Semantic processing and response inhibition

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The present study examined functional MRI (fMRI) BOLD signal changes in response to object categorization during response selection and inhibition. Young adults (*N*=16) completed a Go/NoGo task with varying object categorization requirements while fMRI data were recorded. Response inhibition elicited increased signal change in various brain regions, including medial frontal areas, compared with response selection. BOLD signal in an area within the right angular gyrus was increased when higher-order categorization was mandated. In addition, signal change during response inhibition varied with categorization requirements in the left inferior temporal gyrus (lIT). lIT-mediated response inhibition when inhibiting the response only required lower-order categorization, but lIT mediated both response selection and inhibition when selecting and inhibiting the response required higher-order categorization. The findings characterized mechanisms mediating response inhibition associated with semantic object categorization in the 'what' visual object memory system. *NeuroReport* 24:889–893 © 2013 Wolters Kluwer Health | Lippincott Williams & Wilkins.

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Introduction

Depending on the circumstances, actions might require higher-order or lower-order semantic categorization [1]. For example, driving often requires rapidly and correctly determining whether something that appears on the road merits rapid braking or not. The default response is to brake, but when an object is recognized as innocuous (e.g. leaves, a plastic bag, etc.), the prepotent response to brake can be inhibited. Response inhibition of this type is operationalized in the Go/NoGo paradigm [2], and involvement of semantic object categorization during Go/NoGo tasks has been shown to influence neural mechanisms underlying response inhibition/selection with electroencephalographic measures [3–5].

To probe brain regions mediating response selection and inhibition contingent upon semantic categorization, in the present study, participants completed a Go/NoGo task with varying semantic categorization requirements while functional MRI (fMRI) data were collected. Participants responded to objects (e.g. cars, tools, etc.) but not to animals (e.g. dogs, cows, etc.) in the superordinate categorization task, but participants responded to a single car or any car but not to a single dog or any dogs in the object identification tasks. Thus, the study allowed for the identification of regions sensitive to degrees of semantic categorization during selection and inhibition of responses.

Methods

Participants

All participants ($N = 16$; women = 10; age range 19–34 years, M = 23.5 years) were right-handed, prescreened for neurological or psychiatric diseases and medication, and provided written informed consent, as per the University of Texas at Dallas and University of Texas Southwestern Medical Center Institutional Review Boards.

Stimuli and experimental procedures

Participants completed three versions of a Go/NoGo task where the categorization requirements differed across the versions, adapted from Maguire *et al.* [3]. Across versions, participants were asked to respond as quickly and accurately as possible to stimuli (right index finger press on an MR-compatible button box) on Go trials but not to respond on NoGo trials. For the superordinate categorization version [i.e. the object/animal (OA) stimulus set], Go stimuli consisted of 160 different exemplars of objects (i.e. 40 food items, 40 cars, 20 clothing items, 20 kitchen items, 20 body parts, and 20 tools) and 40 different exemplars of animals of varying visual typicality (e.g. dog, cat, dolphin, etc.). For the two object identification versions, Go stimuli consisted of an exemplar of a specific

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car [i.e. single car (SC) stimulus set] or 40 different exemplars of cars [i.e. multiple car (MC) stimulus set], and NoGo stimuli consisted of a specific dog or 10 different exemplars of dogs, for the SC and MC stimulus sets, respectively. Response inhibition and selection in Go/NoGo tasks are affected by temporal variability in stimulus onsets [6,7]; thus, fixed stimulus durations (300 ms) and interstimulus intervals (1700 ms) were used, and each task lasted for about 7 min (see Supplementary Materials for details, Supplemental digital content 1, *http://links.lww.com/WNR/A253*).

Image acquisition

Using a Philips 3 T scanner (Philips Medical System, Best, the Netherlands) and a standard eight-channel head coil, a T1-weighted MPRAGE (60 sagittal 256×256 slices; voxel size = $1\,mm^3$) and echo-planar imaging (EPI) (33 transaxial 64×64 voxel slices; voxel size = $3.44 \times 3.44 \times 4$ mm; TR = 1.5 s; TE = 25 ms; flip angle = 60°; each run had 289 EPI images) were acquired.

Image analysis

Using AFNI software (NIMH/NIH, Bethesda, Maryland, USA) [8], EPIs were slice-time corrected, motion corrected (excluding participant data if motion exceeded 3 mm in transition or 2° in rotation, $N = 3$), and spatially smoothed (full-width at half-maximum = 6 mm Gaussian kernel). The BOLD data for each voxel for each run were then scaled so that the regression parameter estimates would be expressed in terms of percent signal change (i.e. $100 \times y_t/M_y$, y_t is the BOLD signal at time t, M_y is the mean of the time series).

For each participant, signal change was then estimated using conventional, modified linear regression for fMRI [9]. Regressors were constructed by convolving a gamma-variate function ($b = 8.6$, $c = 0.547$; maximal amplitude = 1.0; [10]) with impulse functions at the onsets of correct NoGo trials and an equivalent number of correct Go trials. Baseline was implicit and not modeled, assumed to have a 0% signal change after previous scaling. Although temporal variability in stimulus onsets affects inhibition and selection [6,7], temporal regularity in interstimulus intervals can lead to extreme collinearity, and possibly singularity, between canonical-based fMRI Go and NoGo regressor models to the point where linear regression is not accurate and in the case of singularity where it is computationally impossible [11,12]. To optimize signal detection and reduce potential collinearity, a covariate was created using correct Go trials not used in the above-described Go regressor. For this covariate, trial gamma functions were modulated for both amplitude and duration by the reaction time (RT) for each trial. Creating canonical Go and RT-modulated Go regressors allowed for Go-trial signal-changes estimates with an equivalent number of trials used to estimate NoGo-trial signal change and induced temporal variability into the regression design matrix to avoid collinearity issues while still accounting for signal-change variability associated with RT-modulated Go regressors. Nuisance regressors for incorrect trials (including RTs beyond ± 2.5 SD from the mean), motion, and temporal drift (i.e. linear, quadratic, and cubic trends) were also included in the design matrix. Signal-change matrices were spatially normalized to a Talairach–Tornoux template. With FSL linear and non-linear spatial transformation functions [13], each participant's MPRAGE was fit to a Talairach–Tornoux template brain. The warping parameters were then applied to the signal-change matrices (see Supplementary Materials for details, Supplemental digital content 1, *http://links.lww.com/WNR/A253*).

The spatially normalized beta matrices were then used for voxel-wise two factorial repeated-measures analyses of variance (two levels of Response Condition: Go/NoGo; three levels of Categorization Task: SC/MC/OA), with a cluster-wise 90 voxel threshold applied, cluster-level of $P = 0.05$, and voxel-level of $P = 0.005$ on the basis of the simulations with a smoothing kernel of full-width at half-maximum = 6 mm [14]. Post-hoc follow-up tests for the main and interaction effects were restricted to voxels with peak F-values within the clusters. One-sample t-tests, comparing the mean signal change to zero (i.e. no signal change), were also used to determine whether significant 'activation' or 'deactivation' was present for any condition in the post-hoc analyses.

Results and discussion

RT and accuracy were analyzed using separate 2×3 analysis of variance (two Response Conditions and three Categorization Tasks). Go RT differed significantly between categorization tasks [$F(2, 30) = 40.2$, $P < 0.001$]. Participants were slower in the OA (M = 467.7, SD = 72.3 ms) than in the SC (M = 380.9, SD = 63 ms) and MC (M = 388, SD = 60.7 ms) tasks, $t(15) = 6.98$, $P < 0.001$ and $t(15) = 7.38$, $P < 0.001$, respectively. Accuracies were significantly greater in Go (M = 99.4, SD = 0.8%) than in NoGo (M = 89.9, SD = 7.7%), $F(1, 15) = 26.64$, $P < 0.001$, and across categorization tasks, $F(2, 30) = 26.52$, $P < 0.001$. However, these main effects were qualified by a significant Response Condition × Categorization Task interaction, $F(2, 30) = 6.12$, $P = 0.016$. Further tests showed that Go accuracies remained relatively high, with no significant difference across all three tasks, $F(2, 30) = 0.37$, $P = 0.67$, but NoGo accuracies differed significantly across tasks, $F(2, 30) = 4.35$, $P = 0.022$, with SC significantly higher than OA, $t(15) = 2.76$, $P = 0.015$ (Table 1). Overall, with involvement of category-level processing introduced in the OA task, Go RT was slower and NoGo accuracy was lower.

The main effects of response condition for BOLD signal (Fig. 1) were shown to be in the left middle occipital gyrus, right supramarginal gyrus, right inferior occipital gyrus, right middle temporal gyrus, right inferior

frontal gyrus, left precentral gyrus, left middle cingulate cortex, right middle frontal gyrus, right precentral gyrus (in the above clusters NoGo trials elicited greater BOLD signal change than did Go trials; also NoGo trials had increased activation from baseline; Supplementary Table, Supplemental digital content 2, *http://links.lww.com/WNR/A254*), left postcentral, right cerebellar vermis, left angular gyrus (AG), and right parahippocampal gyrus (in the above clusters, Go responses elicited greater BOLD signal than did NoGo stimuli; also, Go trials had increased activation from baseline, except for the left AG and right parahippocampal gyrus; Supplementary Table, Supplemental digital content 2, *http://links.lww.com/WNR/A254*). The BOLD findings associated with NoGo/Go differences are consistent with previous literature [15,16] and show greater responses on NoGo trials than on Go trials, spanning from posterior (parietal and occipital) regions to more anterior (frontal) regions. This widespread network has been suggested to be involved in stimulus recognition, maintenance, and manipulation of stimulus–response associations and response inhibition [15]. Go responses elicited activity in the left precentral gyrus and right cerebellum, reflecting the roles of these regions in motor execution and coordination [15]. Interestingly, one focus in the medial frontal area (middle cingulate cortex, BA32, in close proximity to pre-Supplementary Motor Area, or pre-SMA, BA6; Supplementary Table, Supplemental digital content 2, *http://links.lww.com/WNR/A254*) showed greater than baseline activation for both Go and NoGo trials. The finding is consistent with the hypothesis of the medial frontal areas playing a role in both response selection and inhibition [17]. Nevertheless, we also found this medial frontal activation to be significantly higher in NoGo than Go, suggesting that some additional recruitment would still be needed to mediate response inhibition.

Table 1 Means (SDs) of percent accuracy and reaction times across tasks

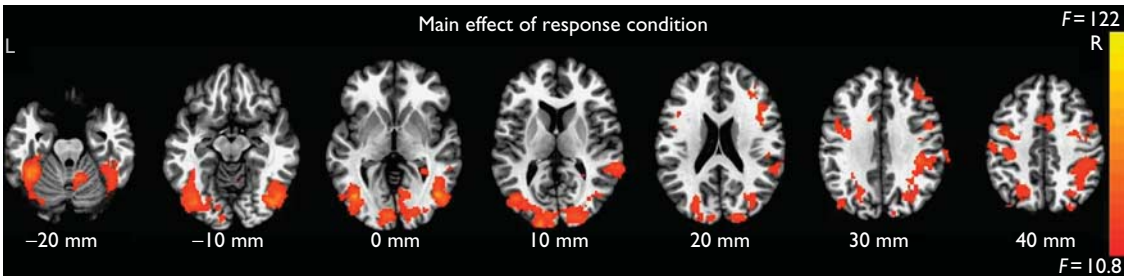
Experiment	Go correct (%)	NoGo correct (%)	Reaction times (ms)
SC	99.5 (0.9)	92.5 (4.4)	380.9 (63.0)
MC	99.5 (0.8)	90.8 (8.4)	388.0 (60.7)
OA	99.3 (0.6)	86.4 (8.7)	463.7 (72.3)

MC, multiple car task; OA, object animal task; SC, single car task.

A main effect of categorization task was observed in the right AG (rAG; Fig. 2). Lower BOLD signal change occurred in the SC task compared with the other tasks [post-hoc comparisons: MC > SC, $t(31) = 6.14$, $P < 0.001$; OA > SC, $t(31) = 3.04$, $P = 0.005$]. There was also a statistically significant difference between MC and OA [MC > OA, $t(31) = 3.06$, $P = 0.005$]. Significant activation against baseline was observed in both MC [M = 0.367, $t(31) = 6.64$, $P < 0.001$] and OA [M = 0.216, $t(31) = 5.49$, $P < 0.001$], but not SC [M = 0.05, $t(31) = 1.08$, $P = 0.288$]. To put the results in context, when the object categorization requirements became more complex, from the SC task to MC and OA tasks, the rAG showed a greater degree of signal increase. This effect was not associated with the need to stop a response, as both Go and NoGo trials elicited similar magnitudes of signal change within each type of task. The potential role of the rAG, in the vicinity of intraparietal sulcus and superior temporal sulcus as part of the parietal regions along the dorsal stream of visual processing, could thus be associated with an increase in visuospatial/perceptual variability [18–20] required for higher-order object categorization.

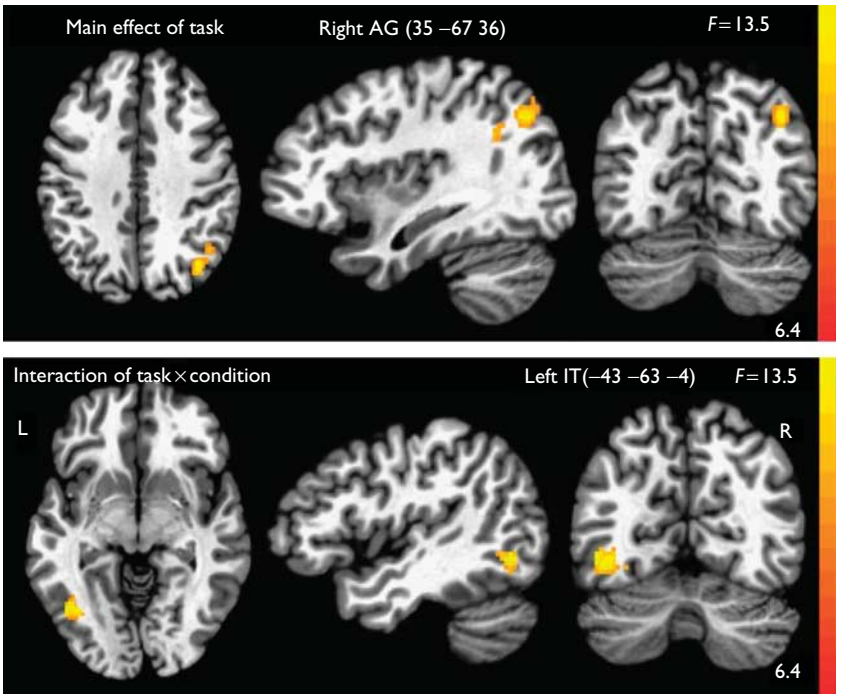
A significant Response Condition × Categorization Task interaction was observed in the left inferior temporal gyrus (Fig. 2). Significantly greater BOLD signal change was observed on NoGo compared with Go trials for both SC, $t(15) = 4.75$, $P < 0.001$ and MC, $t(15) = 5.35$, $P < 0.001$, but signal change did not differ significantly between Go and NoGo trials for OA, $t(15) = 0.14$, $P > 0.1$. Significant activation against baseline was tested by one-sample *t*-tests with each peak voxels at the participant level and was observed on NoGo trials in SC [M = 0.214, $t(15) = 3.71$, $P = 0.002$], MC [M = 0.207,

Fig. 1



Regions that showed the main effect of response condition (Go/NoGo). Yellow/red colors indicate increased signal change. The color bar represents the range of *F*-values (from 10.8 to 122). Coordinates are represented in Talairach space (*Z*-axis) and shown in neurological convention.

Fig. 2



Regions that showed the main effect of Categorization Task (top) and Categorization Task by Response Condition interaction (bottom). The color bar represents the range of *F*-values (from 6.4 to 13.5). Coordinates are represented in Talairach space in neurological convention. AG, angular gyrus; IT, inferior temporal (gyrus).

$t(15) = 4.06$, $P = 0.001$], and OA [M = 0.13, $t(15) = 3.15$, $P = 0.007$], but for Go trials only in the OA condition [M = 0.127, $t(15) = 3.65$, $P = 0.002$]. It appears that lIT mediates semantic processing related to inhibition even when lower-order categorization is required. In other words, higher-order categorization elicits lIT activation for both selection and inhibition, but lower-order categorization elicits lIT activation only during inhibition.

Semantic categorization of objects has been shown to involve multiple brain areas, including several frontal and temporal regions. However, IT and ventral temporal (VT) areas have previously been observed to mediate categorization in object identification and recognition tasks [21–25]. Furthermore, IT/VT have been proposed to mediate levels of categorization (i.e. superordinate through subordinate) through differential responses to conceptual versus perceptual object processing [21,23,25].

Our finding that lIT mediates object identification on NoGo trials (but not Go trials) suggests that lIT-mediated semantic/conceptual processing is involved in inhibition under lower-order categorization requirements. Although previous studies have shown increased activity in the IT/VT regions during NoGo trials, even in the absence of any component of explicit semantic memory in the task [15], none of these studies varied depth of cognitive processing during a Go/NoGo task. Our data suggest that the IT/VT regions play a potential role in mediating and facilitating object processing in response to increased cognitive demand in processing stimuli that require inhibiting a prepotent response.

Conclusion

Activity in the left inferior temporal region is engaged in superordinate categorization, irrespective of Go or NoGo conditions. This same region is engaged only in NoGo but not in Go trials during object identification requiring not as much semantic processing as superordinate categorization does. This suggests regional specialization in the 'what' visual object memory system for semantic processing that might also mediate response inhibition in relation to objects.

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Conflicts of interest

There are no conflicts of interest.

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