# Integration of diverse information in working memory within the frontal lobe

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**Ability to integrate diverse forms of information in current thought, or working memory, is essential for human reasoning and problem solving. We used functional imaging to identify brain regions preferentially involved in maintaining integrated versus unintegrated information in working memory. For equal amounts of verbal and spatial information, activation of prefrontal cortex was greater for maintaining integrated rather than unintegrated representations. Posterior brain regions showed the opposite pattern. These results demonstrate frontal-lobe specialization in maintaining working-memory representations that integrate verbal and spatial information. The role of prefrontal cortex in integrating multiple forms of information in working memory may underlie its unique contribution to high-level cognition that demands flexible mental representations.**

Working memory involves the short-term maintenance of information relevant to current goals. Neuroimaging studies show that working memory is mediated by frontal and posterior cortical regions differing in the types of information maintained (for instance, verbal, spatial or object) and in the kinds of contributions made to working memory (for instance, directing rehearsal versus storing information *per se*)[1–26]. Whereas posterior cortical regions seem to specialize in the type of information held in working memory[5,10,17,22,23,27–29], several findings suggest that prefrontal areas have a special role in integrating different types of information in working memory. Electrophysiological studies in nonhuman primates reveal frontal lobe cells that maintain both spatial and object information in working memory[30–32]. Neuroanatomical tracing in nonhuman primates suggests prefrontal cortex as a region of polymodal sensory convergence from posterior cortical areas (parietal, temporal and visual regions)[33,34]. Neuroimaging studies in humans have shown proximal foci of activation in frontal cortex for maintaining different types of information (for example, letters, objects, locations or faces) in working memory. The present study aimed to test directly the hypothesis that human frontal cortex has a specialized role in maintaining integrated information in working memory[35,36].

Six subjects (right-handed; mean age, 24.5 years) were scanned via functional magnetic resonance imaging (fMRI). Each subject performed four different tasks in four successive scans. Subjects performed two scans in which they were asked to maintain either spatial information or verbal information (**Fig. 1**). In the spatial scan, subjects saw a target display of four spatial locations appear for two seconds and then disappear. In the verbal scan, subjects saw a target display of four letters appear for two seconds and then disappear. Over a retention interval, subjects then had to maintain those letters or locations in working memory. Subsequently, they saw a single lower-case probe letter in the verbal scan or a single probe location in the spatial scan, and decided whether the letter or the location,

respectively, had appeared in the previous display. For the verbal scans, the letters were shown at study and test in different cases, so that subjects coded the verbal identity rather than the visual appearance of letters.

In two other scans, subjects were asked to maintain both spatial and verbal information either in an integrated or in an unintegrated fashion. In both scans, subjects saw a target display of four letters and four spatial locations appeared for two seconds and then disappeared (**Fig. 2**). In the integrated scan, the four letters to be remembered were displayed in the four locations to be remembered; thus verbal information and spatial information were bound together. In the unintegrated scan, the four letters were presented centrally and separately from the four indicated locations; thus, verbal information and spatial information were separate. Subjects then had to maintain those letters and locations in working memory over a retention interval. Subsequently, they saw a single probe letter in a single probe location and had to judge whether both the letter and the location had been shown in the previous display (regardless of whether that particular letter had been in that particular location). Positive-probe trials presented a letter and a location that had been in the target display; negative probe trials presented either a different letter or a different location or both.

Scans using a 5-second retention interval between the target and probe displays were compared to a baseline identical in all regards except the retention interval between the target and probe displays was only 250 ms, so that information did not have to be maintained in working memory. This allowed for isolation of areas involved in maintaining different types of information (spatial, verbal, verbal and spatial/integrated, verbal and spatial/unintegrated) in working memory. As processes involved in encoding the target information and in responding to the probe were equivalent for the delay (5-second interval) and no-delay (250-ms interval) trials, our scans did not allow identification of areas involved in these processes.

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**Fig. 1.** Spatial and verbal trial types. For the spatial trials, subjects viewed for two seconds and were asked to remember a target display comprising four locations enclosed by parentheses. Locations were selected randomly on the circumference of an imaginary ellipse. In the spatial condition (left panel), subjects had to maintain location information for either 5 s (upper halves of each panel) or 250 ms (lower halves of each panel). Subsequently, subjects were probed and had 2.5 s to determine whether the probe location was one of the locations in the target display. For the verbal trials, subjects viewed for two seconds and were asked to remember a target display comprising four upper-case consonants in the center of the display. They had to maintain letter information for either 5 s (upper halves of each panel) or 250 ms (lower halves of each panel). Subsequently, subjects were probed and had 2.5 s to determine whether a single lower-case letter had been in the target display. A 4.75-s delay was added to the trials with short delays to equalize the time between target displays.
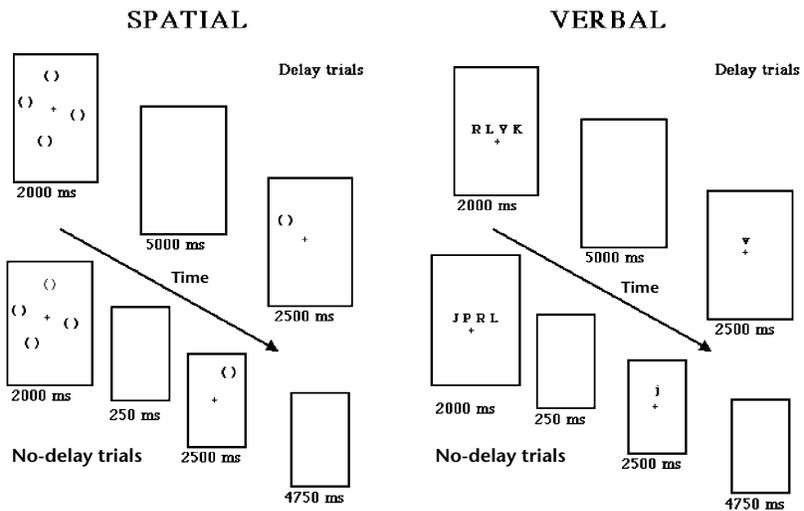
## RESULTS

In general, subjects found the spatial and verbal conditions easier than the bound and separate conditions. Subject reaction times (RTs) were significantly shorter in the spatial condition [average RT, 979 ms; $F_{1,5} = 50.5$, mean squared error (MSE) = 293654, $p = 0.0009$] and the verbal condition (average RT, 834 ms, $F_{1,5} = 391.8$, MSE = 805951, $p = 0.0001$) than in the bound and separate conditions (1200 ms). Subjects were not significantly different in accuracy in the spatial condition (average accuracy, 83.3%; $F_{1,5} = 0.49$, MSE = 52.44, $p = 0.51$), but were significantly more accurate in the verbal condition (average accuracy, 97.6%; $F_{1,5} = 82.35$, MSE = 763.04, $p = 0.0003$) than in the bound and separate conditions (87.1%).

Maintaining only spatial information resulted in prominent activations in right frontal and bilateral superior parietal regions.

Maintaining only verbal information, in contrast, resulted in prominent activations in left inferior frontal (Broca's area), left inferior parietal and temporal regions (**Fig. 3**). The different locations of activation reflect the neural separation of short-term memory for spatial versus verbal information. Both imaging results were consistent with previous imaging studies of maintenance of spatial or verbal information in working memory[7,10,11,20,22,23,26].

When maintaining both spatial and verbal information, for both positive and negative probe trials, subjects were significantly more accurate in the bound (88.5%) than in the separate (85.7%) condition ($F_{1,5} = 7.18$, MSE = 46.62, $p = 0.044$) and tended to be faster in the bound (1139 ms) than in the separate (1261 ms) condition ($F_{1,5} = 4.59$, MSE = 105186.7, $p = 0.076$). There was no significant effect of delay or condition × delay interaction. Further examination of only the positive-probe tri-

**Fig. 2.** Bound and separate trial types. For all trials, subjects viewed for two seconds and were asked to remember a target display comprising four upper-case consonants and four locations enclosed by parentheses. Locations were selected randomly on the circumference of an imaginary ellipse. In the bound condition (left panel), letters were placed in the locations to be remembered. In the separate condition (right panel), letters were located elsewhere. Subjects had to maintain both letter and location information for either 5 s (upper halves of each panel) or 250 ms (lower halves of each panel). Subsequently, subjects were probed and had 2.5 s to determine whether a single lower-case letter had been in the target display and whether its location was one of the locations in the target display (not necessarily the same letter). A 4.75-s delay was added to the trials with short delays to equalize the time between target displays. Examples of two kinds of positive probes are shown in the bound condition. In the delay trial, a positive congruent probe is shown; the probe is congruent with the target because the same letter was presented in the same location. In the no-delay trial, a positive incongruent probe is shown; the probe is incongruent because the letter had been presented in a different location. For both kinds of probes, subjects would answer affirmatively because both the letter and the location had been presented in the target.
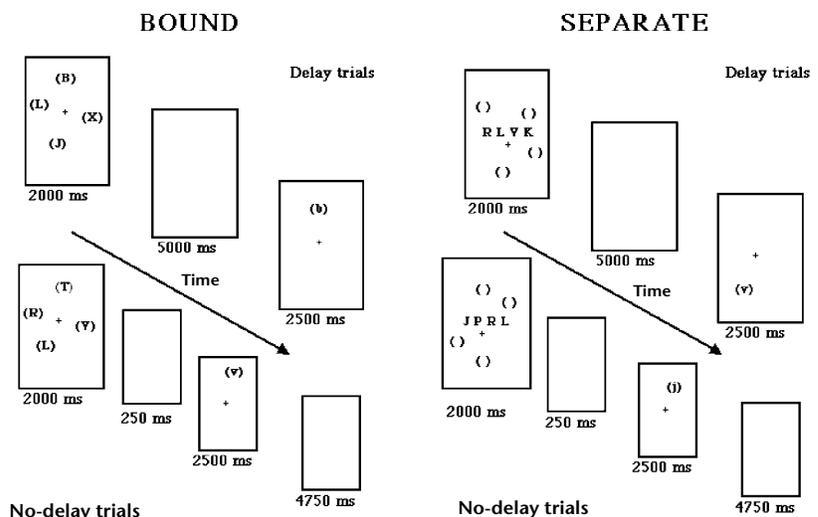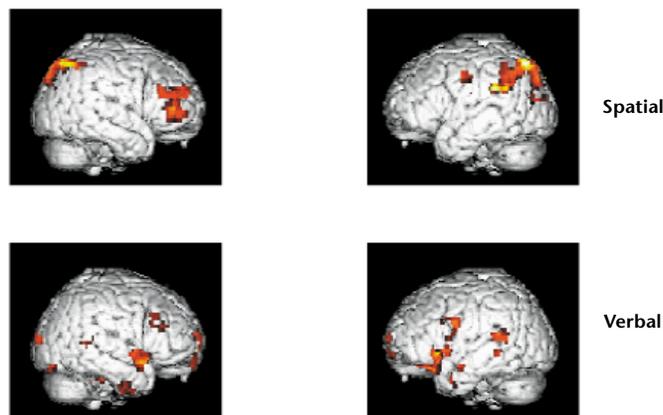
**Fig. 3.** Composite activation maps of spatial and verbal conditions. Images show regions significantly more active in the delay than in the no-delay conditions coded in red/yellow. Right-hemisphere and left-hemisphere views of the brain are shown for each condition. Regions that were more active when subjects maintained spatial information for 5 s rather than 250 ms are shown in the upper row. Right frontal and bilateral parietal regions show activation. Regions that were more active when subjects maintained verbal information for 5 s rather than 250 ms are shown in the lower row. Left inferior frontal, left posterior parietal and temporal regions show activation.

gruent (1123 ms) than the incongruent (1251 ms) positive probes ($F_{1,5} = 7.04$, MSE = 115585.75, $p = 0.038$); they also tended to be more accurate for the congruent (95.8%) than the incongruent positive probes (81.9%; $F_{1,5} = 4.31$, MSE = 1157.59, $p = 0.09$).

These findings indicate that subjects maintained the target displays in the bound condition in an integrated fashion, such that they could quickly compare the congruent probes to the similar, integrated content of working memory. They were slower, however, when they had to reorganize the information in working memory to compare to the incongruent probes. These results validate the conclusion that verbal and spatial information in the bound displays were maintained in an integrated fashion in working memory during the delay period and before probe presentation.

Congruent and incongruent positive-probe trials occurred equally often in the 5-second delay and 250-millisecond 'no-delay' conditions. There was no congruency × delay interaction in either reaction time ($F_{1,5} = 0.02$, $p = 0.90$) or accuracy ($F_{1,5} = 0.00$, $p = 1.0$). Therefore, the imaging results do not reflect the behavioral differences between congruent and incongruent trials. Rather, they reflect the mental representation of information before appearance of the positive (congruent or incongruent) and negative probe types.

Many brain regions were activated in both the bound and separate conditions as subjects maintained verbal and spatial information in working memory for 5 seconds versus 250 milliseconds. These regions included frontal, parietal and temporal areas that were involved in maintaining verbal and spatial information (**Fig. 3**). Scans under bound or separate conditions were directly compared to identify areas preferentially involved in maintaining integrated versus unintegrated information in working memory (**Fig. 4**). Maintenance of integrated information resulted in greater activity than maintenance of unintegrated information in the right frontal cortex, specifically right middle and superior frontal gyri. This

als in the bound condition provided evidence that subjects maintained verbal and spatial information in an integrated working-memory representation (**Fig. 3**). The positive-probe trials consisted of two types of probe trials. Positive congruent-probe trials presented the same letter in the same location congruent to what had been shown in the target display. Positive incongruent-probe trials presented a previously seen letter in a location that had been occupied by a letter different from that shown in the target display. Subjects responded affirmatively for both positive-probe trials, because the letter and location had been in the target display. Subjects responded significantly faster for the con-

**Fig. 4.** Difference maps of bound versus separate scans. Images show regions that were significantly more active in the bound than in the separate condition coded in red/yellow and regions that were significantly more active in the separate than in the bound condition coded in blue. Four slices were selected to highlight the different regions that are involved in the different conditions. Difference maps were created by performing paired subtractions between statistical parametric maps (SPMs) for each subject after warping to the reference template (structural image averaged across all subjects) and then averaging the difference images across subjects. The resulting functional maps were then overlaid on the reference template.
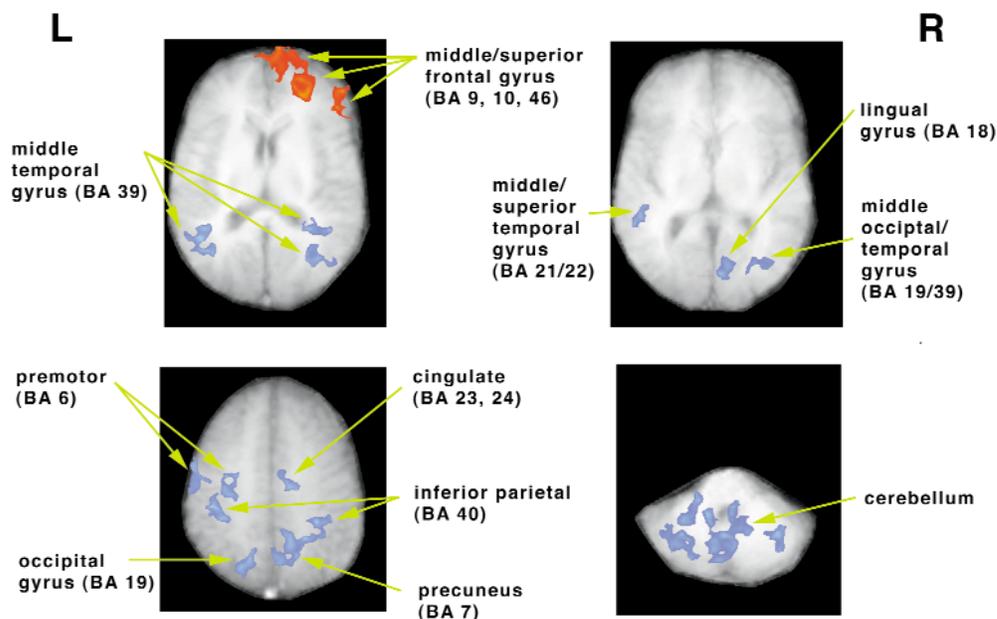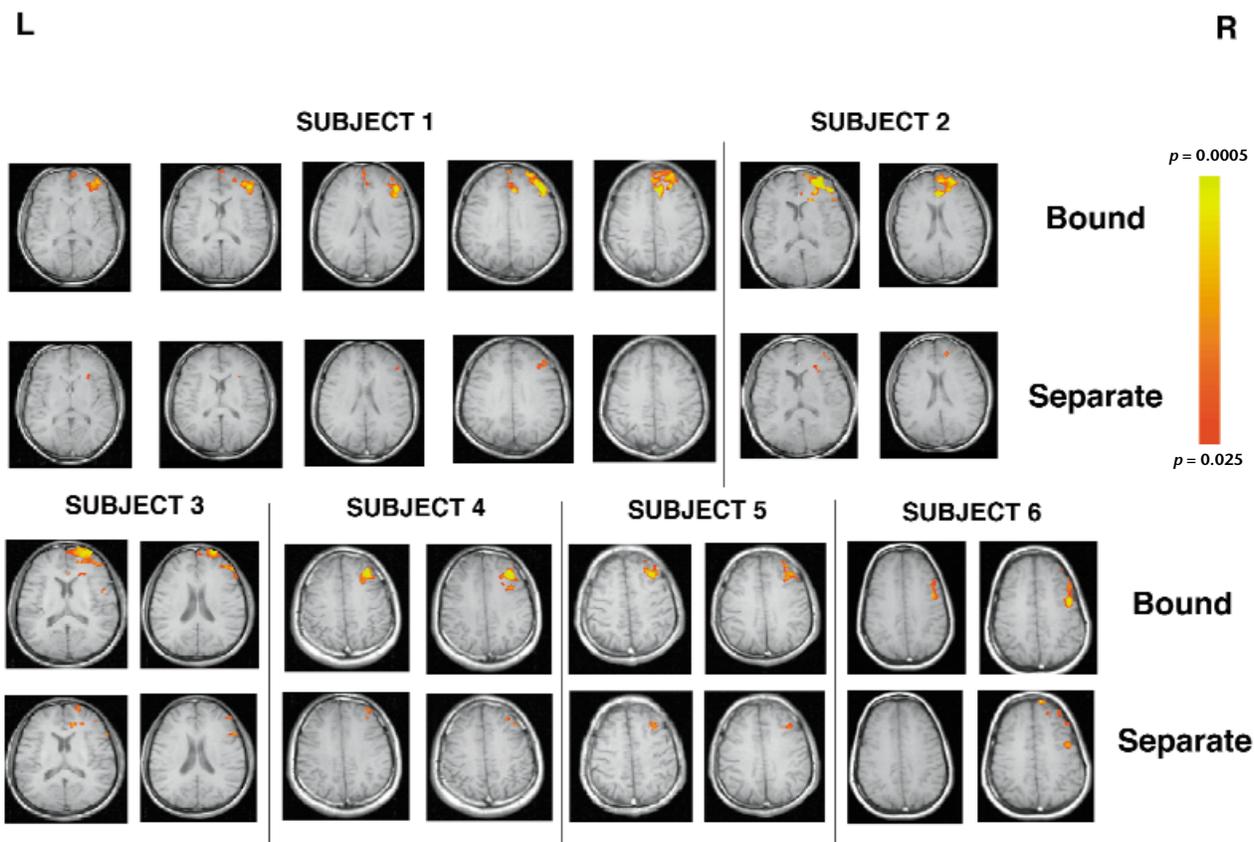
**Fig. 5.** Activation in the right frontal cortex in six subjects. For each subject, a minimum of two slices depicting differential activation levels in the right frontal cortex were chosen. The right frontal cortex was identified anatomically as a region of interest (ROI) in these slices. Statistical analyses were confined to that ROI and superimposed on each subject's anatomical MR image. The upper row shows robust right frontal activation for maintaining bound information for 5 s versus 250 ms; the lower row shows that this region was minimally activated while maintaining separate information for 5 s versus 250 ms.

was evident not only in the group average, but also in each individual subject (**Fig. 5**). Maintenance of unintegrated, relative to integrated, information resulted in greater activity in multiple posterior brain areas, including bilateral parietal, temporal and cerebellar regions.

In a second analysis, bound and separate conditions were compared to the combination of the purely spatial and verbal conditions. Here also, the bound versus spatial and verbal comparison revealed substantially greater involvement of the right prefrontal cortex in maintaining integrated spatial and verbal information than in maintaining either spatial or verbal infor-

mation alone (**Fig. 6**). Comparison of separate versus spatial and verbal scans revealed posterior regions that were more involved in maintaining unintegrated verbal and spatial information than in maintaining either spatial or verbal information alone. There was not, however, any difference in the right prefrontal cortex for maintaining unintegrated verbal and spatial information. Thus, both analyses provide convergent evidence for a dissociation of the right frontal region preferentially involved in the maintenance of integrated working-memory representations, and multiple posterior brain regions preferentially involved in the maintenance of non-integrated working-memory representations.

**Fig. 6.** Difference maps of bound or separate condition versus spatial (SPA) and verbal (VER) conditions. Left column, posterior view of brain; right column, anterior view. Images show regions that were significantly more active in the bound or separate condition than in the spatial and verbal conditions coded in red/yellow. Regions that show greater activation in the bound condition than in both the spatial and verbal conditions are depicted in the top row. The anterior regions show robust activation, specifically in the right prefrontal region, whereas posterior regions are minimally active. Regions that show greater activation in the separate condition than in both the spatial and verbal conditions are depicted in the bottom row. The posterior regions show robust activation, whereas there is no activation in the anterior regions. Difference maps were created by performing a contrast analysis between the bound or separate condition versus spatial and verbal conditions.
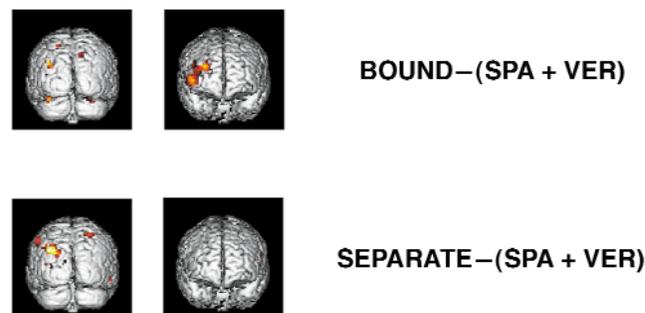
## DISCUSSION

The right prefrontal activation associated with the integration of verbal and spatial information is in agreement with meta-analyses showing right prefrontal involvement in both spatial and nonspatial working memory[9,35,36]. In contrast, left prefrontal regions show involvement only in nonspatial working memory. Thus, right prefrontal regions seem to have a flexible representational architecture that processes both spatial and nonspatial information. Posterior activations have been more material specific, with specific areas in parietal and temporal regions involved either in verbal or spatial working memory[5,10,17,22,23].

Many studies have shown greater activation in prefrontal cortex due to increased demands of load, duration or manipulation on working memory[1–23]. In contrast, greater prefrontal activation in the present study occurred in the easier condition: subjects were more accurate and faster in the bound than in the separate condition. The prefrontal activation, therefore, reflected the nature of the working-memory representation, rather than working-memory load or duration, which were equal in the two conditions.

Baddeley has proposed separate 'slave system' buffers that allow for temporary retention of discrete information in working memory, including a visuospatial buffer and a phonological buffer[37]. Logie and others have further decomposed the visuospatial buffer into separate visual and spatial buffers[38]. The present fMRI results provide evidence for another type of buffer, namely, one that allows for temporary retention of integrated information.

The capacity to integrate information in working memory may enhance the efficiency of working memory in several ways. For example, a study examining the capacity of short-term memory for visuospatial information found that subjects show equivalent accuracy in maintaining the memory of a single feature of objects (for instance, color of an object) as in maintaining four features of objects (for instance, color, size, orientation and shape)[39]. However, performance decreases as the number of objects that need to be remembered increases. In other words, more information could be maintained for visuospatial information in a bound rather than separate display. In our study, the finding subjects were significantly more accurate and tended to be faster in the bound than in the separate condition suggests more efficient access to integrated relative to unintegrated information. Further, the mean volume of brain area preferentially activated by the unintegrated information (11,483 mm³) was more than twice that activated preferentially by the integrated information (4,368 mm³). The greater activity seen in the posterior regions suggests that more neural resources are required when maintaining separate information than bound information. Thus, integration may provide for efficient working-memory representations.

Human lesion and neuroimaging studies show that prefrontal cortex is essential in reasoning and problem solving[40–45]. The capacity to integrate, or relate[43], different kinds of information may endow frontal cortex with a flexible representational structure important for the fluid, innovative thinking that underlies successful reasoning and problem solving. More generally, the prefrontal activation in the present study may reflect one solution to the binding problem in the human brain—the problem of integrating the outputs of multiple, specialized processing pathways.

## METHODS

All studies were done in full compliance with the guidelines of the Institutional Review Board (Assurance #M1272-02) of Stanford University. Subjects performed four scans: bound, separate, verbal and spatial. Each scan consisted of six cycles, with each cycle comprising blocks of 5-s maintenance trials alternated with blocks of 250-ms maintenance trials. There were 4 trials per block with a total of 24 (12 negative-probe trials and 12 positive-probe trials) 5-s maintenance trials and 24 (12 negative-probe trials and 12 positive-probe trials) 250-ms maintenance trials in each scan. In the bound scan, the positive-probe trials were equally divided into congruent and incongruent trials. The scan order was counterbalanced across the subjects. Stimuli were generated from a computer and back-projected onto a screen located above the subject's neck via a magnet-compatible projector. Visual images were viewed from a mirror mounted above the subject's head. The sequence of the presentations of the stimuli were synchronized with the imaging sequence of the scanner.

**fMRI methodology.** Imaging was performed with a 1.5T whole-body MRI scanner (General Electric Medical Systems Signa, Rev. 5.5, Waukeshau, Wisconsin). A T2* sensitive gradient echo spiral sequence[46] was used for functional imaging with parameters of TR = 1440 ms, TE = 40 ms, flip angle = 83°, FOV = 20 cm, inplane resolution = 1.56 mm², sampling interval = 2.88 s and number of temporal frames or image volumes = 160. Sixteen 7-mm thick slices with a 0-mm inter-slice interval and covering the whole brain were acquired in the horizontal plane of the Talairach and Tournoux atlas[47].

**fMRI analysis.** Functional images were motion-corrected and normalized using SPM96, interpolated to $2 \times 2 \times 4$ mm³ voxels and spatially smoothed with a Gaussian filter (full width at half maximum, 8 mm). Low-frequency noise and differences in global signal were removed. Single subject data were analyzed with a fixed-effects model. Group data were analyzed using a random-effects model. For the group analysis, images were averaged to create one image of mean activity per condition and subject. These average images were used to create a series of SPM{Z} maps depicting differences in brain activity between task conditions. Activation maps for both fixed-effects model and random-effects model analysis were created with SPM96 software (http://www.fil.ion.ucl.ac.uk/spm)[48] with an intensity threshold of $p < 0.025$ and spatial-extent threshold of $p < 0.05$.

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