An Event-related Functional MRI Study of the Stroop Color Word Interference Task

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In this study we have attempted to define the neural circuits differentially activated by cognitive interference. We used event-related functional magnetic resonance imaging (fMRI) to identify areas of the brain that are activated by the Stroop word-color task in two experiments. In the first experiment, we used infrequent, incongruent colored word stimuli to elicit strong Stroop interference (the 'conventional Stroop' paradigm). In the second experiment, we used infrequent, congruent colored words (the 'inverse Stroop' paradigm) to confirm that the regions identified in the first experiment were in fact specifically related to the Stroop effect and not to nonspecific oddball effects associated with the use of infrequent stimuli. Performance of the conventional Stroop specifically activated the anterior cingulate, insula, premotor and inferior frontal regions. These activated regions in the current experiment are consistent with those activated in fMRI experiments that use a more traditional block design. Finally, analysis of the time course of fMRI signal changes demonstrated differential onset and offset of signal changes in these activated regions. The time course results suggest that the action of various brain areas can be temporally dissociated.

Introduction

Selective attention plays a critical role in our ability to process task-related stimuli, and to filter task-unrelated stimuli so as to guide the execution of task-relevant responses. Selective attention is therefore engaged in tasks that produce cognitive interference, or competing information-processing demands. The Stroop task (Stroop, 1935) has been used for many years as a test that exploits the conflict between one well-learned or automatic behavior (reading) and a decision rule that requires this behavior to be inhibited. Given that the Stroop task has been routinely used in normal and patient cognitive studies, there is a continuing interest in better understanding the neural circuitry recruited during the Stroop task.

The classic Stroop test relies on the observation that color naming can be slowed by the concomitant presence of a color-word (competing information). For example, naming the ink color of the word *blue* that is printed in red color is typically slower than naming *blue* displayed in blue color. This is because subjects must filter or inhibit their automatic reading in order to engage in color-naming. Many previous behavioral studies have established the features of the Stroop task that produce cognitive interference (MacLeod, 1991). Recent neuroimaging studies have indicated that several brain regions are involved in the performance of the Stroop task (Pardo *et al.*, 1990; Bench *et al.*, 1993; Taylor *et al.*, 1994; Carter *et al.*, 1995; Bush *et al.*, 1998), although these imaging studies do not all agree on which brain areas are most centrally involved in resolving Stroop interference. Pardo and colleagues, for example, have suggested that the anterior cingulate is the most relevant region (Pardo *et al.*, 1990), whereas others have suggested that the anterior cingulate activation is not specific for the interference effect (Bench *et al.*, 1993). Most of these imaging studies have thus far been performed using a 'block' design, in which activations of brain regions are obtained by subtracting images from blocks recorded in an 'off' condition from blocks recorded in an 'on' condition.

We previously used a block-design in an functional magnetic resonance (fMRI) study to investigate Stroop interference (Peterson *et al.*, 1999). In that report, we postulated that different parts of the brain are functionally connected and contribute to specific aspects of task performance. However, experiments that use block designs suffer a number of limitations. They are more susceptible to habituation and to changes in behavioral strategies [e.g. practice effects (Bush *et al.*, 1998)] within and between blocks. The more recently developed event-related design allows more flexible experimental designs, and the advantages of this technique have recently been demonstrated in various fMRI studies (Buckner *et al.*, 1996; Robson *et al.*, 1998). In a typical event-related study, the hemodynamic responses evoked by repeated presentations of single stimuli are recorded and the average transient response is calculated. Event-related imaging thus allows the study of the transient brain activation directly resulting from an immediately preceding cognitive event so that activations evoked by a cognitive task can be studied repeatedly while minimizing habituation to the main effect (Buckner *et al.*, 1998).

We therefore implemented an event-related fMRI version of the Stroop task to better determine the neural circuitry that underlies this task. We aimed to elucidate the time course of signal changes to better understand how brain regions work in concert in complex cognitive tasks. We also compared the pattern of activation recorded in this new design with our previous block-design study. Studies in clinical settings have suggested that performance on the Stroop task correlates with function within the frontal cortical region (Perret, 1974; Golden, 1976) and the anterior cingulate cortex (Carter *et al.*, 1997). We therefore aimed in particular at quantifying the differential activations of frontal and anterior cingulate structures in this study.

In the current study, we performed two variants of the Stroop color-word interference task. In the first experiment, we maximized Stroop interference by presenting incongruent words randomly and infrequently among stimuli in which color words were presented most often in their congruent color. The transient hemodynamic changes evoked by the incongruent color words were then evaluated relative to the responses corresponding to the congruent color words. We measured the magnitude of the activation as well as the signal changes across time after each incongruent color-word event. We then performed a second experiment to evaluate the possible novelty effect of the stimulus presentation in the first experiment by presenting less frequently the congruent and more frequently the incongruent color words. We thereby were able to identify

the regions differentially activated by interference and facilitation, as well as those that responded mainly to novelty.

Materials and Methods

Subjects

Nineteen right-handed (age 20–45) subjects, who denied previous history of neurological disorders or head injury, were recruited from the university community. Handedness was assessed with the Edinburgh scale (Oldfield, 1971). For the first study, five subjects were male and eight were female and their average age was 28. For the second study, four were male and nine were female and the average age was 26 (seven subjects from experiment 2 participated in the first experiment). All subjects gave informed consent to the protocol that was reviewed and approved by the Human Investigations Committee of the Yale University Medical School.

Task 1 — Conventional Stroop

In this experiment the conventional Stroop effect was emphasized (Fig. 1). While scanning, a continuous series of color words was displayed. Most of the stimuli were words that were displayed in their congruent colors (e.g. *blue* displayed in blue color). Only a few of the stimuli were incongruent color words (e.g. *blue* displayed in red color). Both congruent and incongruent stimuli were presented randomly, except no word or color of an incongruent stimulus was the same as the preceding congruent color word to avoid priming effects. Four colors and words (red, blue, yellow and green) were used in various combinations in the incongruent stimuli. Each stimulus was presented for 1300 ms, with an intertrial interval of 350 ms [similar to previous work (Pardo *et al.*, 1990) and to our block design study (Peterson *et al.*, 1999)]. There were six or seven incongruent stimuli in each run of 102 events. Incongruent epochs were pseudorandomly spaced at least 13–16 stimuli apart, i.e. 21.45–26.4 s. Each run was 2 min 48 s long. We collected at least five runs from each subject, and usually (in 10 subjects) 8–10 runs were obtained. Thus, each set of data had at least 30, but more often 48–60 incongruent events for analysis.

Task 2 — Inverse Stroop

We performed a second experiment to determine whether the effects seen in the first experiment can be explained by novelty of the incongruent stimulus or by an attentional shift to the infrequently presented stimulus feature. The task format was similar to the first experiment, but now the infrequent events were the congruent color-words and the incongruent color-words were shown more frequently as a baseline (Fig. 1).

General Experimental Setup

Words were presented against a black background and back-projected onto a screen that was positioned at the front of the magnet bore opening. Subjects viewed this display through a mirror that was mounted above their eyes in the scanner's head coil. The words were situated directly above (0.53°) gaze-fixation (a white crosshair). The word stimuli subtended 1° vertical and 3.92° horizontal of the visual field. For one subject with severe near-sighted vision (>500D), visual stimuli were presented through television screens in a set of goggles (Resonance Technology Inc.). All subjects were instructed to silently name the color as rapidly as possible and to avoid making mistakes. Silent naming without or with minimum vocalization was requested to minimize head or jaw motion artifacts. All visual stimuli were presented with PSYSCOPE software (Cohen *et al.*, 1993) running on a Macintosh Power PC (Apple Computer, Cupertino, CA). A digital interface enabled the Macintosh to record when each image was acquired, and this information was used to synchronize the presentation of stimuli with the acquisition of images [within 20 ms (Robson *et al.*, 1998)].

Subjects practiced aloud one or two runs before the scanning session and they all indicated clear understanding of the task. The interference effect was measured after the scanning session by recording from each subject at least one run of verbal responses to displayed color-words using the same stimulus parameters as inside the scanner. Subjects were asked to report their performance after each run in the scanner. Subjects reported that they made few or no mistakes during the scanning runs.

MRI Techniques

Subjects were positioned in the coil and head movements were restrained using foam pillows and a band across the forehead. Imaging was performed on a GE 1.5 T Signa (Milwaukee, WI) scanner with an ANMR (Advanced NMR, Wilmington, MA) resonant gradient echo-planar imaging system. All images were acquired using the standard quadrature head coil and a T_2*-sensitive gradient-recalled single shot echo planar pulse sequence. Ten axial–oblique slices parallel to the anterior–posterior commissural (AC–PC) line were prescribed based on sagittal localizers acquired at the beginning of each scanning session. Functional images were acquired at the same locations in runs of 1020 images (102 per slice). fMRI acquisition parameters were as follows: repetition time (T_R) = 1650 ms, echo time (T_E) = 60ms, flip angle = 60°, acquisition matrix 128 × 64, and field of view (FOV) = 40 × 20 cm. Voxel resolution was 3.12 × 3.12 mm in-plane by 7 mm thickness. Spaces of 1–2 mm between slices were adjusted for each subject such that the ninth slice above the AC–PC plane was at the vertex of the brain. This method was chosen to better register individual brains to the standard Talairach coordinates (Talairach and Tournoux, 1988) by reducing interpolation between slices for data analysis.

Image Analysis

Before data analysis, all functional images were screened for obvious artifacts and by looking at variations in parameters including the center of mass, the number of voxels above intensity threshold, and overall intensity. Images showing visible motion or other kinds of artifacts (such as ghosting) were removed from the analysis. A version of the SPM96 algorithm (Friston *et al.*, 1996) was used to correct for motion between successive images in each run. Low-intensity voxels in images such as ghosts outside of the brain were removed. The EPI images were then smoothed with a Gaussian filter with a full-width at half maximum of 6.3 mm.

Data for each individual subject were analyzed pixel by pixel using three statistical approaches. The timing of each of the infrequent stimuli in each sequence was used to define the start of an epoch. First, a *t*-test was used to create individual activation maps by comparing image values recorded after the start of each epoch with those that occurred just before. For each individual data set, the images were sorted to align epochs at the times of the infrequent stimuli. The three images starting from the third image after the infrequent event were used as a measure of the activated signal (the first two images were discarded to account for the delay in hemodynamic response). The six images immediately preceding each infrequent event were used as a baseline. Using the same grouping of images, the average percentage differences in MRI signal before and after the start of each epoch were also calculated for each pixel. Finally, a correlation analysis was performed. The time course data of each pixel in each image series was cross-correlated with a candidate time course, which consisted of a hemodynamic response function (HRF) derived from a previous study from this laboratory (Robson *et al.*, 1998). The function was a gamma-variate function of the form:

$$\mathrm{HRF} = (t - t_0)^{\alpha} \exp[-(t - t_0)/\beta],$$

where $t_0 = -0.25$, $\alpha = 14$, $\beta = 0.344$.

The onset of the hemodynamic response function was placed at the image in the time series when each infrequent event occurred. The correlation coefficient (r) for each voxel was calculated, and pixels with r above a threshold were overlaid on a conventional image in order to represent which voxels were activated.

For each individual, the same *t*-test and percent difference methods were also used to calculate activation time course maps by separately comparing each of the eight images following the infrequent event with the baseline (the six preceding images). In other words, at each time step (separated by 1.65 s) over a 13.2 s period, the percent signal change of each voxel in a slice was calculated by dividing the signal by the averaged baseline signal. Adjustments were made in the time course data for the variations in the time of acquisition of each slice during each T_R. Each voxel was time-smoothed by a Gaussian filter with a full-width at half maximum of 1.98 s prior to interpolation and data resampling.

The individual statistical maps were then transformed into the

standardized Talairach atlas coordinate system (Talairach and Tournoux, 1988) using eight anatomical anchor points (AC, PC, and the superior, inferior, anterior, posterior, left and right most points on the cortical surface). The individual activation data were then used to compute group composite images. Statistical maps of group composites were separately derived for different statistics, by performing *t*-tests comparing individual statistical maps of *t*-values, *r*-values or average percentage differences with zero (Figs 2 and 3). Composite activation maps from the percentage difference analysis are shown in the Results section, and similar maps were demonstrated by the *t*-test and cross-correlation analysis.

Comparisons between Studies

Comparisons between the results of the first and second experiments were made using a region of interest (ROI) analysis. Sixteen ROIs were defined according to the Talairach and Tournoux atlas (Talairach and Tournoux, 1988). The densities of activation for individual ROIs were calculated by summing *t*-values for pixels above a threshold (0.1) and by normalization by region size and total number of activated pixels in one hemisphere. For each ROI, significant differences between the Stroop and inverse Stroop studies were assessed using Student's *t*-test. A difference was considered significant if $P < 0.025$ (two-tailed tests and corrected for number of comparisons).

We also compared results from the current study with that of a previous block design by overlapping the activation maps based on composite analysis. Details of the methods can be found in the original paper (Peterson *et al.*, 1999). Briefly, the same color words were presented in congruent and incongruent blocks of 16 trials each. Each experiment consisted of two runs, while each run had four blocks of each condition. Images were acquired from the same scanner as the current study.

Results

Stroop Behavior

We estimated subjects' performance of color naming outside the magnet based on one behavioral run from each subject after the scanning session. On average subjects demonstrated a significant difference of 224 ms (SE = 32 ms, $n = 11$, $P < 0.0005$) between reaction times obtained from naming colors of incongruent versus congruent color words during the Stroop task. Subjects made an average of 0.8 errors (range 0–2) over six incongruent color-words during the conventional Stroop task. On the other hand, subjects showed an insignificant mean reaction time difference of –10 ms (SE = 27, $n = 13$, $P > 0.05$) when naming colors of congruent versus incongruent color words during the inverse Stroop task. Subjects made an average of 5.6 errors (range 1–12) over 96 incongruent color words in this latter task.

Composite Brain Maps for the Stroop Effect

Results from the composite statistical analysis of all subjects in the first experiment showed that a number of brain areas were activated by incongruent stimuli in comparison with congruent events. Since the various statistical analyses that we examined showed similar results, we display here only the results from the composite maps obtained from our percentage difference analysis (Fig. 2*A*). These results show consistent changes in the MRI signals evoked by incongruent stimuli across subjects ($P < 0.005$ uncorrected) in the anterior cingulate, insula, inferior frontal, middle frontal, parietal and mid-temporal regions. The activation indices and coordinates of these regions (based on an ROI analysis) are shown in Table 1. Decreases in signal, as well as negative correlations with our reference waveform, following the incongruent stimuli were also observed in regions of the ventral part of the anterior and posterior cingulate (Fig. 2*A*). Most ROIs showed no significant difference between left and right hemispheres, except the middle frontal regions (areas 9 and 46) and posterior cingulate gyrus ($P < 0.05$).

Table 1
Normalized regional activations associated with infrequent incongruent (Stroop) and congruent (inverse Stroop) tasks

Region	Stroop					Inverse Stroop					
	Average	SE	*x*	*y*	*z*	Average	SE	*x*	*y*	*z*	*P*
Positive activation											
All ROI	1.57	0.05				1.14	0.06				**
	1.54	0.04				1.20	0.05				**
Premotor, 6	1.55	0.16	7	1	60	1.01	0.13	8	–2	59	*
	2.01	0.16	–7	0	59	1.13	0.19	–9	–4	60	**
ACG, 32	1.92	0.20	6	23	39	0.85	0.10	8	26	37	**
	1.79	0.35	–6	23	38	1.09	0.13	–9	24	39	
MFG, 46	2.46	0.31	39	33	23	1.48	0.21	39	32	23	*
	2.03	0.21	–40	32	23	1.54	0.25	–40	33	24	
IFG, 44	2.49	0.22	44	8	30	1.45	0.16	46	8	30	**
	2.57	0.16	–46	8	31	1.61	0.14	–44	8	33	**
IFG, 45	2.40	0.39	44	22	11	1.44	0.22	45	22	14	
	2.91	0.37	–44	21	11	1.09	0.20	–43	22	14	**
BG	1.48	0.12	18	1	10	0.95	0.13	18	0	11	*
	1.47	0.13	–19	–1	10	0.92	0.10	–19	0	9	**
GTM, 21	1.72	0.18	53	–40	3	1.02	0.19	53	–41	3	*
	1.42	0.12	–53	–42	4	1.05	0.21	–52	–42	3	
insula	2.00	0.16	34	4	10	1.24	0.14	34	–2	10	**
	2.02	0.17	–34	6	11	1.21	0.11	–33	0	10	**
Negative activation											
PCG, 23/31	–1.88	0.18	8	–52	28	–1.26	0.15	8	–48	26	*
	–2.24	0.22	–8	–52	27	–1.43	0.19	–8	–47	26	*
ACG, 32	–2.17	0.39	6	47	5	–1.75	0.31	8	48	1	
	–3.44	0.71	–7	47	5	–1.32	0.20	–9	49	0	*
ACG, 24	–2.57	0.55	6	37	–3	–1.29	0.21	8	37	–7	
	–2.93	0.31	–6	37	–2	–1.39	0.23	–7	36	–9	**

Average activation index, SE (standard error) and Talairach coordinates (*x*, *y*, *z*) of the center of mass of activation within each ROI were determined. Right and left hemisphere measurements are shown in top and bottom rows respectively. For each subject, individual ROI activation indexes were calculated by summing t-values for pixels above a threshold (0.1) and that sum was normalized by region size and total number of activated pixels in one hemisphere. No significant differences in positive activations between the two studies are found for bilateral ACG (24), MFG (9), IFG (47), LPI and thalamus. Broadmann's areas are indicated after the named structure. ACG, anterior cingulate gyrus; MFG, middle frontal gyrus; IFG, inferior frontal gyrus; BG, basal ganglia; GTM, middle temporal gyrus; LPI, inferior parietal lobule; PCG, posterior cingulate gyrus. *$P < 0.025$, **$P < 0.005$.

Composite Brain Maps for the Inverse Stroop Effect

The inverse Stroop experiment was performed to clarify that activations obtained from the conventional Stroop experiment were not due to oddball effects associated with the infrequent presentation incongruent events. Figure 2*B* shows results from the second experiment in which congruent color-words were used as the infrequent stimuli relative to the greater frequency of incongruent stimuli presentation. These maps show much less

Figure 1. Example runs for experiment 1 with incongruent color-words as infrequent events and experiment 2 with congruent color-words as infrequent events.

Figure 2. (*A*) Composite maps of 13 subjects performing the Stroop task (experiment 1) with incongruent color-words as the infrequent events. (*B*) Composite maps obtained from the inverse Stroop task (experiment 2) with congruent words as the infrequent events. All maps are threshold at $t = 3.43$ ($P < 0.005$ uncorrected) with a cluster filter of nine contiguous pixels. Red–yellow represents activated pixels that are significantly greater than zero. Negative pixels are in blue–purple. The numbers in gray background are the *z* (mm) position of the slices.

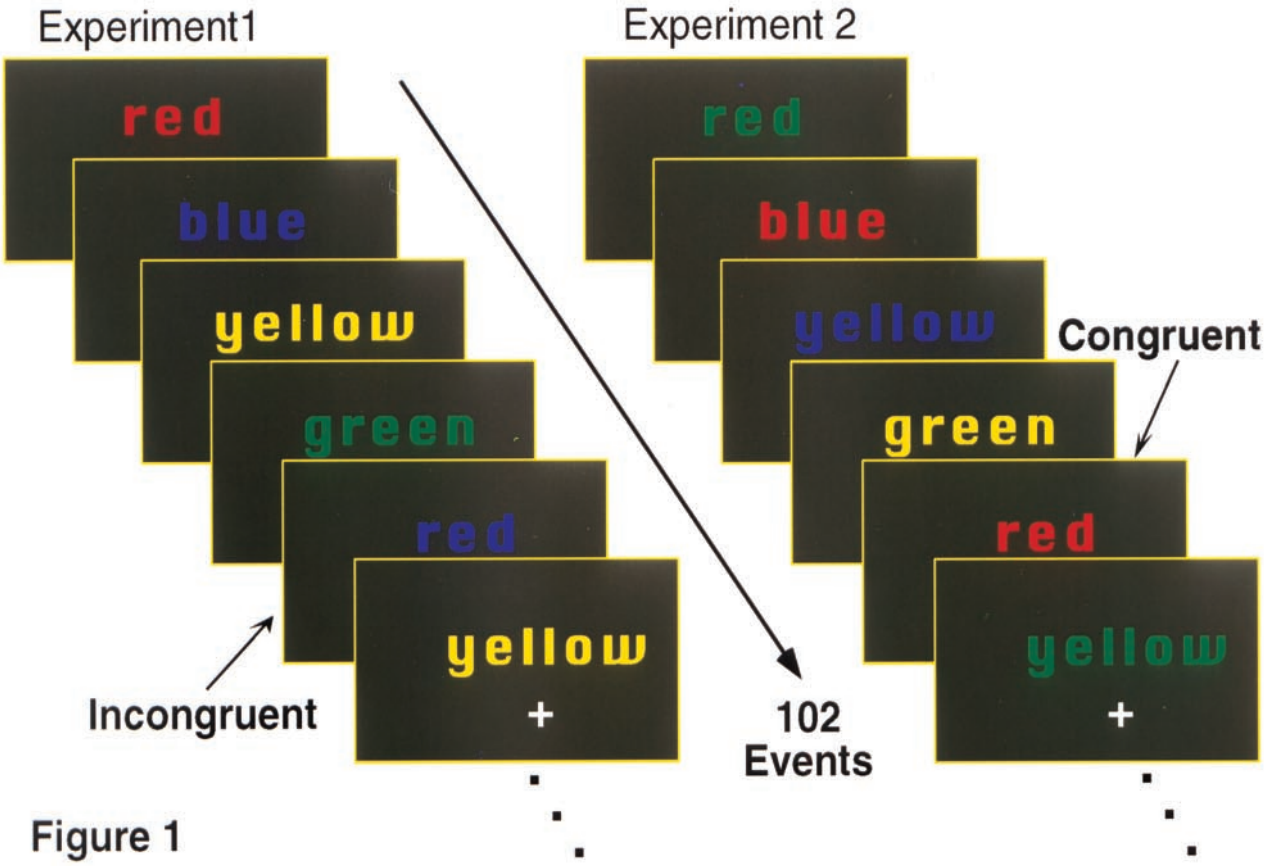

Figure 1

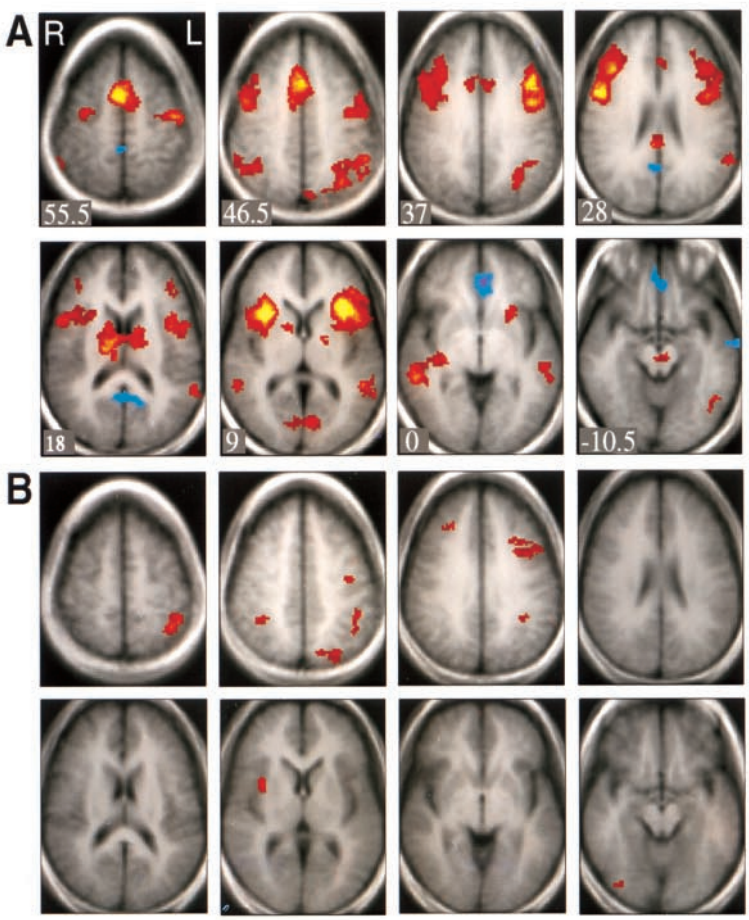

Figure 2

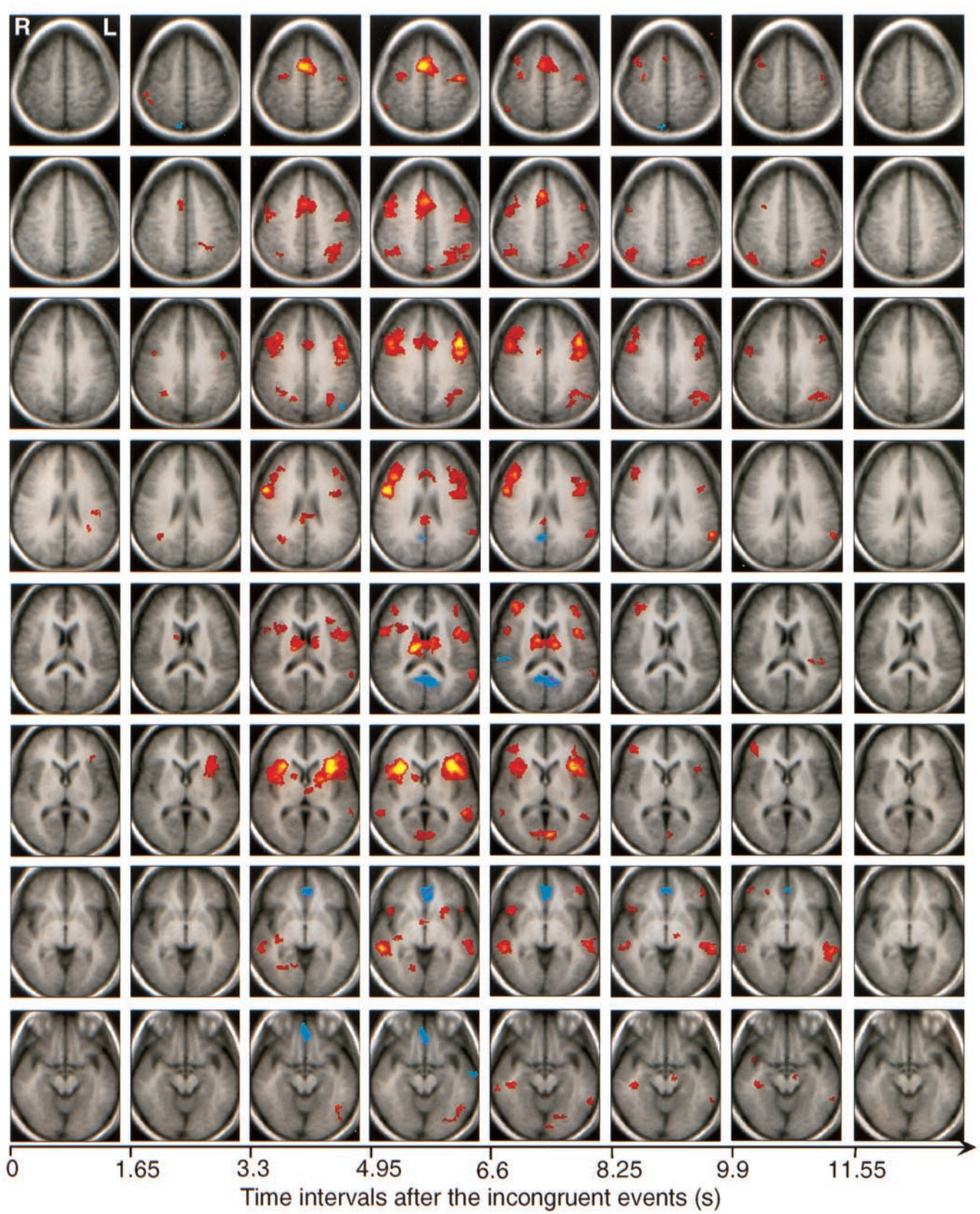

Figure 3. Time course composite maps. Slices from top to bottom of the brain are presented at regular intervals in columns after the presentation of incongruent color-words (the beginning of the first column). The maps are created in the same format as maps in Figure 2.

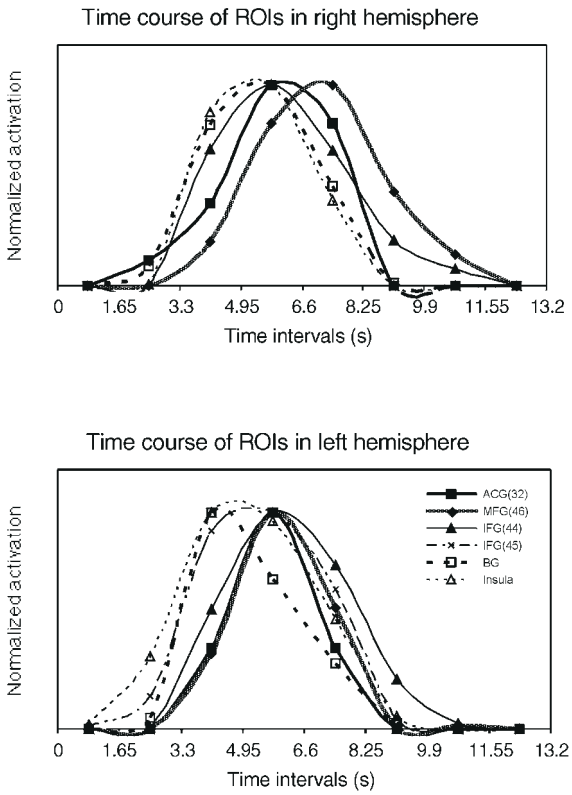

Figure 4. Temporal patterns for ROIs in the right (upper panel) and left hemispheres (lower panel) are extracted from Figure 3. In order to visualize the temporal differences between regions, we plotted the normalized sum of activation for each time step (data points are interpolated with a smoothed line). The sum of activation for each ROI in the composite map (Fig. 3) is calculated by summing *t*-values of voxels above threshold ($t = 3.43$). Normalization is obtained by dividing the values at each time point by the maximum value. ROIs are defined the same way as those in Table 1. For simplicity, we only plotted results from a few ROIs that are found significantly different from the second experiment (see Table 1). The right IFG (45) is not shown because it has much weaker activation than other regions.

activation than in experiment 1. These maps are shown at the same threshold as Figure 2*A*. We did not observe many more activated areas even when lowering the threshold. Significant differences in activation indices between the two studies were found for a number of ROIs (Table 1). There are overlapping activations in Figure 2*B* and Figure 2*A*. The most obvious regions of overlap are in the left middle frontal and inferior parietal areas; these regions showed insignificant differences in activation between the two studies (Table 1).

Time Course Data

To visualize the average time course of signals after a Stroop (incongruent) event, Figure 3 shows the composite time course maps. Each row shows a different slice and each column corresponds to a different time point. The first column was recorded 1.65 s after the start of the incongruent visual stimulus. Each successive column is one time step (1 T_R or 1.65 s) later. Differential activation was observed for those brain structures described in Table 1. To illustrate different temporal patterns, Figure 4 shows the differential onsets and durations of the normalized activation within several ROIs. The normalized integrated activation was measured from the composite statistical maps in Figure 3 by summing the *t*-values of all activated voxels within an ROI after setting a threshold at $t = 3.43$ (with $P < 0.005$, uncorrected). These activations clearly begin at and/or last for different times for different regions. For example, in the right hemisphere (top figure of Fig. 4), the insula, inferior frontal and anterior cingulate areas have earlier onsets and peak times than do the middle frontal regions. The right middle frontal and inferior frontal areas also have more prolonged activations than the other regions. The basal ganglia activity is shown to have a relatively shorter duration than other regions.

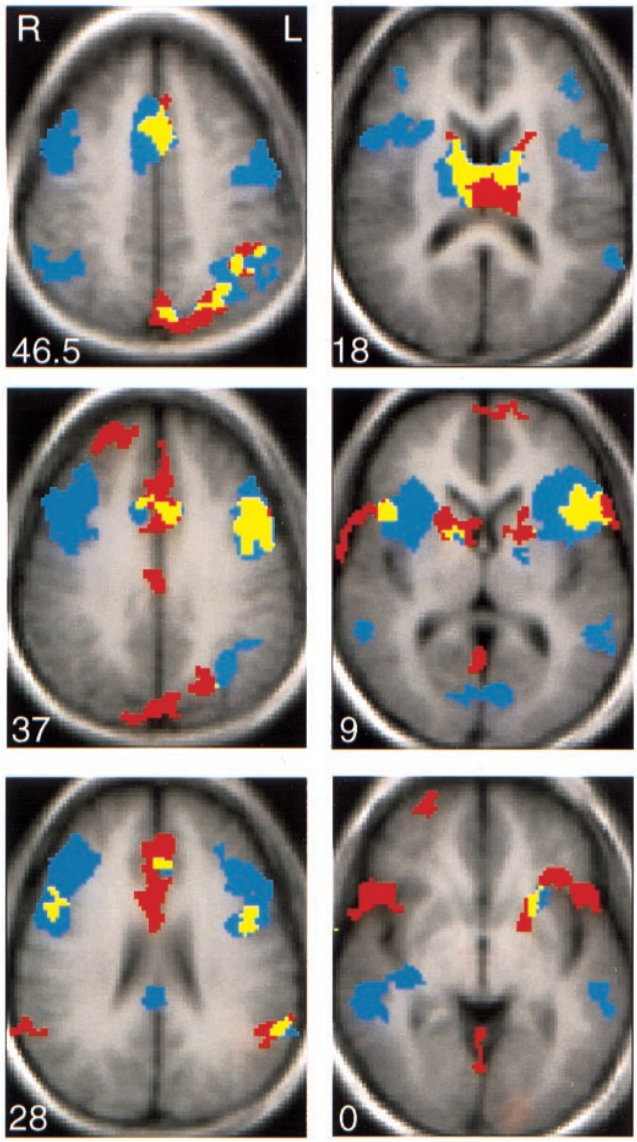

Figure 5. Comparison of Stroop effect with a previous block study (Petersen *et al.*, 1999). Composite maps of the two studies are overlapped on top of each other for positive activation. Yellow color indicates the overlapped activated areas, blue color the event-related study (experiment 1) and red color the block study.

Comparison with a Block Design Study

Activations detected in the current experiment were compared with results of a previous block design study of the Stroop task from this laboratory (Peterson *et al.*, 1999). Figure 5 shows the results from the block design study superimposed on the current study. For simplicity, only positive activations are shown in these images. Qualitative visual inspection suggests the results from

both studies are similar in terms of which regions were strongly activated. To estimate the extent of overlap, we counted the number of pixels that were above threshold for equivalent slices in both studies. Since the number of stimuli and subjects and other aspects of the tasks differed, an arbitrary threshold was set so that the top 5% of all the voxels within each composite map were assigned as activated voxels. The calculation indicates a 26% overlap for the positively activated voxels. Similarly, the negatively activated voxels overlapped by 22%. To indicate the consistency, the threshold was also set equal to 10%, 34% and 26% of overlap were estimated for the positively and negatively activated voxels respectively. The major differences between the two data sets appeared to be in the distribution of insula and inferior frontal activations. Also, the event-related study showed more bilateral activation in the middle frontal and parietal areas, whereas the block-design study showed mainly unilateral (left) activation.

Discussion

The current study demonstrates that transient brain activation produced by single cognitive events can be reliably detected by event-related fMRI and used to extend our understanding of the processes involved in tasks such as the Stroop. Our results indicate that a group of brain regions is activated by single incongruent events (color-words) and that these regional activations are not just simple oddball effects. In particular, our results illustrate the differential activation of the anterior cingulate and other frontal areas between the event-related conventional Stroop and inverse Stroop studies. Interestingly, temporal differences were found in signal changes between regions.

Implications of Multiple Regions Participating in the Stroop Effect

Finding the neural substrates that underlie the Stroop effect may advance our understanding of how humans maintain attention and perform a task by eliminating 'irrelevant' sensory input and suppressing automatic responses in favor of a task-relevant response. Failure to disregard or ignore irrelevant sensory inputs from the environment has often been implicated as a determinant of Stroop performance. Pardo and colleagues suggested that the anterior cingulate was the most strongly activated area while performing the Stroop task (Pardo *et al.*, 1990), while other brain-imaging studies have shown activations in inferior frontal gyrus and basal ganglia (Bench *et al.*, 1993; Taylor *et al.*, 1997; Peterson *et al.*, 1999). Our data also indicate that in addition to the anterior cingulate, a number of other brain regions are activated in this task. These areas include: the middle frontal regions, areas 9 and 46; inferior frontal regions, areas 44, 45; medial wall frontal regions, areas 6; temporal areas, middle temporal cortex; parietal regions, inferior parietal (area 40); insula; and the basal ganglia. Insula, inferior frontal (areas 44 and 45), ACG and middle frontal (area 46) are the most strongly activated regions. The insula plays a role in many non-cognitive and language functions (Augustine, 1996). The role of the insula in cognition is intriguing and has yet to be more clearly defined. It has been shown previously to be involved in verbal working memory (Paulesu *et al.*, 1993) and selective attention (Corbetta *et al.*, 1991). The anterior cingulate and other frontal activations are discussed further below. The large number of brain regions involved in the Stroop task is not surprising, as one would expect a network of multiple brain regions to be involved in an important and fundamental cognitive process such as selective attention.

Anterior Cingulate

The anterior cingulate has been postulated to be a crucial area for attention, motor modulation, and response selection (Pardo *et al.*, 1990; Corbetta *et al.*, 1991; Paus *et al.*, 1993; Carter *et al.*, 1998). In the event-related Stroop task, the superior part of the anterior cingulate shows an early onset but later time to peak after the incongruent event, and it is much more active when the infrequent event interferes with, rather than facilitates, the response. The anterior cingulate may therefore play a role in guiding the execution of a correct response by online error detection or performance monitoring (Carter *et al.*, 1998; Peterson *et al.*, 1999), by the selection of an appropriate response, and by conveying decisions to the motor system (Paus *et al.*, 1993). Our data are consistent with Paus' hypothesis that the dorsal portion of anterior cingulate participates in motor control by 'facilitating the execution of the appropriate responses and/or suppressing the execution of the inappropriate responses' (Paus *et al.*, 1993). The more inferior part of the ACG seems to be activated at a slightly later time, which is consistent with previous studies suggesting that this part of the ACG is involved in vocalization and emotional judgment (Vogt *et al.*, 1992).

Frontal Cortex

While Stroop interference activates the ACG, a number of other frontal cortical areas were shown to be highly activated in the current study. Historically, the Stroop task was proposed by Perret (Perret, 1974) as a potential means to indicate frontal dysfunction. It has been used to imply frontal dysfunction in various psychiatric patient groups that have no focal frontal lesions, such as schizophrenia (Cohen and Servan-Schreiber 1992), depression (Trichard *et al.*, 1995) and obsessive-compulsive disorder (Martinot *et al.*, 1990). The abnormalities in frontal connections in these disorders were shown in regional cerebral blood flow studies (Mellet *et al.*, 1998). However, some studies demonstrated that patients with right lateral frontal lesions, but not left frontal lesions, made more errors than normal controls in Stroop performance (Vendrell *et al.*, 1995; Kingma *et al.*, 1996). Our data clearly show that multiple bilaterally activated regions in the frontal cortex are related to the Stroop task. Even though it might not be specific to the Stroop effect (Vendrell *et al.*, 1995), the involvement of these frontal structures is quite dominant in our study.

A number of lateral and medial frontal regions, including areas 6, 9, 46, 45 and 44, were activated during the Stroop task. Subjects were involved in generating correct color names and suppressing reading. Processes such as selective retrieval (Thompson-Schill *et al.* 1997) and the inhibition of verbalization or reading (Jonides *et al.* 1998) can engage areas 45 and 44. Area 6 may participate in motor preparation and planning. Interestingly, area 46 — an area considered to be related to working memory (Goldman-Rakic 1987) — is also activated and its role in this study may be related to task monitoring and reevaluation of task rules during the period immediately following an incongruent stimulus. Area 9 is also involved in the Stroop effect and has a long sustained activation. It could be related to subjects recognizing a potential erroneous response during the Stroop event, since it has been proposed to be an area related to error trials in a cognitive behavior study of lesion patients during the Stroop task (Vendrell *et al.*, 1995). Prefrontal activity in the left hemisphere could also be due in part to novelty effect as discussed below.

Time Course Evaluations

The time course data demonstrate the transient changes produced by single incongruent events (Fig 3). The temporally dispersed activation of areas represent differences produced by incongruent and congruent stimuli in perception of visual stimuli (word and color), word–color form interpretation, selective attention, selection of response, and generation of response (color naming/word reading). Since we obtain images by measuring differences in activation between congruent and incongruent stimulus trials, we do not expect significant additional activation in the primary effects of visual excitation and form perception, in primary motor effects of word generation, or from differences in automatic responses such as word reading. The activation maps should thus reflect changes of brain activation across time related to the selection of the stimulus, the execution of the appropriate response, the monitoring of task performance, and the suppression of inappropriate responses (error correction). Our data demonstrate differential time course patterns between the ACG and frontal activations.

The event-related Stroop results show that different activated regions can be dissociated temporally. The differential onset and offset of activation supports the idea that differential information processing occurs in distributed brain regions in the Stroop task. Potentially, the temporal information from event-related fMRI studies can help us learn more about the differential timing of regional brain activations during a cognitive task, although the physiological basis for different timings remains unclear. For example, patterns of temporal activity may be used to assess the temporal relationships between regions and to provide information on functional connectivity among brain regions. Preliminary results using such data with a larger sample of subjects will be presented in a subsequent report.

Comparison with the Oddball Effect

Some of the activation produced in our first experiment could be due to a so-called 'oddball' effect since the task was based on an infrequent presentation of incongruent color words versus frequently displayed congruent color words. An earlier fMRI study of visual oddball stimuli showed activation of the middle frontal gyri and inferior parietal lobule (McCarthy *et al.*, 1997). The inferior parietal activation in our study is relatively weaker than activations in other regions in the first experiment, but is one of the few regions that also activated in the second experiment. If the oddball effect is accounted by the parietal structures (McCarthy *et al.*, 1997), then the oddball effect in our event-related conventional Stroop study seems to be relatively weak. Furthermore, the event-related fMRI findings presented here are similar to those of our previous block-design study (Peterson *et al.*, 1999), which suggests that either the two processes (oddball and Stroop) have a shared pathway or that these data mainly show the Stroop effect.

Comparison with Block Design

Using event-related fMRI, we observed more robust activations in several regions of the brain than in our previous block design (Fig. 5). This was expected because non-imaging behavioral studies have demonstrated greater Stroop interference effects when single rather than blocked incongruent stimulus trials are used (MacLeod, 1991). Nonetheless, the activated regions from the current event-related fMRI study are in general similar to those of the previous block study. Both techniques could be readily applied to clinical populations for diagnostic or research purposes. However, event-related fMRI has the advantage of probing the time course of the fMRI signal change corresponding to the Stroop effect and may be less influenced by low-frequency variations in baseline, thereby producing higher-quality activation maps. Even though the temporal sequences of the activations are smoothed by the hemodynamic response time course, we postulate that the temporal activation patterns of cognitive events may also have neurobiological relevance for both basic and clinical studies, and that further work to improve the temporal sampling of the Stroop response is justified.

Notes

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