On Verbal/Nonverbal Modality Dependence of Left and Right Inferior Prefrontal Activation during Performance of Flanker Interference Task

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Abstract

■ One of the most prevailing views on the functional localization of human cognition is the hemispheric specialization, wherein the left and right hemispheres are implicated primarily in verbal and nonverbal functions, respectively. Cognitive control is known to involve the lateral prefrontal cortex. However, it remains unclear whether the hemispheric specialization in the lateral prefrontal cortex can be observed in cognitive control per se, independent of sensory aspects of stimulus materials. In this functional magnetic resonance imaging study, we tested whether the verbal/nonverbal hemispheric specialization applies to the lateral prefrontal activation by investigating interference suppression, the ability to filter out irrelevant information in the environment. The flanker task was employed using a compound stimulus that contained a target and a flanker. The flanked stimulus was either a color word flanked by a colored patch or a colored patch flanked by a color word, which allowed us to manipulate the modality of the presented flanker stimulus from which interference originates, keeping the total stimulus modality balanced. The inferior frontal gyrus (IFG) showed prominent Modality-by-Hemisphere interaction in interference suppression, the left IFG being activated when a word flanker (plus a patch target) was presented and the right IFG being activated when a patch flanker (plus a word target) was presented. These results suggest that the verbal/nonverbal hemispheric specialization in the IFG can be explained by cognitive control processes per se, independent of sensory aspects of presented materials. ■

INTRODUCTION

Neuropsychological studies using patients with split brains and unilateral lesions have revealed hemispheric specialization in human higher cognitive functions, implicating the left and right hemispheres in the verbal and nonverbal functions, respectively (Gazzaniga, 2005; Milner, 1971). Previous neuroimaging studies have confirmed this principle primarily in the frontal cortex, demonstrating the left and right frontal activation during memory encoding of verbal and nonverbal materials, respectively (Wig, Miller, Kingstone, & Kelley, 2004; Konishi, Donaldson, & Buckner, 2001; McDermott et al., 1999; Kelley et al., 1998; Wagner et al., 1998). These studies compared conditions where the presented items were not matched across the verbal and nonverbal modalities in the sensory level, leaving the possibility that the observed activation consistent with the hemispheric specialization principle can be interpreted as reflecting sensory processing of the stimulus materials, rather than cognitive control of the presented items.

The present functional magnetic resonance imaging (fMRI) study tested whether the prefrontal activation during cognitive control was modulated by the verbal/nonverbal material modality in accordance with the hemispheric specialization principle, independently of sensory aspects of presented items. The flanker task (Hazeltine, Bunge, Scanlon, & Gabrieli, 2003; Bunge, Dudukovic, Thomason, Vaidya, & Gabrieli, 2002; Bunge, Hazeltine, Scanlon, Rosen, & Gabrieli, 2002; Ullsperger & von Cramon, 2001; Botvinick, Nystrom, Fissell, Carter, & Cohen, 1999; Eriksen & Eriksen, 1974), which is used to probe the ability to filter out irrelevant information in the environment, called "interference suppression" (Vaidya et al., 2005; Bunge, Dudukovic, et al., 2002), provides a unique opportunity to easily manipulate the modality of the stimulus from which interference originates. The present study devised a modality-compound flanked stimulus that contained a central target and a flanker of verbal or nonverbal modality: a color word flanked by a colored patch or a colored patch flanked by a color word (Figure 1). The compound stimulus allowed us to examine the activation associated with suppression of interference that originated from verbal or nonverbal flanker materials. Importantly, Japanese morphogram (Kanji words) was presented as a word stimulus because just one character of the Japanese morphogram is capable of representing a color, which is suitable to present as a

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Figure 1. (A) Stimuli and trials presented in the flanker task of this study: flanked and control stimuli presented in the word and patch trials. (B) An example of the S–R mapping used in one subject. The target stimuli presented in the word and patch trials were associated with the R and L button presses according to the table. (C) Task sequence of the flanker task. The flanked and control stimuli presented in the word and patch trials were pseudorandomly presented in a sequence that allowed event-related fMRI to be employed.

flanker in the close vicinity of a target (Yamaguchi, Toyoda, Xu, Kobayashi, & Henik, 2002). Moreover, to keep the total (target plus flanker) visual effects of the stimulus balanced across modalities, only one flanker was presented, instead of presenting two flankers to the right and left of a central target. Such word and patch trials were intermixed and contrasted using event-related fMRI, and the verbal/nonverbal hemispheric specialization hypothesis was tested by detecting brain activity associated with suppression of interference that originated from verbal and nonverbal flanker stimuli.

METHODS

Subjects and fMRI Procedures

Written informed consent was obtained from 34 healthy right-handed subjects (13 men, 21 women; age = 20–28 years). They were scanned by experimental procedures approved by the Institutional Review Board of the University of Tokyo School of Medicine. The experiments were conducted using a 1.5-T fMRI system. Scout images were first collected to align the field of view

centered on the subject's brain. T2-weighted spin-echo images were obtained for anatomical reference [repetition time (TR) = 6660 msec; echo time (TE) = 30 msec; 90 slices, slice thickness = 2.0 mm; in-plane resolution = 2 × 2 mm]. For functional imaging, a gradient-echo, echo-planar sequence was used (TR = 3000 msec; TE = 50 msec; flip angle = 90°). Each functional run consists of 72 whole-brain acquisitions (21 × 4 mm slices with 2 mm gap; in-plane resolution = 4 mm), and six runs were administered to the subjects. The first four functional images for each run were excluded from analysis to take into account the equilibrium of longitudinal magnetization.

Behavioral Procedures

Visual stimuli were presented to subjects by projecting the stimuli onto a screen. Subjects viewed the screen through prism glasses. A magnet-compatible button press based on a fiber-optic switch was used to record the performance of the subjects. The stimulus presented during performance of the flanker task consisted of a central target and a flanker (Figure 1A). The modality of the flanked stimulus was a compound of both a word and a patch: a color word flanked by a colored patch or a colored patch flanked by a color word, and each of the words/patches indicated one of four colors (red, yellow, green, and blue). The Japanese morphogram was employed as a color word, which represents a color in just one character and is suitable for generating interference from the flanker stimulus in the close vicinity of a target. To keep the modality effect balanced across verbal and nonverbal modalities, only one flanker was presented to the left or right of the central target, and the number of pixels constituting the color word and the colored patch was matched. The total number of the flanked stimuli was 32: the combination of color words (×4) and colored patches (×4), with the distinction of the central target versus flanker (×2). In order to control for the cognitive processes that are not associated with interference suppression, a control stimulus was presented that has an asterisk instead of a color-related flanker stimulus (Figure 1A). The total number of the control stimuli was 8: four color words and four colored patches presented centrally.

Each central target, either a color word or a colored patch, is associated with a left or right button press (Figure 1B). The color assignment in the stimulus–response (S–R) mapping was fixed in the same subject and was rotated across subjects. In each trial, subjects were required to press a left or right button on the basis of a fixed S–R mapping assigned to each of the central target stimuli of color words (word trials) and colored patches (patch trials), ignoring the flanker stimulus. One trial was presented every 2 sec, with 571 msec for stimulus presentation and 1429 msec for fixation baseline. One run consisted of 96 trials: 64 trials for the

flanked stimuli (2 trials per each flanked stimulus), 16 trials for the control stimuli (2 trials per each control stimulus), and 16 fixation trials intermixed as a baseline. Six runs were administered to each subject. The flanked, control, and fixation trials were pseudorandomly presented (Figure 1C), and the trial sequences were rotated across runs and subjects. Because there were 48 trial types to be rotated (32 flanked, 8 control, and 8 fixation trials), two sets of rotations were performed in one run, and full (48 sets) rotation took 24 runs performed by four subjects. Six additional trials (12 sec, 4 TRs) were included prior to the 96 trials to stabilize the subjects' performance, and were discarded due to the premature equilibrium of longitudinal magnetization.

Prior to the scanning sessions, subjects received training sessions that took about 30 min. First, each subject was shown an S–R mapping table assigned to the subject. Next, color word or colored patch stimuli without a flanker were given in separate blocks. Then, the non-flanked stimuli were presented intermixed across words and patches. Finally, the same sequence as that used in fMRI scans were administered. The criteria for the final session were 90% correct trials in the 80 flanked and control trials in the last one run.

Data Analysis

Data were analyzed using SPM2 software (www.fil.ion.ucl.ac.uk/spm/). Functional images were realigned, slice timing was corrected, normalized to the baseline template with interpolation to a $2 \times 2 \times 2$ mm space, and spatially smoothed (full width, half maximum = 6 mm). Event timing was then coded into a general linear model (Worsley & Friston, 1995). Transient events at the time of the correct flanked and control trials were modeled as events, time-locked to the onset of stimulus presentation using the canonical function in SPM2. Each of the 40 (32 flanked and 8 control) events consisted of 12 trials at a maximum (2 trials × 6 runs). There were 40 separate regressors in the initial analysis, and each specific contrast was created in each subject by summing up weighted signal estimates for the regressors. The contrasts were then subject to a second-level group analysis using a random effect model. After whole-brain multiple comparisons, the present dataset failed to reveal any peaks, which may indicate the lower sensitivity of the present dataset to interference suppression. One possible factor for the lower sensitivity would be the use of only one flanker, rather than two flankers used in most of the studies of flanker interference tasks, which made it possible to equalize the visual stimulus effects between verbal and nonverbal modalities. For the activation in the inferior frontal gyrus (IFG) and inferior frontal junction (IFJ), a corrected threshold was applied using small volume correction (SVC) (Worsley et al., 1996). Anatomically defined IFG was used as volume of interest, and the estimated volume of gray matter in the entire bilateral IFG was 27 cm³ (Maldjian, Laurienti, & Burdette, 2004; Maldjian, Laurienti, Burdette, & Kraft, 2003). In addition to the above exploratory analysis, a region-of-interest (ROI) analysis was also performed in the IFG and IFJ regions, in order to investigate detailed activation patterns across different types of trials.

In making a contrast of interest between the flanked and control stimuli, the following two distinctions were also considered in a confirmatory analysis shown in Figure 5C. First, the target stimuli were classified as "EASY" and "DIFFICULT" based on the consistency of the S–R mapping in the word and patch target modality (Hester, D'Esposito, Cole, & Garavan, 2007; Jiang & Kanwisher, 2003; Schumacher, Elston, & D'Esposito, 2003). In the case of the Figure 1B, for instance, both the word for "red" and the red patch were associated with "right" responses, and this target was regarded as "EASY." On the contrary, the word for "green" was associated with "left" responses, whereas the green patch was associated with "right" responses, and this target was regarded as "DIFFICULT."

The other distinction was made based on the relationship between the target and the flanker, unlike the EASY/DIFFICULT distinction based on the target stimuli alone. The flanker effect originates from the incongruency between the target and the flanker in terms of the stimulus semantics, the related responses, and both (Egner, Delano, & Hirsch, 2007; van Veen & Carter, 2005; Milham et al., 2001). In the case of the word "green" flanked by the yellow patch shown in Figure 5C, labeled as "S-IN, R-CON," the target and the flanker indicate different color (incongruent: "green" and "yellow"), but indicate the same response (congruent: "left"), based on the S–R mapping shown in Figure 1B. In the case of the green patch flanked by the word "green" shown in Figure 5C, labeled as "S-CON, R-IN," the target and the flanker indicate the same color (congruent: "green"), but indicate different responses (incongruent: "right" and "left"). In the case of the yellow patch flanked by the word "blue" shown in Figure 5C, labeled as "S-IN, R-IN," the target and the flanker indicate different color (incongruent: "yellow" and "blue"), and also indicate different responses (incongruent: "left" and "right"). The stimuli that correspond to S-CON, R-CON were not included in the flanked stimuli in making the "flanked minus control" contrast that is expected to extract cognitive processes associated with interference suppression.

RESULTS

Behavioral Data

Behavioral performance was high: 97.7 ± 0.5% (mean ± *SEM*) in the flanked stimuli in the word trials, 98.2 ± 0.4% in the control stimuli in the word trials, 97.9 ± 0.5% in the flanked stimuli in the patch trials, and 98.0 ± 0.5% in the control stimuli in the patch trials (Figure 2A). No

**Figure 2.** (A) Performance accuracy and reaction time to the flanked and control stimuli presented in the word and patch trials. (B) Flanker effects in the four types of congruency relationships between the target and the flanker (S-CON and R-CON, S-CON and R-IN, S-IN and R-CON, and S-IN and R-IN; see Methods for details). **p < .001, based on a paired t test.

significant difference was detected in the two-way analysis of variance (ANOVA). Reaction time in each condition was 647 ± 16 msec in the flanked stimuli in the word trials, 624 ± 14 msec in the control stimuli in the word trials, 628 ± 15 msec in the flanked stimuli in the patch trials, and 614 ± 15 msec in the control stimuli in the patch trials (Figure 2A). Two-way ANOVA revealed significant main effects for the flanked/control stimuli [$F(1, 33) = 83.7, p < .001$] and word/patch trials [$F(1, 33) = 7.7, p < .01$], but not for the interaction. The significant difference between the flanked and control stimuli was also confirmed in both the word [$t(33) = 6.8, p < .001$] and patch trials [$t(33) = 5.4, p < .001$].

The reaction time difference (flanker effect) was divided into four categories: "S-CON, R-CON," "S-IN, R-CON," "S-CON, R-IN," and "S-IN, R-IN" based on the incongruency between the target and the flanker in terms of the stimulus semantics, the associated responses and both (see Methods for details). The reaction time difference was significant in the three conditions "S-IN, R-CON"

[$t(33) = 6.3, p < .001$], "S-CON, R-IN" [$t(33) = 3.9, p < .001$], and "S-IN, R-IN" [$t(33) = 8.7, p < .001$] (Figure 2B). The between-condition difference was also significant between "S-IN, R-CON" and "S-CON, R-CON" [$t(33) = 6.3, p < .001$], "S-CON, R-IN" and "S-CON, R-CON" [$t(33) = 4.7, p < .001$], and "S-IN, R-IN" and "S-CON, R-CON" [$t(33) = 8.7, p < .001$] (Figure 2B). These behavioral results suggest significant contribution of interference suppression during performance of the flanker interference task.

Imaging Data: Whole-brain Analyses

Previous neuroimaging studies have revealed hemispheric specialization in the frontal cortex, particularly in the region near the IFJ, during processing of verbal and nonverbal materials (Wig et al., 2004; Konishi et al., 2001; McDermott et al., 1999; Kelley et al., 1998; Wagner et al., 1998). This basic material effects were tested as a positive control using the simplest stimuli used in the present study: the control stimuli (without a flanker), whose S–R mapping is consistent across the word and patch modalities (EASY condition: see Methods for details). The material effects "Control (Easy Only) minus Fixation" were applied to the two-way ANOVA with modality (word/patch) and hemisphere (left/right) as main effects (see Konishi et al., 2002). This ANOVA analysis revealed prominent Modality-by-Hemisphere interaction effects in the IFJ region [peak coordinates: $x = ±50, y = 8, z = 44, F(1, 33) = 23.7, p < .001$, 29 contiguous voxels; Figure 3, left]. The interaction was significant after correction for multiple comparisons using SVC based on the entire IFG ($p = .03$). This significant interaction is consistent with the previous studies of the material specialization that demonstrated the material-dependent asymmetry in the IFJ activation (Wig et al., 2004; McDermott et al., 1999; Kelley et al.,

Figure 3. Statistical activation maps for the Modality-by-Hemisphere interaction of the target material effect (Control-Easy minus Fixation) (left) and of the flanker effect (Flanked minus Control) (right). Activation maps are displayed as transverse sections and are overlaid on top of the anatomic image averaged across subjects. Statistical significance is indicated using the color scale to the right, and the transverse section level is indicated by the z coordinates of Talairach space (Talairach & Tournoux, 1988).

1998; Wagner et al., 1998), and also validates the use of the Japanese morphogram and patch stimuli in the present study.

Figure 3 (right) shows the main contrast of interest in this study: the Modality-by-Hemisphere interaction for the contrast "Flanked minus Control." This analysis was aimed at examining whether brain activity related to flanker interference suppression (Vaidya et al., 2005; Bunge, Dudukovic, et al., 2002) in the left and right frontal cortex depended on the verbal/nonverbal modality of the flanker stimulus. More specifically, in the word trials, suppression of flanker interference derived from patch flanker stimulus may activate the right frontal cortex, whereas in the patch trials, suppression of flanker interference derived from word flanker stimulus may activate the left frontal cortex. Prominent interaction was revealed in the IFG region [peak coordinates: $x = \pm54$, $y = 16$, $z = 28$, $F(1, 33) = 26.8$, $p < .001$, 37 contiguous voxels]. The interaction was significant after correction for multiple comparisons using SVC ($p = .01$).

Imaging Data: ROI Analyses

Figure 4A shows the results using ROIs with a radius of 6 mm for the target material effects "Control (Easy Only) minus Fixation." The Modality-by-Hemisphere interaction for the target material effects was not significant in the IFG ($x = \pm54$, $y = 16$, $z = 28$) (Figure 4A, top). On the other hand, the IFJ region ($x = \pm50$, $y = 8$, $z = 44$) naturally exhibited a clear Modality-by-Hemisphere interaction, with the left hemisphere activity during word processing and the right hemisphere activity during patch processing (Figure 4A, bottom). The Modality-by-Hemisphere interaction was directly visualized in Figure 4B, which shows the interaction for the target material effects in the regions highlighted in Figure 4A. The Modality-by-Hemisphere interaction for the target material effects was calculated as follows: (word trials in the left hemisphere − word trials in the right hemisphere) − (patch trials in the left hemisphere − patch trials in the right hemisphere). Naturally, the interaction in the IFJ was significant [$t(33) = 4.9$, $p < .001$], whereas the interaction in the IFG was not. The interaction difference was significant between the IFJ and the IFG [$t(33) = 2.9$, $p < .01$]. To examine the interaction difference between these regions in a more unbiased way,
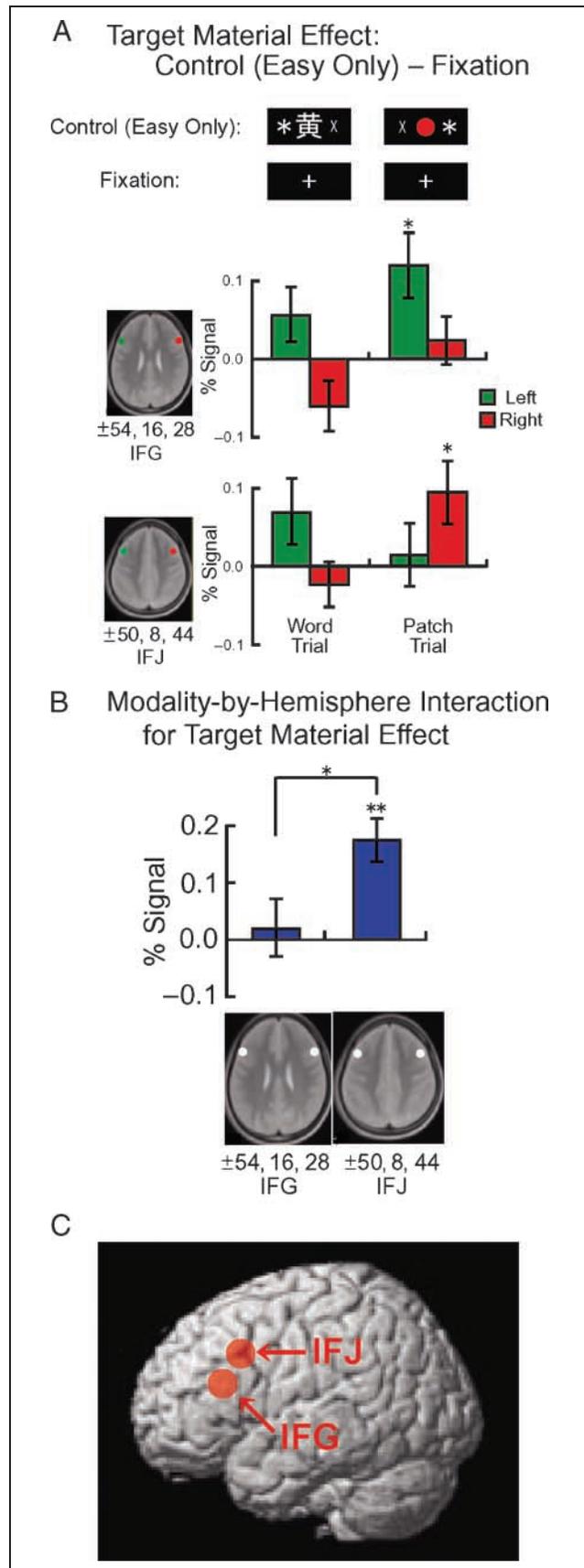
Figure 4. (A) Effects of target materials in the ROI, the IFG and the IFJ, defined based on the activation in Figure 3. Signals are obtained by the contrast "Control (Easy Only) minus Fixation" and are displayed in the left and right hemispheres in the word and patch trials. *$p < .05$. (B) Modality-by-Hemisphere interaction for the target material effects in the same regions. Details of the calculation of the interaction are described in the Results section. *$p < .05$, **$p < .001$. (C) Three-dimensional anatomical reference showing the approximate location of the IFG and the IFJ.

a replication approach was employed for the IFJ, wherein the dataset of 34 subjects was divided into two (17 and 17), and the first dataset generated an ROI in the IFJ, and the second dataset was applied to the generated ROI (Buckner, Raichle, Miezin, & Petersen, 1996). The first dataset generated significant signal interaction at the IFJ (± 48, 10, 44) ($t = 3.5$), and the interaction in the second dataset was significant in this ROI [$t(16) = 3.3$, $p < .005$]. The interaction difference was also significant between the IFJ and the IFG [$t(49) = 2.0$, $p < .05$]. Figure 4C provides anatomical reference to the IFG and the IFJ in the 3-D image.

An ROI analysis was also applied to the flanker effects using the contrast "Flanked minus Control." The IFG region naturally showed a clear Modality-by-Hemisphere interaction pattern, with the left hemisphere activity during word flanker interference suppression and the right hemisphere activity during patch flanker interference suppression (Figure 5A, top). On the other hand, the IFJ did not show a significant interaction (Figure 5A, bottom). The Modality-by-Hemisphere interaction in the regions was directly visualized in Figure 5B. The Modality-by-Hemisphere interaction for the flanker effects was calculated as follows: [patch trials (word flanker) in the left hemisphere − patch trials (word flanker) in the right hemisphere] − [word trials (patch flanker) in the left hemisphere − word trials (patch flanker) in the right hemisphere]. Note that the trial types (word trial/patch trial) were opposite to the definition of the interaction in the target material effects because when the target is a word, the flanker is always a patch, and vice versa. Naturally, the interaction in the IFG was significant [$t(33) = 5.2$, $p < .001$], whereas the interaction in the IFJ was not.

To investigate the Modality-by-Hemisphere interaction more thoroughly, two analyses were made in the IFG region. First, the trials were divided into two conditions: "EASY" and "DIFFICULT" based on the consistency of the S–R mapping in the word and patch target modalities (see Methods for details). The Modality-by-Hemisphere interaction was significantly only in the "DIFFICULT" condition in the IFG (Figure 5C). Second, the trials were divided into three conditions: "S-IN, R-CON," "S-CON, R-IN," and "S-IN, R-IN" based on the incongruency between the target and the flanker in terms of the stimulus semantics, the associated responses, and both (see Methods for details). The Modality-by-Hemisphere interaction

in these three conditions was significant in the IFG (Figure 5C). There were no other regions in the brain that showed significant interaction in the "S-IN, R-CON," "S-CON, R-IN," or "S-IN, R-IN." Additional analyses were further made on the distinctions of high versus low

Figure 5. (A) Effects of flanker interference in the ROIs, the IFG and IFJ regions. Signals are obtained by the contrast "Flanked minus Control." Formats are similar to those of Figure 4A. (B) Modality-by-Hemisphere interaction for the flanker interference effects in the same regions. Details of the calculation of the interaction are described in the Results section. (C) The interaction effects in the IFG were also presented in each of the subdivision of the entire trials: EASY and DIFFICULT on one hand and S-IN & R-CON, S-CON & R-IN, and S-IN & R-IN on the other (see Methods).
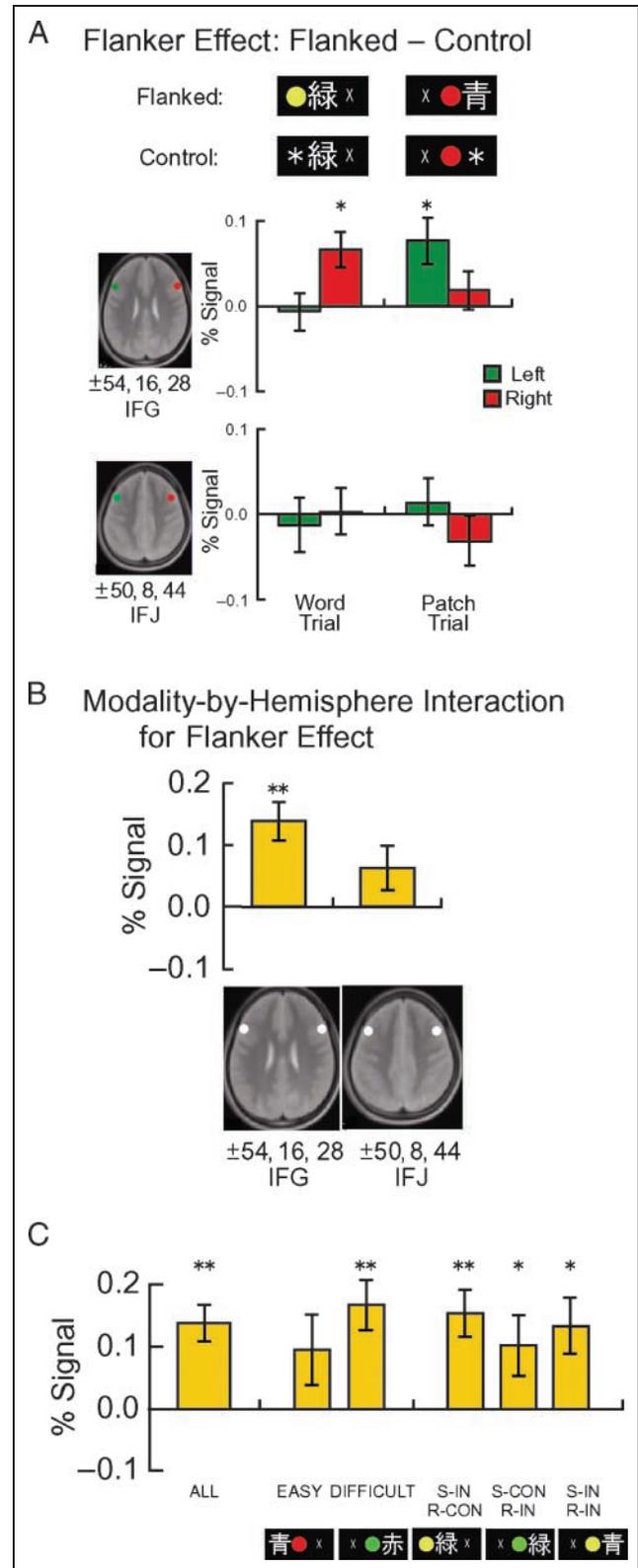
accuracy and of long versus short reaction time. In the IFG, the Modality-by-Hemisphere interaction was significantly different in the low-accuracy group than in the high-accuracy group [$t(32) = 2.2, p < .05$], but not in the reaction time groups.

DISCUSSION

The present study investigated the Modality (verbal/nonverbal)-by-Hemisphere (left/right) interaction during suppression of interference that originated from the verbal/nonverbal flanker. The Modality-by-Hemisphere interaction in the stimulus materials was first replicated in the IFJ region. The Modality-by-Hemisphere interaction during flanker interference suppression was then explored, and prominent interaction was found in the IFG region. These results suggest that cognitive control processes, in this case, interference suppression, activate the lateral prefrontal cortex in accordance with the hemispheric specialization principle, independently of sensory aspects of presented items.

The activation in the IFJ regions shows the Modality-by-Hemisphere interaction during memory encoding, a sort of executive processing that forms long-lasting memory traces (Wig et al., 2004; McDermott et al., 1999; Kelley et al., 1998; Wagner et al., 1998). The significant interaction demonstrated in the present study, therefore, may reflect the material effects related to executive processing of the target stimuli. Such material-dependent executive processes in the IFJ regions are also consistent with previous studies of flanker tasks demonstrating a similar Modality-by-Hemisphere interaction (Hazeltine et al., 2003).

The IFG regions are activated during performance of several tasks requiring cognitive control. On one hand, the Wisconsin Card Sorting Task (WCST) and task switching task activate the left IFG (Parris, Thai, Benattayallah, Summers, & Hodgson, 2007; Crone, Donohue, Honomichl, Wendelken, & Bunge, 2006; Barber & Carter, 2005; Konishi, Chikazoe, Jimura, Asari, & Miyashita, 2005; Brass & von Cramon, 2004; Cools, Clark, & Robbins, 2004; Braver, Reynolds, & Donaldson, 2003; Konishi, Jimura, Asari, & Miyashita, 2003; Monchi, Petrides, Petre, Worsley, & Dagher, 2001; Dove, Pollmann, Schubert, Wiggins, & von Cramon, 2000), which can be attributable to control of interference from verbalized cognitive set. The Stroop task also activates the left IFG, which can be attributable to control of inherent word reading tendency (Laird et al., 2005; van Veen & Carter, 2005; Derrfuss, Brass, & von Cramon, 2004; Milham et al., 2001; Leung, Skudlarski, Gatenby, Peterson, & Gore, 2000; Taylor, Kornblum, Lauber, Minoshima, & Koeppe, 1997). Moreover, control of interference from previously learned verbal items also activates the left IFG (Caplan, McIntosh, & Rosa, 2007; Snyder, Feigenson, & Thompson-Schill, 2007; Feredoes, Tononi, & Postle, 2006; D'Esposito, Postle, Jonides, & Smith, 1999; Jonides, Smith, Marshuetz, Koeppe, & Reuter-Lorenz, 1998; Thompson-Schill, D'Esposito, Aguirre, & Farah, 1997). On the other hand, the go/no-go task and the stop task activate the right IFG (Chikazoe, Konishi, Asari, Jimura, & Miyashita, 2007; Hodgson et al., 2007; Zheng, Oka, & Yamaguchi, 2007; Aron & Poldrack, 2006; Rubia et al., 2005; Wager et al., 2005; Hester et al., 2004; Bunge, Dudukovic, et al., 2002; Durston, Thomas, Worden, Yang, & Casey, 2002; Garavan, Ross, & Stein, 1999; Konishi et al., 1999), which can be attributable to control of prepotent motor set, which is nonverbal. The results of these previous studies appear to support the verbal/nonverbal hemispheric specialization principle in the IFG activation associated with cognitive control, and suggest that the hemispheric asymmetry of brain activation observed in these tasks can be explained by the modality of the processing/materials to be controlled.

The cognitive control processes of central interest in the present study concern "interference suppression" based on Vaidya et al. (2005) and Bunge, Dudukovic, et al. (2002). The Modality-by-Hemispheric interaction observed in the present study is consistent with their view that the left IFG was activated because children may have adopted a verbal strategy during performance of the flanker task (Bunge, Dudukovic, et al., 2002). However, it is not tested in the present study whether activation related to response inhibition, which has repeatedly been shown to activate the right IFG (Kelly et al., 2004; Garavan, Ross, Murphy, Roche, & Stein, 2002; Garavan et al., 1999; Konishi et al., 1999), is modulated by the verbal strategy. The right IFG is activated during response inhibition in tasks where verbal materials are used (Kelly et al., 2004; Garavan et al., 1999, 2002). If the material used in inhibition of motor tendency is critical in determining the hemispheric lateralization, then the conclusion of the present study is not necessarily consistent with extant literature. However, if the motor tendency itself, which is the target of inhibitory control and is apparently nonverbal, is critical in determining the hemispheric lateralization, then the conclusion of the present study is consistent with extant literature. Interestingly, activation in the anterior cingulate cortex was not detected in the contrast "Flanked minus Control trials" in the present study. In a similar flanker task presented in two modalities (verbal/color) (Hazeltine et al., 2003), on the other hand, the anterior cingulate activation was detected. One possible explanation for the difference in the anterior cingulate activation is that, unlike the flanker task in Hazeltine et al. (2003), the present flanker task contained the "DIFFICULT" (see Methods) condition in both flanked and control trials, which might have led to the ceiling effect in the anterior cingulate activation during the flanked and control trials. Although it still remains open to questions what other factors modulate lateral prefrontal activation (e.g., Dolcos, Rice, & Cabeza, 2002; Tulving, Kapur, Craik, Moscovitch, & Houle, 1994), the

present study suggests one obvious and important factor that explains lateralized activation during cognitive control: the verbal/nonverbal hemispheric specialization principle.

Acknowledgments

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