Two distinct neural mechanisms for category-selective responses

Uta Noppeney, Cathy J. Price, Will D. Penny, Karl J. Friston

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Correspondence should be addressed to:
U. Noppeney
Wellcome Department of Imaging Neuroscience
University College London
12 Queen Square
WC1 N3BG London, UK
Tel.: +44-(20)-7833 7483
Fax.: +44-(20)-7813 1420
e-mail: u.noppeney@fil.ion.ucl.ac.uk

Abstract

The cognitive and neural mechanisms mediating category-selective responses in the human brain remain controversial. Using fMRI and effective connectivity analyses (Dynamic Causal Modelling), we investigated animal and tool-selective responses by manipulating stimulus modality (pictures vs. words) and task (implicit vs. explicit semantic). We dissociated two distinct mechanisms that engender category-selectivity: In the ventral occipito-temporal cortex, tool-selective responses were observed irrespective of task, greater for pictures and mediated by bottom-up effects. In a left temporo-parietal action system, tool-selective responses were observed irrespective of modality, greater for explicit semantic tasks and mediated by top-down modulation from the left prefrontal cortex. These distinct activation and connectivity patterns suggest that the two systems support different cognitive operations, with the ventral occipito-temporal regions engaged in structural processing and the dorsal visuo-motor system in strategic semantic processing. Consistent with current semantic theories, explicit semantic processing of tools might thus rely on re-activating their associated action representations via top-down modulation. In terms of neuronal mechanisms, the category-selectivity may be mediated by distinct top-down (task-dependent) and bottom-up (stimulus-dependent) mechanisms.

Keywords: semantic memory, dynamic causal modelling, category-selectivity, effective connectivity, functional imaging

Introduction

A central question in cognitive neuroscience is how object concepts are represented and processed in the human brain. Category-selective impairments in patients with focal cortical lesions suggest specialized neuronal systems that are engaged by different semantic categories such as animals and tools (Warrington and Shallice, 1984;Gainotti *et al.*, 1995;Capitani *et al.*, 2003). These category-selective deficits have been found at multiple processing levels, ranging from structural to semantic (Humphreys and Forde, 2001). Similarly, functional brain imaging studies have reported category-selective activations in multiple cortical regions. Activations within the fusiform gyrus have been found medially for tools and laterally for animals (Chao *et al.*, 1999). In addition, tools have been associated with activations in a visuo-motor action system encompassing a left posterior middle temporal area (lpMT; Martin *et al.*, 1996;Devlin *et al.*, 2002;Damasio *et al.*, 1996;Kellenbach *et al.*, 2002), the anterior intraparietal sulcus (AIP; Chao and Martin, 2000) and the ventral premotor cortex (Rizzolatti *et al.*, 1996;Grabowski *et al.*, 1998;Grafton *et al.*, 1996). Despite this extensive evidence for category-selective regions, the associated cognitive processes and their neural implementation remain unclear.

The present fMRI study addressed two key questions: First, we asked whether category-selective fMRI responses were differentially modulated by stimulus modality (i.e. pictures vs. words) and/or task-context. Second, using effective connectivity analyses (Dynamic Causal Modelling; DCM; Friston *et al.*, 2003), we investigated the neural mechanisms that mediate context-sensitive, category-selective responses entailed by our first question.

The aim of DCM is to make inferences about the coupling among brain areas within a simple but reasonably realistic neuronal model. DCM is a generalization of the linear convolution model used in conventional analyses of regionally specific effects. However, in a conventional analysis, the experimental effects are expressed through a direct or extrinsic influence of experimental effects on each region. In contrast, DCM tries to explain regional responses in terms of interactions among brain regions and, critically, an effect of experimental manipulations on connections between brain regions.

Subjects were engaged in a one-back-task on animals and tools that were presented as pictures, written words or spoken words. The one-back-task used either implicit (i.e. stimulus identity) or explicit semantic (i.e. typical action or real-life-size of the stimulus) attributes. This design allowed us to segregate category-selective regions into two classes: In one class, category-selectivity was stimulus modality-dependent and observed primarily for pictures. In the other class, it was task-dependent and observed when subjects were engaged in explicit semantic tasks.

Using DCM, we then investigated the neural mechanisms underlying category-selectivity in two representative brain regions, one exhibiting modality-dependent, the other one task-dependent tool-selective responses. The model included bottom-up input from early visual areas and top-down influences from left prefrontal areas. This allowed us to address the following three questions: (1) Are stimulus modality-dependent tool-selective responses mediated by forward connections from early visual areas that are enabled when tools are presented as pictures? (2) Are task-dependent tool-selective activations mediated via increased backward influences from left prefrontal regions during explicit semantic tasks? (3) Can the distinct category-selective activation patterns in the two modality- and task-dependent regions be explained by differential modulation of forward or backward connections?

Materials and Methods

Subjects

22 healthy right-handed English native speakers (14 males; mean age: 25; range: 19-35) gave informed consent to participate in the study. All subjects had normal or corrected to normal vision and no diagnosis of dyslexia. All of them reported good reading abilities. 21 were either currently university students or reported having been educated to degree level. The study was approved of by the joint ethics committee of the Institute of Neurology and University College London Hospital, London, UK.

Experimental Design

The activation conditions conformed to a 2 x 3 x 3 factorial design manipulating

(i) Semantic category: animals or tools,

(ii) Stimulus modality: pictures, written words or spoken words. This manipulation allowed us to investigate whether category-effects are elicited by verbal (written or spoken words) and non-verbal (pictures) material. We hypothesized that verbal material would elicit category-effects primarily at the semantic level, while pictures would also induce category-effects at the structural level.

(iii) Task: Subjects were engaged in a one back-task and decided whether subsequent stimuli within a block were identical (= implicit semantic task; e.g. sparrow, sparrow), performed a similar action (=explicit action semantic task; e.g. stork, butterfly) or were of similar size in real life (=explicit visual semantic task; e.g. pigeon, rabbit). Irrespective of task, subjects were instructed to view the pictures, read the written words silently and listen to the spoken words. While the identity task elicits only stimulus-driven implicit semantic activations that are not required for task performance (see (Price *et al.*, 1996)), we expected the action and size tasks to evoke additional task-induced, strategic semantic activations necessary for explicit semantic categorization.

Altogether, there were 90 animals and 90 tools that were matched for word frequency and number of letters. Each stimulus was presented once in each stimulus modality and during each task (i.e. three times during the entire experiment) yielding 270 animal and 270 tool events. ~30% of the stimuli were targets. As the identity task inevitably required successive repetitions of the targets, 16 additional target stimuli were used for the implicit condition to avoid repetition priming confounds. Yes/No responses to all conditions were indicated (as quickly and as accurately as possible) by a two-choice key press. The stimuli (SOA = 3.3 s; stimulus duration = 1.2 s) were presented in blocks of 5 stimuli interleaved with 5.5 s fixation. The category and modality factors were manipulated across the activation blocks, the task factor in long periods covering one third of each session. The order of semantic conditions was counterbalanced within and across subjects.

fMRI scanning

A 1.5 T Siemens Sonata system was used to acquire both T1 anatomical volume images and T2*-weighted axial echoplanar images with blood oxygenation level-dependent (BOLD) contrast (gradient echo, Cartesian k-space sampling, TE=50ms, TR 2.97 s, 33 slices acquired sequentially in descending direction, matrix 64X64, spatial resolution 3X3X3.4 mm^3 voxels, interslice gap 1.4 mm, slice thickness 2.0 mm, tilted from transverse to coronal orientation by –30 degree to reduce susceptibility artefacts). To avoid Nyquist ghost artefacts a generalized reconstruction algorithm was used for data processing (Josephs *et al.*, 2000). There were three sessions with a total of 340 volume images per session. The first six volumes were discarded to allow for T1 equilibration effects.

Conventional SPM analysis

The data were analysed with statistical parametric mapping (using SPM2 software from the Wellcome Department of Imaging Neuroscience, London; http//www.fil.ion.ucl.ac.uk/spm;Friston *et al.*, 1995). Scans from each subject were realigned using the first as a reference, spatially normalised into standard space (Talairach and Tournoux, 1988), resampled to 3X3X3mm^3 voxels and spatially smoothed with a Gaussian kernel of 8mm FWHM. The time series in each voxel were highpass filtered to 1/128 Hz and globally normalized with proportional scaling. The fMRI experiment was modelled in an event related fashion with regressors (i.e. explanatory variables) made by convolving each event-related stimulus function with a canonical hemodynamic response function and its first temporal derivative. Stimulus functions were a series of delta or “stick” functions encoding the occurrence of each trial type. In addition to modelling the 18 conditions in our 2 x 3 x 3 factorial design, the statistical model included instructions, targets during the implicit condition and non-responses. Covariates of no interest included the realignment parameters (to account for motion artefacts). The analysis was performed twice: (i) including all trials, (ii) including only the trials that were equated for reaction times with respect to the main effect of category and the interaction between category and modality/task. This involved excluding (1) tool trials with reaction times that were 1.25 std above the mean and (2) animal trials with reaction times that were 1.25 std below the mean during the explicit semantic conditions (the excluded trials that accounted for less than 10% of all trials in any subject, were modelled as an extra confounding effect). Condition-specific effects for each subject were estimated according to the general linear model and passed to a second-level or subject-level analysis as contrasts. Here each contrast was the estimated response for each condition. This involved creating 18 contrast images (i.e each of the 18 conditions averaged across the three sessions) for each subject and entering them into a second level ANOVA. This ANOVA modelled the 18 effects in our 2 x 3 x 3 factorial design. Inferences were made at the second level to allow a random effects analysis and inferences at the population level (Friston *et al.*, 1999).

The random effects analysis tested for the main effects of tools relative to animals and animals relative to tools. Pooling over written and spoken words, we tested for the interactions between category and stimulus modality i.e. tool or animal selective responses that were increased or decreased for pictures relative to words. Pooling over action and visual explicit semantic tasks, we tested for the interactions between category and task i.e. tool or animal selective responses that were increased or decreased for explicit relative to implicit tasks.

All effects were inclusively masked with all stimuli > baseline (at $p<0.001$ uncorr.). The interactions were further characterized by inclusively masking each contrast with (i) tools > animals or (ii) animals > tools (at $p<0.001$ uncorr.). Unless otherwise stated, we only report activations that are significant ($p<0.05$) corrected for the entire brain volume.

DCM analysis

DCM treats the brain as a dynamic input-state-output system. The inputs correspond to conventional stimulus functions encoding experimental manipulations. The state variables are neuronal activities and the outputs are the regional hemodynamic responses measured with fMRI. The idea is to model changes in the states, which cannot be observed directly, using the known inputs and outputs. Critically, changes in the states of one region depend on the states (i.e. activity) of others. This dependency is parameterized by effective connectivity. There are three types of parameters in a DCM (i) input parameters which describe how much brain regions respond to experimental stimuli, (ii) intrinsic parameters that characterise effective connectivity among regions and (iii) modulatory parameters that characterise changes in effective connectivity caused by experimental manipulation. This third set of parameters, the modulatory effects, allows us to explain context-sensitive category-selective activations by changes in coupling among brain areas. Importantly, this coupling (effective connectivity) is expressed at the level of neuronal states. DCM employs a forward model, relating neuronal activity to fMRI data, that can be inverted during the model fitting process. Put simply, the forward model is used to predict outputs using the inputs. The parameters are adjusted [using gradient descent] so that the predicted and observed outputs match. This adjustment corresponds to the model-fitting.

22 subject-specific DCMs were constructed. The regions (see Table 3) were selected using the maxima from the random effects analysis. The left posterior medial fusiform and AIP were selected as representative regions for modality- and task-dependent category-selectivity respectively. Region-specific time-series (concatenated over three sessions and adjusted for confounds) comprised the first eigenvariate of all voxels

within a 4 mm radius centred on each location. The DCM (Figure 4) included five regions, (i) a left superior temporal area that was activated by spoken words relative to fixation (STG), (ii) a left occipital region that was activated for both written words and pictures and did not show any category-selectivity (OCC), (iii) a task-sensitive left prefrontal region (PF), (iv) tool-selective AIP and (v) the tool-selective left posterior medial fusiform area. Based on our scientific question (see introduction), the tool-selective regions were selected that showed an interaction-effect i.e. we selected a modality-dependent fusiform and a task-dependent AIP tool-selective region. In other words, we used DCM to understand how regionally-specific interactions are mediated by changes in coupling. Visual input ($\text{words}_{\text{written}}$ and pictures) was connected to OCC, the auditory input ($\text{words}_{\text{spoken}}$) to STG. The main effect of task entered directly in the left prefrontal area. Tool pictures, tool $\text{words}_{\text{written}}$ and pictures modulated or enabled the forward connections from OCC to the category-selective regions. These three effects were chosen to cover the main effect of category, stimulus modality and their interaction. Category-effects (tools in all modalities) were entered to modulate the backward connection from PF to the category-selective regions.

The subject-specific modulatory effects were entered into t-tests at the group level (see Table 4). This allowed us to summarize the consistent findings from the subject-specific DCMs using classical statistics. First, we tested whether tool pictures relative to tool words increased the strength of forward connections (i.e. we tested for a modulatory effect of the category x modality interaction on forward connections). Second, we tested whether tools increased the backward connections from the left prefrontal to the category-selective regions. As the left prefrontal response is caused primarily by the main effect of task, this effectively tests for a category x task interaction mediated by backward connections. Finally, we tested for differences in modulatory effects between connections to the fusiform and AIP regions using a paired t-test. This allowed us to characterize category-selective effects in terms of a differential enabling of dorsal and ventral pathways.

Results

Behavioural results

For performance accuracy, a three-way ANOVA with category (tools, animals), stimulus modality (pictures, spoken words, written words) and task (identity, action, real life size) identified a significant main effect of stimulus modality (F(1.7,36.5)=9.6; $p < 0.01$) and of task (F(1.8,39)=247; $p < 0.001$) after Greenhouse-Geisser correction. Importantly, there was no significant effect of category or the interactions between category and task/modality. For reaction times, the three-way ANOVA identified (i) main effects of category (F(1,21)=66; $p < 0.001$), stimulus modality (F(1.5,31)=597; $p < 0.001$) and task (F(1.7,35)=203; $p < 0.001$) and (ii) significant interactions of category by stimulus modality (F(1.9,41)=7; $p < 0.01$) and category by task (F(1.8,38)=13; $p < 0.001$) following Greenhouse-Geisser correction. After equating the reaction times with respect to the main effect of category and the interaction between category and modality/task, the three-way ANOVA only identified (i) main effects of stimulus modality (F(1.2,26)=597; $p < 0.001$) and task (F(1.7,34)=203; $p < 0.001$) following Greenhouse-Geisser correction.

Table 1, Figure 1 about here

Conventional SPM analysis

The SPM analysis was performed in two steps: First, we identified regions that responded selectively to tools or animals. Second, we tested for category-selective responses that were significantly modulated by stimulus modality or task-context. Analyses including all trials or only the trials that were equated for reaction times (see methods) gave nearly identical results. We report the results of the latter conventional analysis.

Tools evoked increased responses relative to animals, in the left posterior medial and anterior fusiform regions. At a lower significance threshold, we observed increased responses in the right medial fusiform (co-ordinates: [27 –42 –21]; $z=4.4$; $p<0.001$ uncorr.). In addition, tools evoked selective responses in a visuo-motor system encompassing a left posterior middle/inferior temporal area (lpMT), the anterior intraparietal sulcus (AIP) and several left prefrontal regions. Left prefrontal activation was found in the ventral pre-motor area and along the left inferior frontal sulcus extending into the triangular part of the left inferior frontal gyrus. Critically, tool-selective responses in the occipito-temporal areas showed a significant interaction with stimulus modality and were greater for pictures. For pictures relative to written words only (i.e. excluding spoken words) a left medial fusiform, middle and superior occipital region showed increased tool-selective activations, the right middle and superior occipital regions showed increased animal-selective activation. This demonstrates that the interaction effect reflects the difference between verbal and non-verbal stimuli. In contrast, responses in lpMT and AIP exhibited a significant interaction with task and were greater for explicit semantic tasks that required retrieval of an associated action or the real life size of the stimulus. The apparent increased activation for animals relative to tools in AIP (see Figure 2) during the implicit condition was not significant at $p<0.05$ uncorrected.

We did not detect any tool-selective activation that was enhanced for (i) words relative to pictures or (ii) implicit relative to explicit semantic tasks.

Figure 2, Table 2 about here

Animals increased responses relative to tools in the right middle occipital and the lateral fusiform gyri. Animal-selective responses in both regions and additional left and right lateral occipito-temporal areas interacted with stimulus modality and were greater when the stimuli were presented as pictures. No animal-selective responses were detected that (i) were enhanced for words relative to pictures or (ii) interacted with task context.

In summary, a ventral object recognition system, comprising occipito-temporal regions showed modality-dependent category-selective effects, while a dorsal visuo-motor system showed task-dependent category-effects. Our DCM analysis addressed how this dissociation was mediated in terms of functional integration:

Figure 3, Table 3 about here

Effective Connectivity analysis

First, we found that tool pictures enabled the forward connections from OCC to the tool-selective left posterior medial fusiform and AIP areas. Furthermore, this effect was significantly greater for tool pictures than tool words i.e. there was a significant modulatory effect of the stimulus modality by category interaction on the forward connections (Fusiform: $p<0.001$; AIP: $p<0.05$). These results imply that modality-dependent category-selective responses can be explained by modulation or selective enabling of forward connections, in the context of tool pictures (see Table 1).

Second, left prefrontal areas that showed greater responses during explicit semantic tasks exerted more top-down influence on the fusiform and AIP when subjects were actively engaged in semantic tasks on tools than on animals. These results demonstrate that task-dependent category-selective responses can be explained in terms of category-sensitive modulation of backward connections, during explicit semantic tasks on tools.

Finally, the effect of the stimulus modality x category interaction was greater for the forward connections from early visual areas to the fusiform than to AIP ($p<0.01$). Conversely, the task-dependent category-effect of tools was greater for backward connections from the left prefrontal area to the AIP than the fusiform area ($p<0.05$). These results demonstrate that the distinct patterns of category-selectivity over regions can be explained by differences in top-down and bottom-up influences that show a dorso-ventral dissociation (i.e. differences in modulatory effects between connections to the fusiform and AIP).

Table 4, Table 5, Figure 4

In a subsequent analysis, we have investigated the neural mechanisms that mediate modality-dependent animal-selective responses in the ventral occipito-temporal cortex using a DCM model including the STG, OCC and the animal-selective right lateral posterior fusiform area. Similar to our DCM analysis for tools, we found increased forward connections from OCC to the animal-selective right lateral posterior fusiform area for animal pictures relative to animal words i.e. there was a significant modulatory effect of the stimulus modality by category interaction on the forward connections. In short, we reached equivalent conclusions for the modality-dependent animal-selective activations in the ventral occipito-temporal cortex (detailed results not reported).

In summary, we found that ventral category-effects could be explained by a stimulus modality-dependent increase in bottom-up category-specific influences, whereas dorsal regions were subject primarily to category-selective top-down influences of task-related prefrontal activity.

Effect of gender on modulatory effects

At the random effects level, we compared modulatory effects between female and male subjects. This analysis did not reveal any gender effects (p>0.05).

Effect of performance on modulatory effects

To further characterize the connectivity results, we investigated the effect of subject's performance on the modulatory effects (see Buchel *et al.*, 1999;Goncalves and Hall, 2003;Glabus *et al.*, 2003) using subject-specific reaction times as predictors for the connection strengths. First, we used the reaction time difference for tools – animals during semantic decision tasks to predict the tool-effect on backward connections from the prefrontal cortex. Second, we used the reaction time difference for tools – animals during picture conditions to predict the tool picture-effect on the forward connections from the occipital cortex. Finally, we used the reaction time difference for tools – animals during written word conditions to predict the modulatory tool written word-effect on forward connections from the occipital cortex. None of these regression analyses revealed a significant relation between reaction time and connection strength.

Discussion

Our results demonstrate robust category-selective responses in multiple cortical regions: Within the fusiform gyrus, category-selective activations were found medially for tools and laterally for animals. In addition, tools elicited increased responses in a left-lateralized visuo-motor action system encompassing ventral premotor, anterior intraparietal and posterior middle temporal regions. Critically, in the ventral occipito-temporal cortex, tool-selective activations were observed irrespective of task but depended on stimulus modality (picture vs. words). In contrast, tool-selective responses in the dorsal visuo-motor action system emerged irrespective of modality but were modulated by task. Therefore, category-selectivity rests on the interaction of semantic content with either (i) stimulus-bound factors such as modality or (ii) task. From a cognitive perspective, category-selective responses may be better understood in terms of the cognitive operations induced by a semantically invested stimulus in a particular context, rather than its semantic content alone. In particular, our results demonstrate a dorso-ventral dissociation with ventral occipito-temporal regions engaged by stimulus-bound structural processing and dorsal visuo-motor action regions by task-induced semantic operations. In terms of neural mechanisms, our results suggest that the stimulus modality- and task-dependent tool-selective responses are not properties intrinsic to a region but are mediated by changes in the influence of, or the responsiveness to, other regions (McIntosh, 2000;Mesulam, 1990;Friston and Price, 2001;Buchel and Friston, 2000;Horwitz, 2003). These two distinct classes of tool-selectivity can be explained by differential top-down and bottom up influences for task and modality-dependent effects respectively.

The tool and animal-selective responses within the ventral occipito-temporal cortex are consistent with numerous studies of object recognition demonstrating focal regions with preferential responses to various semantic categories including faces, houses and chairs (Haxby *et al.*, 2001;Spiridon and Kanwisher, 2002;Ishai *et al.*, 1999). A recent study reported ventral category-selective activations that were mediated by bottom-up effects during perception and top-down effects during imagery (Mechelli *et al.*, 2004). In our study, category-selective responses in the occipito-temporal cortex were modulated by stimulus modality and were evident only for pictures, irrespective of the task context. According to our DCM, this functional specialization is not an intrinsic property of the ventral occipito-temporal regions, but is mediated via bottom up mechanisms that render them especially responsive to certain patterns of input from early visual areas during object perception. Collectively, these results suggest that the ventral occipito-temporal regions are specialized for processing structural features that are sufficiently abstract to be shared by different exemplars of the same category. These structural features permit object categorization during perception and possibly imagery.

In contrast to the modality-dependent category-selective responses in the ventral occipito-temporal cortex, the tool-selective responses in the dorsal visuo-motor action system showed a distinct activation pattern: The tool-selective responses in the left inferior/middle temporal area (lpMT), anterior inferior parietal sulcus (AIP) and ventral pre-motor cortex (i.e. the putative homologue of area F5) were observed irrespective of the stimulus modality. These three regions correspond to those with the highest lesion overlap in patients with impaired action retrieval (Tranel *et al.*, 2003) and have been implicated in tool and action observation and retrieval by previous functional imaging studies (Grezes and Decety, 2001;Hauk *et al.*, 2004). In the macaque, neurons in areas F5 and AIP have been identified that respond selectively to action execution, observation and presentation of graspable objects (Rizzolatti and Luppino, 2001;Rizzolatti and Arbib, 1998). Our study demonstrates that lpMT and AIP in humans respond to both tool pictures and names suggesting a role in semantic processing. However, their responses were not obligatory but strongly context-sensitive with tool-selective responses being enhanced when subjects process stimuli at a deeper semantic level. Consistent with studies in primates and neuropsychology that have implicated the left prefrontal cortex as a key player in top-down control processes (Fuster, 1989;Miller, 2000), our DCM analysis demonstrated that task-dependent tool-selectivity is mediated via increased backward influences from the left prefrontal cortex to AIP during semantic decisions on tools. Thus, tool-related action responses, for instance in AIP, might be enabled during explicit semantic tasks by top-down modulation from the prefrontal cortex.

The DCMs discussed so far have established bottom-up and top-down modulations as sufficient explanations for modality- and task-dependent category-selectivity. Obviously, most brain regions will -to a certain degree- be exposed to both bottom-up and top-down influences. Our study also demonstrated significant bottom up and top-down influences for AIP and the fusiform region. Directly comparing the modulatory components of connections to the left posterior fusiform and AIP demonstrated that (i) modality-dependent bottom-up category effects were greater for the fusiform than AIP and (ii) task-dependent top-down category effects were greater for AIP than the fusiform. Thus, distinct classes of category-selectivity in AIP and left posterior medial fusiform can result from differential enabling of ventral and dorsal connections.

Further evidence for distinct functional roles of the dorsal visuo-motor system and the ventral occipito-temporal cortex in tool processing is provided by two recent studies: The first (Chao *et al.*, 2002) manipulated semantic category (animals vs. tools) and visual experience (primed vs. unprimed) and demonstrated a priming- induced response reduction selectively for tools in LPMT, but non-selectively in the medial fusiform. The second (Beauchamp *et al.*, 2003) manipulated (i) semantic type (i.e. human motion vs. tool motion) and (ii) stimulus display (real objects vs point light display) in a factorial design and showed a tool selective response in LPMT irrespective of stimulus display but in the medial fusiform primarily for real tool motion. These results suggest that the tool-selective responses in occipito-temporal regions are strongly influenced by stimulus-bound factors such as modality (pictures vs. words), display (real objects vs point lights) or perceptual priming.

In conclusion, our results demonstrate two classes of category-selectivity: In the ventral occipito-temporal cortex, category-selective responses were observed primarily for pictures and mediated by bottom-up effects. In lpMT and AIP, they were observed during semantic decision tasks and mediated by increased top-down modulation from left prefrontal cortex. These distinct activation and connectivity patterns suggest that the two classes of category-selective systems may support different cognitive operations with ventral occipito-temporal regions engaged in structural processing and dorsal visuo-motor regions activated during strategic semantic processing. Consistent with current semantic theories that emphasize the link between tools and action features, we thus provide evidence that explicit semantic processing of tools relies on re-activating their associated action representations via top-down modulation (Damasio, 1989;Martin and Chao, 2001;Barsalou *et al.*, 2003).

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Figure Legends

Figure 1

Top: Main effects of category: Tool- and Animal-selective activations are rendered on an averaged normalised brain. Height threshold: $p<0.05$ corrected. Extent threshold: > 1 voxel, including only voxels that were activated for stimulus > fixation at $p < 0.001$ (uncorrected).

Bottom: Main effects of category and category x task/modality interactions on coronal and sagittal slices of a structural image created by averaging the subjects' normalized images. Red: Tools > Animals; Green: Animals > Tools; Blue: Tools > Animals for Semantic Decision > Implicit task; Yellow: (i) Tools > Animals for Pictures > Words or (ii) Animals > Tools for Pictures > Words. Height threshold: $p<0.001$ uncorrected for illustration purposes. Extent threshold: > 19 voxels restricted to voxels that showed a significant effect of category-selectivity and stimulus > fixation.

Figure 2

Left: Interactions: Stimulus modality- and task-dependent tool-selective activations on transverse slices of a structural image created by averaging the subjects' normalized images. Modality-dependent: Tools > Animals for Pictures > Words. Task-dependent: Tools > Animals for Semantic Decision > Implicit task. Height threshold: $p<0.001$ uncorrected for illustration purposes. Extent threshold: > 19 voxels, restricted to voxels that showed a significant effect of tool-selectivity and stimulus > fixation.

Right: Parameter estimates for Tools (T, grey) and Animals (A, black) relative to fixation during Implicit (I) and Explicit Semantic (S) tasks. The bar graphs represent the size of the effect in adimensional units (corresponding to % whole brain mean) These effects are activations pooled (i.e. summed) over appropriate conditions.

Figure 3

Left: Interactions: Stimulus modality-dependent animal-selective activations on transverse slices of a structural image created by averaging the subjects' normalized images. Animals > Tools for Pictures > Words. Height threshold: $p<0.001$ uncorrected for illustration purposes. Extent threshold: > 19 voxels, restricted to voxels that showed a significant effect of animal-selectivity and stimulus > fixation.

Right: Parameter estimates for Tools (T, grey) and Animals (A, black) relative to fixation during Implicit (I) and Explicit Semantic (S) task.. The bar graphs represent the size of the effect in adimensional units (corresponding to % whole brain mean) These effects are activations pooled (i.e. summed) over appropriate conditions.

Figure 4

DCM for left anterior intraparietal (AIP) and left posterior medial fusiform gyrus (FG) responses. Black: Intrinsic connections; Purple: Extrinsic input; Green: Modulatory effects

Values are the mean (SD) of changes in connection strength (over subjects; at $p<0.001$ in bold). These parameters quantify how experimental manipulations change the values of intrinsic connections. In dynamic systems the strength of a coupling can be thought of as a rate constant or the reciprocal of the time constant. Typically regional activity has a time constant in the order of 1-2 seconds (rate of 1-0.5 s^{-1}). Therefore, a modulatory effect of 0.05 s^{-1}corresponds to a 5%-10% increase in coupling.

Table 1.a Response Accuracy

Task	Implicit	Action	Visual
Words written			
Tools	0.99(0.03)	0.91(0.06)	0.85(0.07)
Animals	0.99(0.02)	0.90(0.07)	0.87(0.07)
Words spoken			
Tools	0.99(0.04)	0.89(0.07)	0.86(0.06)
Animals	0.98(0.09)	0.89(0.07)	0.84(0.09)
Pictures			
Tools	0.99(0.03)	0.87(0.05)	0.81(0.08)
Animals	0.98(0.06)	0.87(0.06)	0.81(0.06)

Table 1.b Reaction times

Task	Implicit	Action	Visual
Words written			
Tools	624(99)	944(118)	951(96)
Animals	617(86)	920(104)	897(98)
Words spoken			
Tools	1057(138)	1432(159)	1419(125)
Animals	1017(136)	1353(174)	1317(97)
Pictures			
Tools	635(77)	1014(132)	953(92)
Animals	638(73)	905(102)	870(80)

Table 1.c Reaction times (equated)

Task	Implicit	Action	Visual
Words written			
Tools	624(99)	902(104)	919(92)
Animals	617(86)	939(108)	911(94)
Words spoken			
Tools	1057(139)	1401(173)	1368(124)
Animals	1022(137)	1399(227)	1353(95)
Pictures			
Tools	636(78)	966(123)	910(76)
Animals	640(72)	931(104)	893(84)

Values are across-volunteer means (SD)

Table 2.Tool-selective activation

Region		Co-ordinates	Z-score	p-value (corr.)	voxels
Tools > Animals					
L. post. middle temporal g.		-51 -66 -6	>8.0	0.0	195
L. medial fusiform		-24 -57 -15	5.9	0.0	14
L. supramarginal g.		-57 -30 39	6.9	0.0	32
L. prefrontal	triangular	-48 36 6	6.2	0.0	64
	opercular	-54 18 15	5.5		
L. ant fusiform		-33 -33 -24	5.8	0.01	5
Interaction: Tool-selective activation for Pictures > Words					
L. medial fusiform g.		-27 -63 -12	5.5	0.0	4
L. middle occipital g.		-45 -66 -9	4.9	0.0	2
Interaction: Tool-selective activation for Semantic Decision > Implicit task					
L. supramarginal g.		-60 -30 42	5.7	0.0	12
					(at p<0.001 uncorr.)
L. post. middle temporal g.		-54 -57 -12	3.8	0.8	27
L. prefrontal, opercular		-54 12 24	3.4	1.0	14

activation at p<0.05 (corr.); extent threshold > 1 voxel

Table 3. Animal-selective activation

Region	Co-ordinates	Z-score	p-value (corr.)	voxels
Animals > Tools				
R. middle occipital g./ Lat. occipital sulcus	51 -78 0	6.2	0.0	17
R. fusiform g.	39 -60 -21	5.2		5
Interaction: Tool-selective activation for Pictures > Words				
R. middle occipital g./ Lateral occipital sulcus	51 -78 0	>8.0	0.0	26
R. fusiform g.	45 -48 -27	5.8		22
	42 -57 -21	4.9		
R. sup. occipital sulcus	15 -102 9	5.7		5
R. inf. occipital sulcus	36 -84 -12	5.4		3
L. middle occipital g.	-45 -84 3	5.5		2

activation at p<0.05 (corr.); extent threshold > 1 voxel

Table 4. DCM Regions

Region	Co-ordinates
L. inf. frontal sulcus	-45 9 27
L. middle occ. g.	-30 -93 6
L. sup. temp. g.	-60 -15 3
L. medial fusiform	-27 -63 -12
L. anterior intraparietal sulcus	-60 -30 42

Table 5. Modulatory Effect on Forward and Backward connections

	Bilinear Effects	Connections	T-value df=21	p-value
Forward and Backward Bilinear Effects				
Forward	Tool Pictures - Tool Words	Occ => AIP	2.78	0.01
	Tool Pictures - Tool Words	Occ => FG	8.06	0.00
Backward	Tools	PF => AIP	7.31	0.00
	Tools	PF => FG	4.18	0.00
Dorso-ventral Dissociation of Bilinear Effects				
Forward	Tool Pictures - Tool Words	(Occ => FG) - (Occ => AIP)	3.3	0.00
Backward	Tools	(PF => AIP) - (PF => FG)	2.5	0.02

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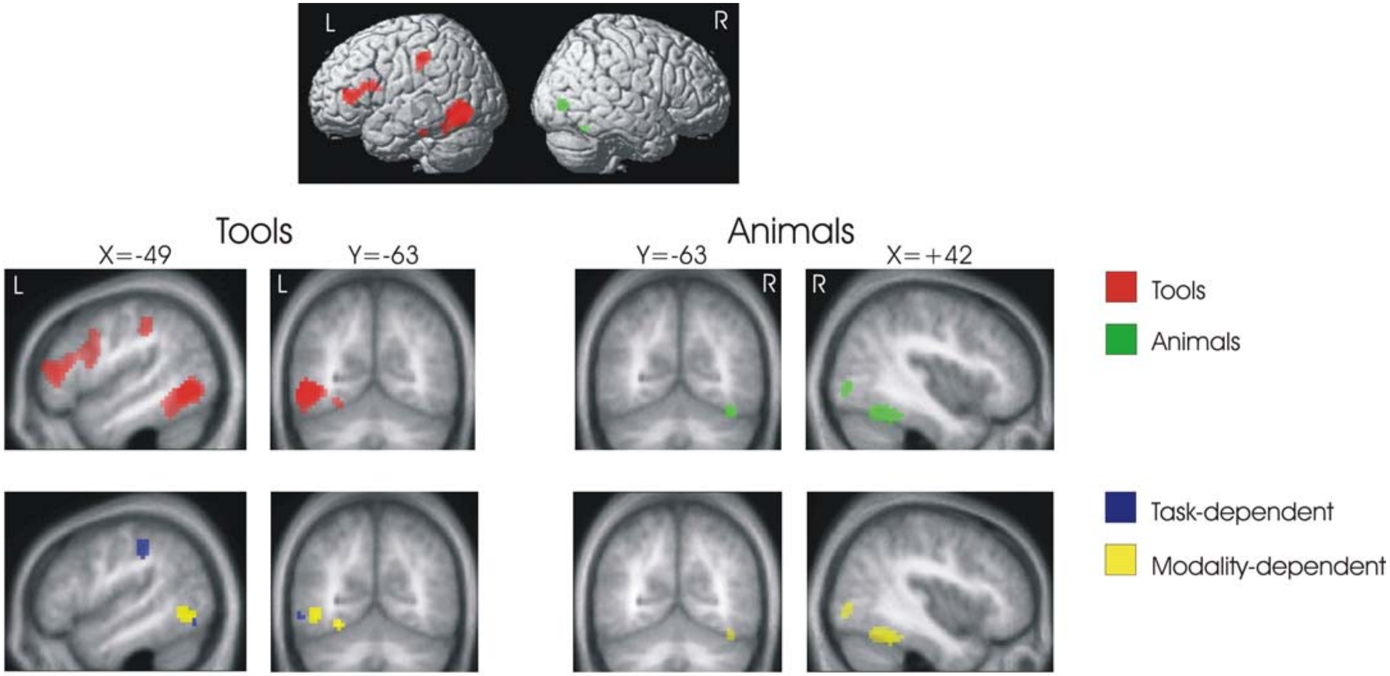
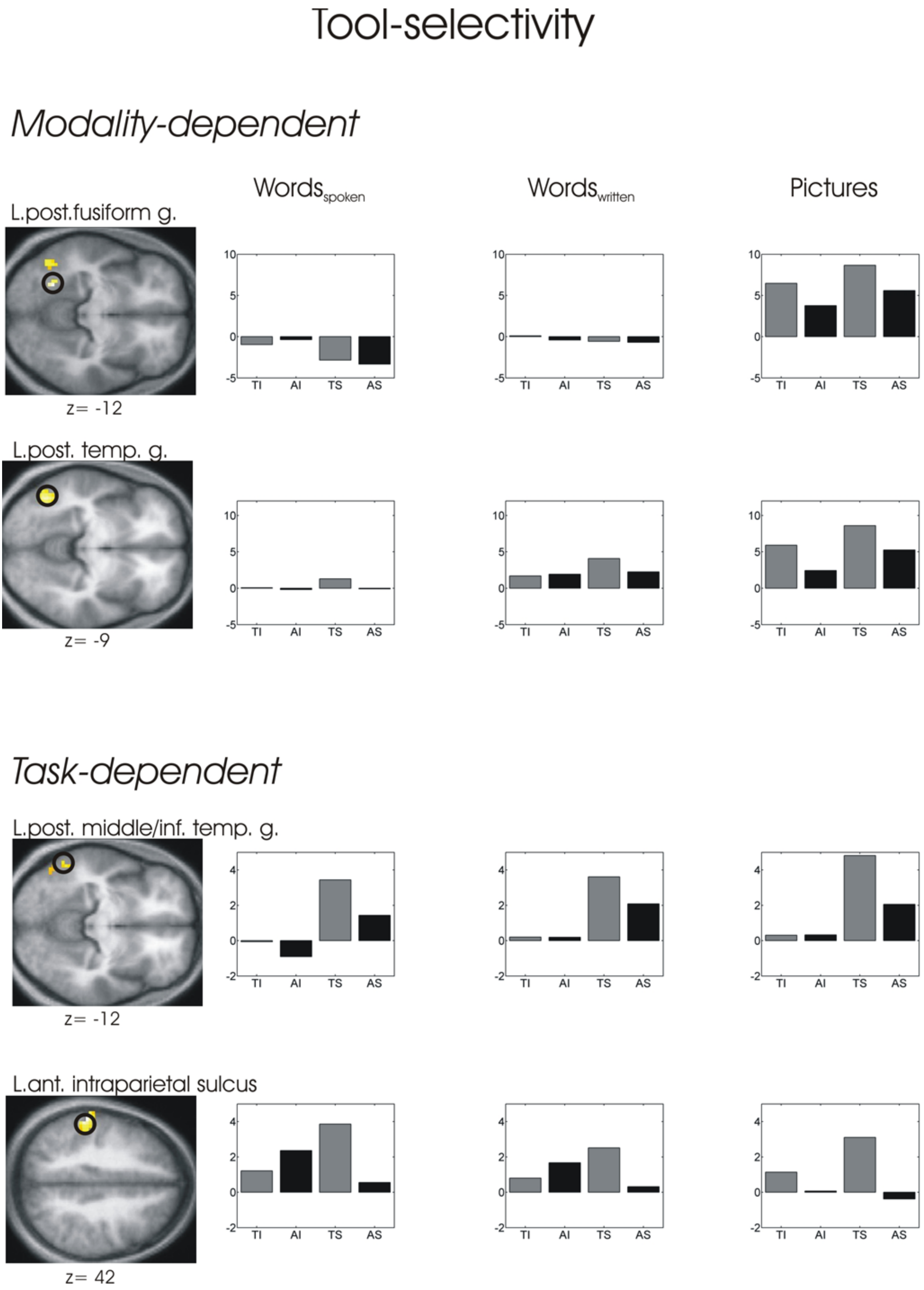

L
R
Tools
Animals
X=-49
Y=-63
Y=-63
X=+42
L
L
R
R
Tools
Animals
Task-dependent
Modality-dependent

Figure 1



Tool-selectivity

Modality-dependent

Task-dependent

Figure 2

Animal-selectivity

Modality-dependent

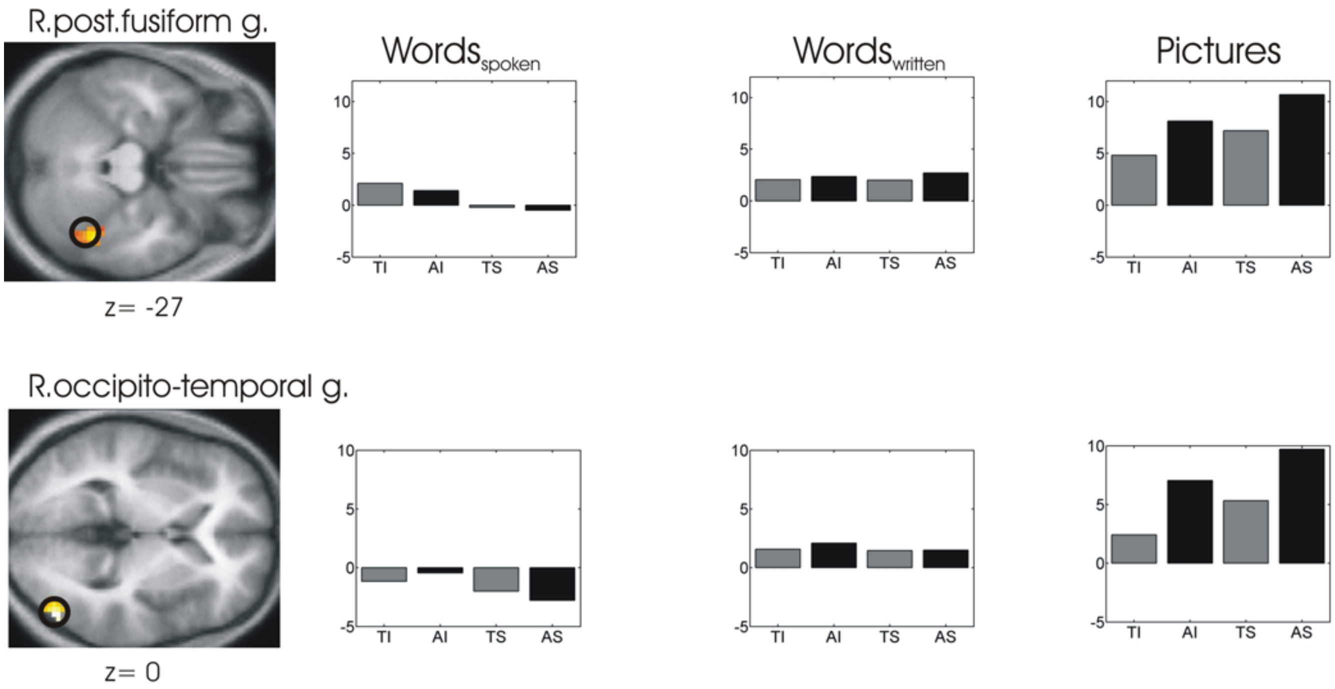


Figure 3

Dynamic Causal Model

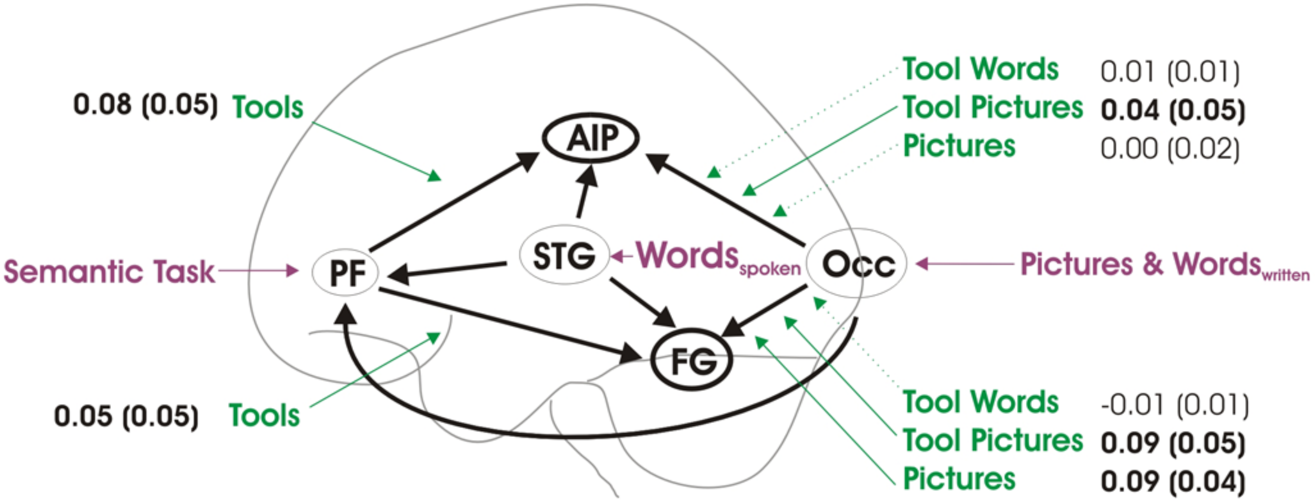


Figure 4