here, Abe is taller than Charles). The integration of two relations will require more complex processing, and impose a higher working-memory load, than simply representing each individual relation. Preschool children typically exhibit understanding of individual ordering relations such as 'taller than', yet are unable to reliably make transitive inferences (Halford, 1984); and patients with prefrontal damage are unable to integrate two relations to solve transitive inference problems (Waltz *et al.*, 1999). Examination of the cognitive tasks that yield activations in DLPFC suggest a unified interpretation: tasks that require processing a small number of relations (perhaps one or two) activate DLPFC, and tasks that require processing additional relational complexity recruit more anterior portions of DLPFC.

We used functional magnetic resonance imaging (fMRI) to measure increases in MR signal that accompany increases in the relational complexity of a reasoning task. The reasoning problems were adapted from the Raven's Progressive Matrices (RPM) (Raven, 1941; Carpenter *et al.*, 1990), a neuropsychological test that has been associated with fluid intelligence and that is impacted by frontal lobe injury (Duncan *et al.*, 1995; Waltz *et al.*, 1999). In the context of the RPM-type problems used in the present study, relational complexity is equivalent to the number of dimensions of stimulus variation that must be integrated to complete the missing cell of the matrix. Each change in a

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dimension (e.g. a circle increasing in size) is equivalent to a binary relation between an initial stimulus and a final stimulus. It has been estimated that normal human adults can reliably integrate up to four dimensions of variation without relying on external memory aids (Halford *et al.*, 1998); accordingly, we used problems that manipulated complexity in the range of 0–4 dimensions of variation (see Fig. 1).

A prior study found that more complex and difficult RPM problems activate more anterior DLPFC (Prabhakaran *et al.*, 1997). A central goal of the present study was to decouple the effects of relational complexity from those of other factors that increase task difficulty. Task difficulty has been shown to increase the magnitude of blood flow changes in DLPFC on a wide variety of tasks (Demb *et al.*, 1995; Baker *et al.*, 1996; Cohen *et al.*, 1997; Carlson *et al.*, 1998), and no studies to date have firmly distinguished the neural basis for integrating multiple relations from the neural response to general task difficulty. In addition, other psychological factors vary across RPM problems and may constitute further confounds with changes in relational complexity (Carpenter *et al.*, 1990).

In order to manipulate relational complexity while controlling for general difficulty and to preclude other confounding factors, we developed a new set of stimuli adapted from the RPM in which we parametrically varied the number of relations required to solve the problem. The level of relational complexity was defined by the number of relations, drawn from a fixed set of possible relations each defined by a monotonic change, which had to be integrated to form the correct figure for the empty cell (see Fig. 1*a*,*b* for examples). To differentiate the impact of relational complexity from other factors that also increase general problem difficulty, we created a set of control problems using the same RPM format that was designed to yield a monotonic increase in task difficulty without increasing relational complexity. In each of these control 'distractor' problems a single relation was varied, while one to four simple forms (e.g. square, circle) that were added to the figures did not vary across the matrix (Fig. 1*c*). The added forms were designed to increase task difficulty across four levels (distractor levels 1–4), by requiring selective attention to segregate the relevant dimensions of variations from the background of constant forms, so that progressively more non-relational information had to be mediated to select the correct answer. The distractor forms could not be ignored altogether, as the correct answer choice had to include the constant forms as well as varying ones, and in some answer choices some of the distractor forms were altered or not present; however, constant forms do not increase the number of dimensions of variation, A behavioral pilot study confirmed that both complexity and distractor manipulations caused monotonic increases in error rates and solution times for the problems. Our prediction was that the variation in relational complexity, but not simply general difficulty, would result in parametrically increased MR signal [which we interpret as increased brain activation (Cohen and Bookheimer, 1994; Cohen, 1997)] in anterior DLPFC at higher complexity levels.

Materials and Methods

Stimuli

Stimuli were constructed starting with basic shapes (e.g. square, circle, infinity sign) to be used as elements in the matrix cells. Various featural details were varied regularly to create a large pool of figures with subtle variations, so that a degree of novelty would exist among the final stimuli to minimize their predictability for subjects. To avoid potential confoundings with difficulty of particular relations, the relations that varied in each problem were restricted to monotonic increases or decreases along five types of dimensions: size, number, position, orientation, and brightness. When multiple relations varied in a matrix, the variations were distributed evenly across the vertical and horizontal directions. Relational changes that resulted in symmetry about the vertical or horizontal matrix center were excluded. A particular type of relational change was used only once in a given matrix.

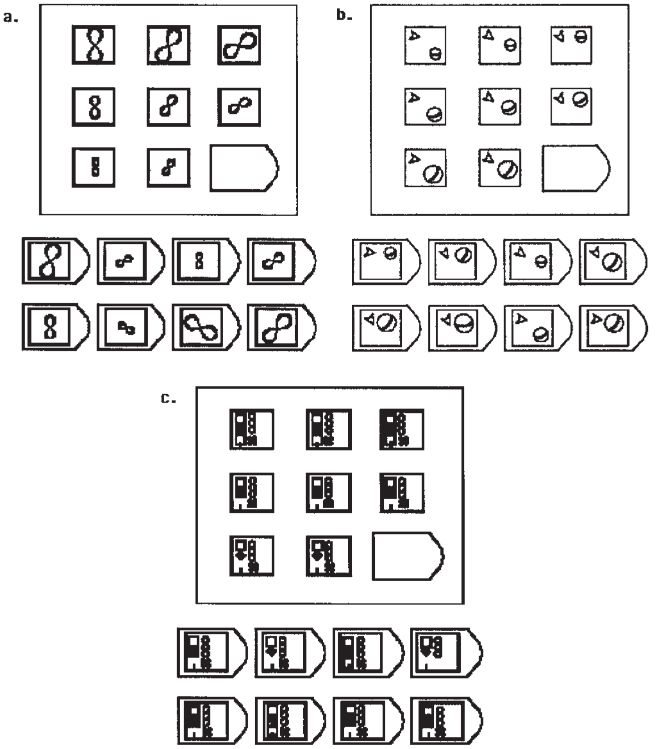

Figure 1. Examples of matrix problems. (*a*) A problem at complexity level 2. Two monotonic relations must be integrated to solve the problem: the size of the object decreases towards the bottom of the matrix, and its orientation progressively changes horizontally across the matrix. (*b*) A problem at complexity level 4 (the highest level). Orientation, size, and position of the ball, as well as orientation of the arrow, all change across the matrix. (*c*) A problem at distractor level 4. The one relevant relation concerns the number of squares on the left. The other four objects are distractors that remain constant in all cells of the problem matrix.

To form a set of stimuli that manipulated relational complexity, problems were constructed in which 0, 1, 2, 3 or 4 relations varied vertically and/or horizontally. In the easiest complexity condition, nothing varied: the stimuli in the matrix were identical, as was the answer. In the complexity level 1 condition, a single monotonic change existed across either the vertical or the horizontal direction. Adding additional monotonic variations from the five types generated problems at complexity levels 2–4.

Behavioral Task

All experimental stimuli were presented by means of an MRI compatible video display system (MRVision, 2000; Resonance Technology, Northridge, CA). This display was connected to a Macintosh computer used for stimulus presentation and collection of reaction time and accuracy data.

Subjects performed practice trials until they were familiarized with the task before being introduced to the scanner. Each subject then completed four scans. Two complexity scans and one distractor scan were used. An additional scan in which brightness contrast was varied was also performed, but not used in the analyses reported here. Each scan included blocks of problems at each level for a given condition. The problems in the two complexity scans for any subject did not overlap. Each level was 1 min long, during which subjects completed problems at their own pace; the mean number of problems completed per block for the complexity levels 0–4 were: 10, 8, 6.5, 3.9 and 3.2; and for the distractor levels 1–4: 5, 4.3, 4.6 and 3.6, respectively. A 24 s baseline, with the word 'rest' appearing to subjects, started and finished every scan. To control for order effects, the variables of order of levels within scan and conditions between scan were counterbalanced, with the constraint that the two complexity scans never occurred consecutively.

On each trial a presentation program first presented the nine cells of a 3 × 3 problem matrix together (with the bottom right cell empty), without the answer choices. Subjects were instructed to form a mental represen- tation of the solution that would complete the empty cell, and then to press one button on a two-button pad to reveal the answer choices below the matrix (with the location of the correct answer location counter- balanced across trials). In debriefing, all subjects reported adherence to this strategy. The choices remained onscreen as subjects used the second button to advance a pointer to the desired choice, and then pressed the first button again to enter their selection and end the trial. After a 2 s blank-screen delay, the next trial began. Before scanning, subjects were trained on the task, performing problems at each level of complexity and distractors until they were familiar with the procedure.

Imaging Procedure

Eight subjects (right-handed college students; six male; aged 19–32 years) solved reasoning problems during fMRI. Scans were conducted at the Ahmanson–Lovelace Brain Mapping Center of the UCLA School of Medicine on a 3 T General Electric scanner (Waukesha, WI, USA), with echo-planar imaging (EPI) capability from Advanced NMR Systems (Wilmington, MA, USA). Axial high-resolution spin-echo scans of the whole brain were collected in the same plane as the functional scans to aid group registration (26 slices; 4 mm slices, 1 mm gap; 128 × 128 matrix; 20 cm field of view; T_R: 4 s; T_E: 54 ms). Sixteen functional scans were acquired (from approximately –15 mm to +65 mm) at 148 time points over 7 min 40 s during which one set of blocks (e.g. five 1 min blocks of complexity trials interspersed by 24 s baselines) was completed (T_R: 3 s; T_E: 42 ms; flip: 80°; 4/1 mm slices; 64 × 64 matrix; 20 cm field of view). Two complexity sets, a distractor set, and an unused Noise set were completed by each subject. Since the distractor set only included four levels, the final block consisted of a blank screen. Events for each set of blocks occurred in multiples of 3 s in order to synchronize the behavioral task explicitly to the scanning parameters. Within each block, problems were presented as fast as subjects completed them, separated by 2 s.

During training, subjects were briefed about the nature of the imaging experiment and the instrument used, and signed informed consents approved by the UCLA Office for the Protection of Research Subjects.

Image Post-Processing

Data from fMRI scans was motion-corrected and warped into a site-specific atlas in Talairach space (Talairach and Tournoux, 1988), using AIR software (Woods *et al.*, 1998). The data were smoothed with a Gaussian filter of 6 mm full-width half maximum. Data were analyzed in SPM99 (Wellcome Department of Cognitive Neurology, http://www.fil.ion.ucl.ac.uk/spm/). All contrasts were run using an uncorrected threshold of $P \leq 0.001$ and a 'k' extent of 40 voxels that corresponded approximately to a corrected cluster threshold of $P \leq 0.009$. Planned contrasts included comparisons of each of the nine individual levels of complexity (0–4) and of distractors (1–4) to baseline. In order to identify specific areas selectively activated by increases in relational complexity, linear-trend analyses were performed separately for the complexity conditions and the control distractor conditions. Linear contrasts were set up to reflect an increase in activity with increasing load for a given condition type. Additional analyses were performed in order to identify areas selectively activated by the highest levels of relational complexity while controlling for general problem difficulty. This analysis used a contrast based on subtraction of the two highest levels of distractors from the two highest levels of relational complexity. For comparison the opposite contrast was also performed. Finally, time-series graphs were generated for regions of interest identified in the linear-trend analysis for relational complexity, showing mean percent signal change across the 60 s period (20 T_Rs) of task performance and the 24 s (8 T_Rs) baseline periods preceding and following the task period.

Results

Behavioral Analyses

In order to assess subjects' performance on the various types of problems, analyses of variance were performed on solution times (time to internally generate a solution and make the initial button press) for problems solved correctly, and on error rates (Fig. 2). For both dependent variables means were calculated for each level of complexity and distractors for each subject (averaging over the two complexity sets). Solution times increased as a function of both complexity (levels 0–4) and distractors (levels 1–4). For complexity, the increase in solution time across levels was highly significant [$F(4,28) = 17.16$, mean squared error (MSE) = 2 362 476, $P < 0.001$], with a reliable linear component [$F(1,7) = 22.24$, MSE = 6 639 151, $P = 0.002$]. The quadratic component was also reliable [$F(1,7) = 6.23$, MSE = 2 063 178, $P < 0.05$], reflecting the fact that solution times increased more than linearly for the two highest complexity levels (3–4). Solution times also increased across levels of distractors [$F(3,21) = 3.84$, MSE = 1 938 866, $P < 0.025$], with only the linear component being reliable [$F(1,7) = 10.33$, MSE = 2 122 689, $P = 0.015$]. The complexity and distractor manipulations yielded comparable solution times. Notably, mean solution times were longer for distractor level 4 (5.549 s) than for complexity level 3 (4.416 s), making it possible to separate the impact of relational complexity from that of general task difficulty. The greater variance in response time across complexity levels than across distractor levels was probably due to inter-problem and inter-subject differences in the time required to detect the nature of relations changing across the matrix; in contrast, additional distractors increased general difficulty but did not require additional inferences.

An analysis of errors rates provided converging evidence that

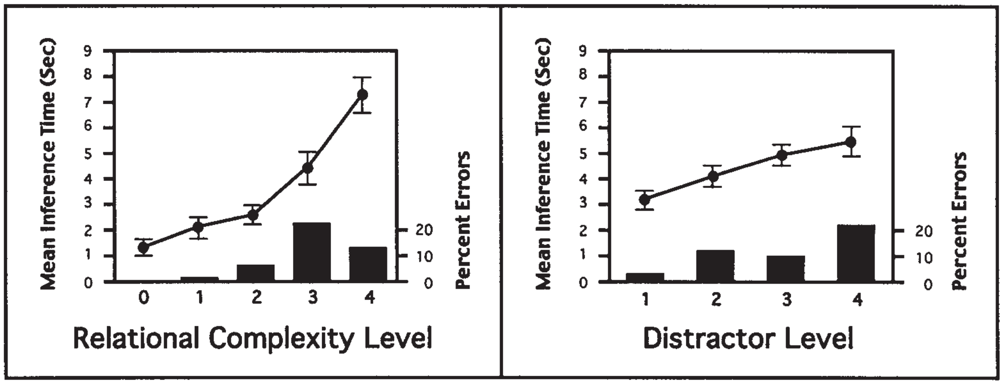

Figure 2. Mean solution times (correct trials only) and percent errors as a function of complexity and distractors. Error bars indicate 1 SE.

both manipulations influenced ease of solving the matrix problems. Error rates tended to increase across the five complexity levels [$F(4,28) = 6.02$, MSE = 111.81, $P = 0.001$], with a reliable linear component [$F(1,7) = 17.94926$, MSE = 99.24, $P < 0.005$]. The cubic trend was also reliable [$F(1,7) = 7.38$, MSE = 91.57, $P < 0.05$], reflecting the lower error rate at complexity level 4 relative to complexity level 3. It thus appears that the large increase in solution times from complexity level 3 to complexity level 4 (4.416–7.055 s) was at least partially attributable to a speed–accuracy trade-off. Error rates also tended to increase across the four distractor levels [$F(3,21) = 2.61$, MSE = 208.13, $P = 0.08$], with a reliable linear component [$F(1,7) = 6.01$, MSE = 206.88, $P < 0.05$]. Although solution times were longer for complexity level 4 than distractor level 4, accuracy showed the reverse trend. When both solution times and error rates are considered, the overall difficulty of the two highest levels of complexity was comparable to that of the two highest levels of distractors.

Results of Imaging Analyses

Initial analyses of each separate level of complexity and of distractors (subtraction of task minus rest) are shown in Figure 3. The results revealed a broad bilateral frontoparietal network within which signal changes were associated with solving matrix problems. As relational complexity increased beyond level 0, increasingly more extensive DLPFC activation was observed, first on the left side (level 1) and then bilaterally (level 2), with yet more anterior activation apparent at levels 3 and 4. This anterior DLPFC activation was much less apparent in the distractor conditions.

We then examined changes in fMRI signal as task difficulty increased across levels for the complexity and distractor tasks separately, using the linear-trend analyses described above. The resulting images in Figure 4 show all pixels in the brain in which increased task difficulty produced increases in MRI signal intensity; Table 1 provides a more detailed description of the regions of activation. The two analyses of linear trends yielded patterns of activation in multiple cortical areas. Activity in the inferior frontal gyrus (around BA 47) was apparent in both, as well as increases in DLPFC, although the complexity conditions seemed more left lateralized.

Specifically for complexity conditions, linear increases in activation were observed bilaterally in the posterior parietal lobe (BA 7). The complexity analysis also revealed activation around Broca's area (BA 44 and 47), as well as a broad strip extending anteriorly in left middle frontal gyrus (BA 9/46). In distractor conditions specifically, MR signal increased monotonically in the right middle frontal gyrus (BA 9). Activity correlated with level of distractors was also observed bilaterally in the inferior frontal gyrus (BA 47), the anterior cingulate, and the supplementary motor area (BA 6).

An additional analysis was performed to identify regions selectively activated by the highest levels of relational complexity, controlling for task difficulty. A subtraction of the two highest distractor conditions from the two highest complexity conditions revealed activation in the anterior and posterior cingulate, the medial frontal gyrus (BA 8), the right middle frontal gyrus (BA 9/46) and left middle frontal gyrus (BA 46/10) (Table 2 and Fig. 5).

When the opposite subtraction was examined (the two highest distractor conditions minus the two highest complexity conditions), significant activations were observed in bilateral posterior parietal cortex (BA 7), bilateral peri-sylvian cortex (BA 45, 47), and anterior cingulate (BA 32). The latter area was more posterior and superior (Talairach coordinates 2, 26, 32; k extent 103) to the anterior-cingulate area that yielded significant activation in the subtraction of the highest complexity conditions minus highest Distraction conditions (Table 2). In general, the areas of activation for the subtraction of the two highest distractor conditions minus the two highest complexity

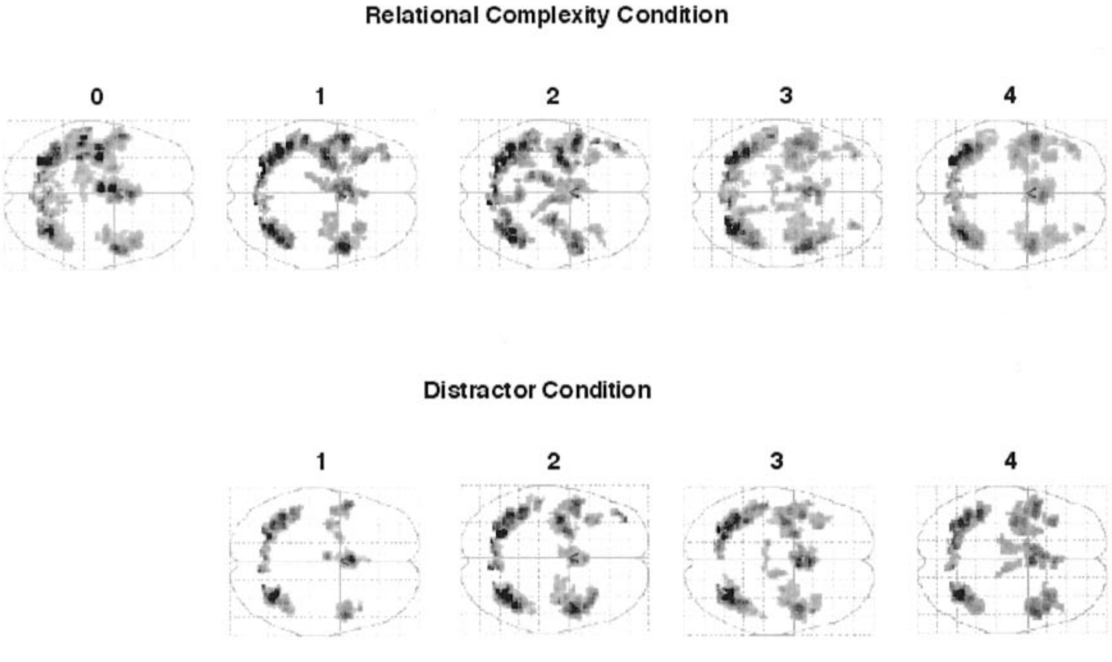

Figure 3. A subtraction analysis revealed responses to increasing levels of relational complexity (top row, increasing from left to right) and to increasing the number of distractors (bottom row, increasing from one on the left to four on the right). Each figure depicts an axial view of all brain voxels which were significantly ($P < 0.001$) more active during that block than during the resting baseline which was interspersed between blocks of matrix trials. The extent of frontal lobe activity appears to increase for both factors, but its consistent progression anteriorly occurs only for increasing relational complexity. The distractor conditions were created by adding distractors to a matrix with relational complexity level 1.

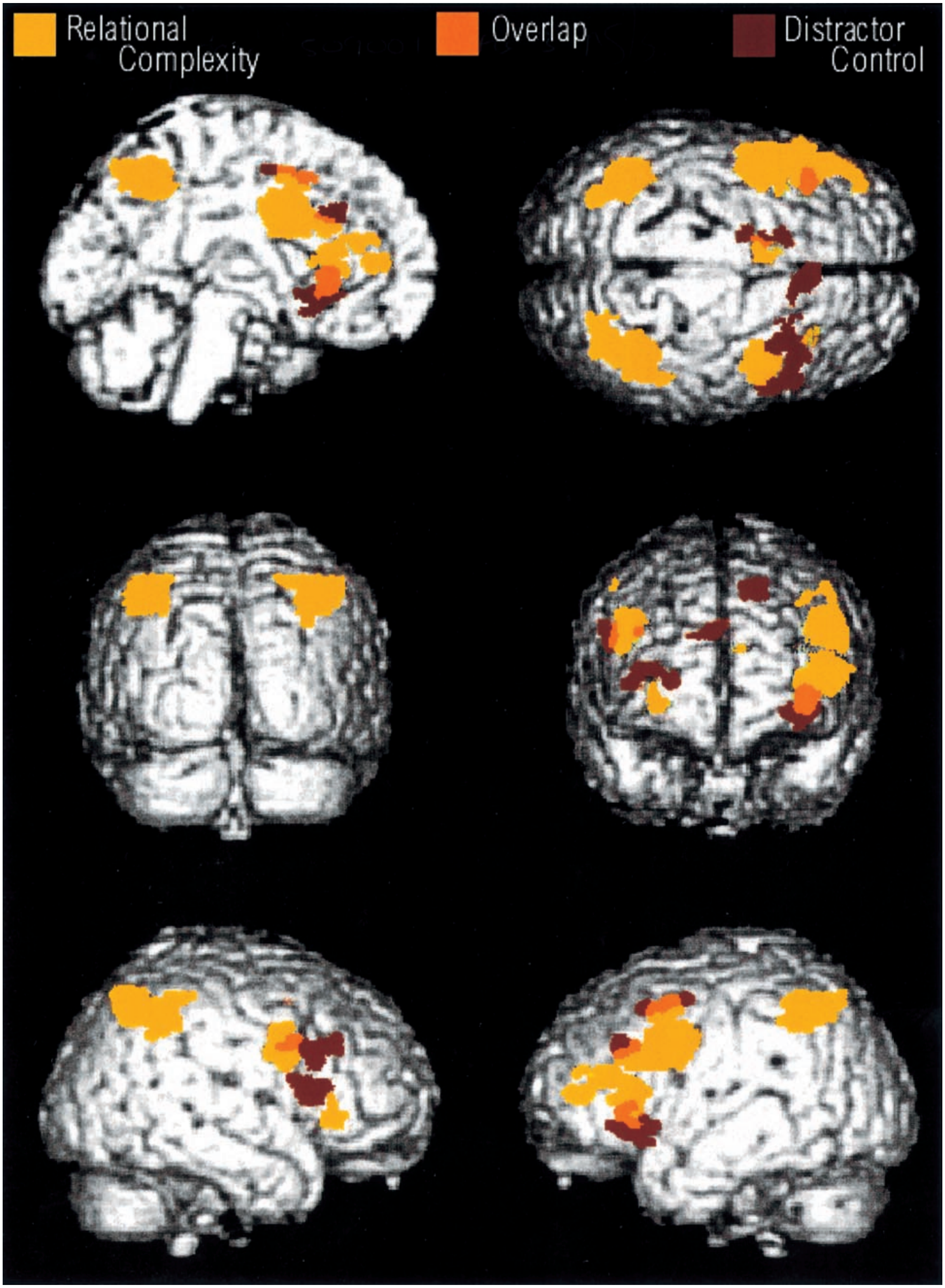

Figure 4. Linear trends for complexity and distractor contrasts on a rendered surface. Yellow represents the complexity conditions; red the distractor; and orange the areas of overlap.

Table 1
Areas of activation obtained in linear-trend analyses for relational complexity and distractor conditions

No.	Location	k extent	Maxima (*t*)	Position		
				x	*y*	*z*
Relational complexity						
1	L middle frontal gyrus	533	7.66	–50	22	26
2	R inferior frontal gyrus	250	7.56	42	6	32
3	L inferior frontal gyrus	392	6.91	–34	26	2
4	R superior parietal lobule	447	6.30	38	–60	52
5	L superior parietal lobule	364	6.11	–34	–68	50
6	R inferior frontal gyrus	54	5.13	28	26	–2
7	L cingulate gyrus	41	4.37	–6	6	24
Distractor control						
1	R middle frontal gyrus	63	6.72	50	18	30
2	R inferior frontal gyrus	117	5.15	36	20	12
3	L inferior frontal gyrus	81	5.04	–34	20	–8
4	R cingulate gyrus	64	4.95	6	26	28
5	L medial frontal gyrus	41	4.22	–14	–2	52

Table 2
Areas of activation: complexity levels 3–4 minus distractor levels 3–4

No.	Location	k extent	Maxima (*t*)	Position		
				x	*y*	*z*
1	L medial frontal gyrus	76	6.06	–8	44	42
2	R middle frontal gyrus	43	5.94	46	24	26
3	R middle frontal gyrus	45	5.91	40	24	38
4	L anterior cingulate gyrus	92	5.85	–4	36	24
5	L middle frontal gyrus	57	5.13	–32	40	22
6	L hippocampal gyrus	72	5.00	–28	–48	4
7	R precuneus	45	4.57	6	–62	42
8	L cuneus	68	4.34	–4	–72	16

conditions are consistent with increased stimulus processing at the highest levels of the distractor conditions.

Time-series graphs were generated for three regions of interest identified in the linear-trend analyses for relational complexity (an anterior frontal region, a dorsolateral frontal region, and a posterior parietal region). The graphs for the anterior DLPFC are presented in Figure 6. Percent signal differences from resting baseline were computed for the anterior frontal region for each subject. The region of interest was defined bilaterally as anterior from +20 anterior and from –4 to +20 superior (Talairach coordinates). This area includes all of BA 10, and also portions of BA 46 and BA 47. The percent signal differences were averaged across subjects and blocks for each trial type, and were then smoothed temporally with adjacent time points. In the complexity graph (Fig. 6*A*), the most notable feature is that the three highest complexity levels (R2–4) consistently show greater activation over the task period than do the lower complexity levels (R0–1). In contrast, the different levels of distractors do not show a clear pattern of differential activation during task performance (Fig. 6*B*). Qualitatively similar patterns were observed in comparable graphs for the other two regions of interest.

Discussion

Our findings reveal that reasoning problems that vary in relational complexity – the number of explicit relations that jointly determine the solution to a problem – recruit a cortical network encompassing several anterior and posterior areas. Moreover, the change in activity observed as relational complexity increased was distinguishable from activity changes resulting from increases in general task difficulty. For the matrix problems used in this study, solution times and error rates showed comparable increases in task difficulty. Yet although both manipulations systematically increased the difficulty of the same type of reasoning problems, increasing relational complexity yielded a distinct pattern of neural activity.

The most prominent areas of activation that correlated with increases in relational complexity included DLPFC (foci in BA 9 and 46, with significant left hemisphere activation extending into the more anterior BA 10). Although increases in number of distractor forms also activated DLPFC, the area activated in this control condition was less left-lateralized and more posterior. A greater degree of anterior left prefrontal involvement was also apparent in the analysis of areas selectively activated by the two highest levels of complexity, subtracting areas activated by the two highest levels of distractors. In addition, time-series analyses revealed greater anterior prefrontal activation in the three highest complexity levels. The latter result is consistent with the neuropsychological findings of Waltz *et al.* (Waltz *et al.*, 1999), who found that prefrontal patients were catastrophically impaired in their ability to solve matrix problems that required integration of multiple dimensions of variation (i.e. complexity level 2 and above). The present results confirm the hypothesis that increasing relational complexity activates DLPFC, with more left and more anterior activation being produced in response to the highest complexity levels.

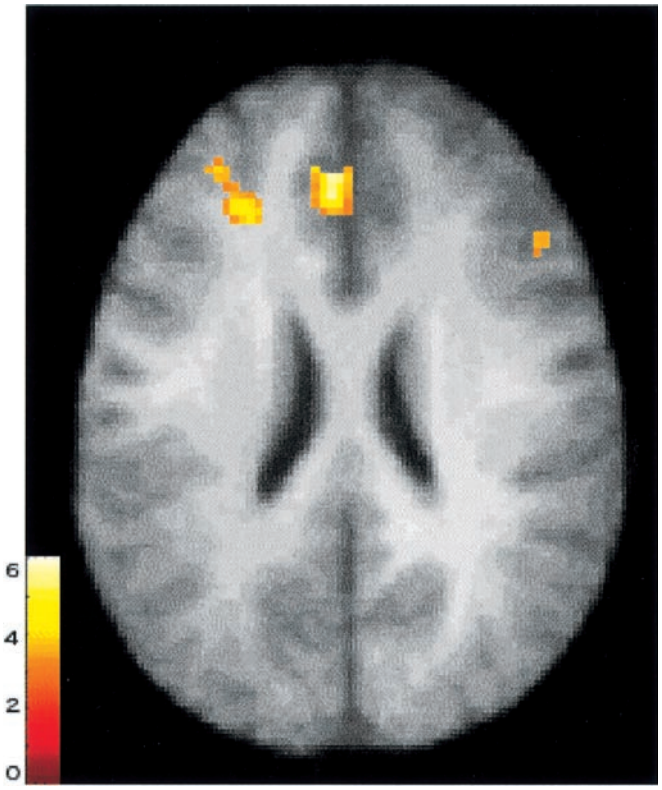

Figure 5. Difference map for the contrast subtracting distractor levels 3–4 from complexity levels 3–4. Slice selection at Talairach $z = 24$. The bar depicts z-score for clusters. This contrast revealed a significant cluster in the anterior portion of the left middle frontal gyrus.

The linear-trend analysis for complexity also specifically revealed extensive bilateral activation in the posterior parietal lobe (BA 7). This area is commonly activated by tasks involving manipulation of spatial relations, including mental rotation (Bonda *et al.*, 1996; Belger *et al.*, 1998; Carlson *et al.*, 1998; Coull and Frith, 1998). The spatial relations that defined the matrix problems were all monotonic changes in visuospatial dimensions such as orientation and size of forms, and solving the problems required analyzing and extrapolating these changes to form a mental representation of the forms in the empty cell. The number of spatial relations that had to be manipulated increased with complexity level; accordingly, increasing complexity progressively activated cortical areas associated with visuospatial processing. The analysis for the highest complexity levels also yielded activation in the medial gyrus (BA 8), which may be associated with the increased demand for comparative inspection of various features of the stimuli that recruits this gaze control center (Petit *et al.*, 1995), though there is some debate as to the precise localization of the frontal eye fields in humans (Luna *et al.*, 1998). The combination of prefrontal and parietal activation that accompanied increasing relational complexity is consistent with a cortical circuit in which visuospatial relations are represented and manipulated in posterior cortical regions under the control of prefrontal cortex (Quintana and Fuster, 1993).

Parietal activation did not increase across levels as much in the control distractors task. Although the addition of constant forms increased the sheer amount of visual information in matrix problems, it did not increase the number of relations that had to be manipulated (which was held constant at one for all problems in the distractor conditions). A comparison of each level of distractor to baseline revealed that while frontal activation increased with level, the parietal region around the intraparietal sulcus activated more consistently across distractor levels; thus the failure to find a linear increase in parietal activation reflected extensive activation at lower levels of distractors, rather than a lack of it at higher levels (see Fig. 3). An increase in the number of distractor forms was also associated with increased activation in the anterior cingulate, a region associated with inhibitory attentional control and response conflict (Paus *et al.*, 1993; Muir *et al.*, 1996; Casey *et al.*, 1997; MacDonald *et al.*, 2000). In the distractor conditions of the matrix task, subjects were required to identify and maintain up to four added distractor forms while also maintaining the critical relation defined on one item across the matrix. Subjects were required to attend to the distractor forms because they varied in the answer choices. Increasing relational complexity also recruited anterior cingulate; the subtraction analysis revealed significantly greater activation in anterior cingulate for the higher complexity trials than for the higher distractor trials. The demands of binding multiple relations into a single answer choice in the highest complexity

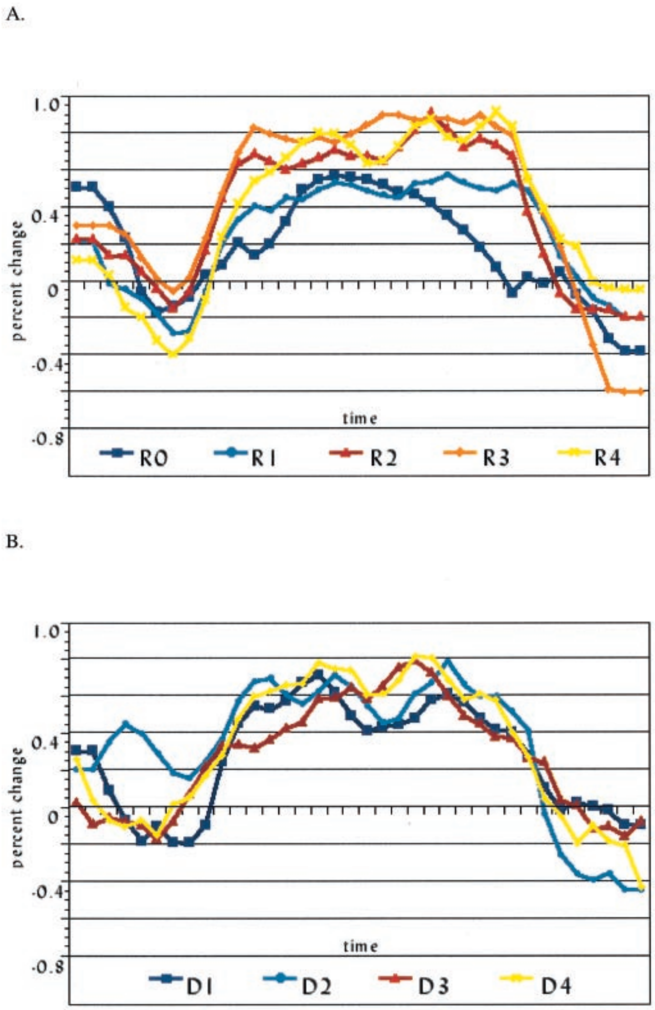

Figure 6. Time-series graphs for (*A*) relational complexity conditions and (*B*) distractor conditions, in bilateral anterior prefrontal cortex (BA 10/46/47). Percent signal differences from resting baseline were computed for each subject and then averaged across all trials for all subjects. The x-axis depicts 36 images collected at 3 s intervals: eight images (24 s) of baseline period, 20 images (60 s) of task period, eight images (24 s) of subsequent baseline period.

levels appear to have elicited the greatest participation of the anterior cingulate.

Both increased complexity and increased number of distractors were associated with activation in inferior frontal gyrus (predominantly in the left anterior region for the complexity condition). Although often associated with semantic retrieval, recent evidence suggests that this region is involved in tasks requiring selection among strongly competing alternatives (Thompson-Schill *et al.*, 1997, 1998). In the matrix task, increasing relational complexity demands selection among a greater number of possible dimensions of monotonic change; and increasing number of distractors requires selection among a greater number of visual forms in each cell of the matrix. Our results thus extend previous findings regarding the role of left inferior frontal gyrus in selection based on semantic information, indicating a similar role for this region in selection among visuospatial elements potentially relevant to a decision.

Activation in anterior prefrontal cortex has been observed in some studies of episodic memory (Buckner *et al.*, 1998; MacLeod *et al.*, 1998; Christoff and Gabrieli, 2000), although not in others (Fletcher *et al.*, 1998; Klingberg and Roland, 1998). Episodic retrieval tasks that recruit this area typically involve either retrieval of information integrated across stimuli presentations or retrieval of deeply encoded information, which may entail synthesis of stimulus materials with existing knowledge. Common to cognitive processing in these studies is the constrained integration of information from long-term memory into a representation meeting current task demands. Binding new information with existing knowledge into a meaningful and useful representation depends on appropriately relating elements of the current situation to previously encoded experience, potentially forming a complex relational structure. The process of binding together relational structure together may involve anterior prefrontal cortex in some episodic memory studies.

A number of other proposals have been made about the nature of the cognitive processes that recruit more anterior regions of prefrontal cortex. These include internal generation of responses (Christoff and Gabrieli, 2000), selection and evaluation of action sequences (Baker *et al.*, 1996), and maintenance of multiple goal contingencies (Koechlin *et al.*, 1999). It may be possible to view such alternatives as special cases of variation in the relational complexity of the task representations required to select goal-appropriate actions. In general, many other aspects of complex cognitive processes, such as selection of actions, manipulation of goal hierarchies, and integration of multiple modalities into a single representation, can be viewed as special cases of processing at high levels of relational complexity. Other tasks, including deductive as well as inductive reasoning (Waltz *et al.*, 1999), can be potentially analyzed in terms of relational complexity. Future neuroimaging studies may reveal the extent to which relational complexity in different types of cognitive tasks activates a shared neural substrate.

Notes

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