Neuroimaging studies of semantic memory: inferring "how" from "where"

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Abstract

For nearly two decades, functional neuroimaging studies have attempted to shed light on questions about the representation, organization, and retrieval of semantic knowledge. This review examines some of the major findings in this area. For example, functional neuroimaging studies have examined the extent to which there is a unitary semantic system or a series of multiple semantic subsystems organized by input modality, knowledge attribute, and/or taxonomic category. Additionally, functional neuroimaging studies have investigated the contributions of frontal cortex to semantic retrieval and selection. Collectively, these studies demonstrate that functional neuroimaging can offer more than neuroanatomical localization information; in addition, these studies offer new insights into longstanding questions about semantic memory.
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1. Introduction

Tulving first made the distinction between our general knowledge of concepts and facts, called semantic memory, and our specific memory for personal experiences, called episodic memory [105]. The information that one ate eggs and toast for breakfast is an example of episodic memory, whereas knowledge that eggs, toast, cereal, and pancakes are typical breakfast foods is an example of semantic memory. Some investigators (e.g. [24,58]) also include encyclopedic knowledge under the term semantic memory, such as the fact that Eggs Benedict are named for a regular patron of a Manhattan restaurant and not for Benedictine monks or Benedict Arnold. For the purpose of this review, however, the term semantic memory will be used synonymously with conceptual knowledge (i.e. excluding encyclopedic memory).

Investigations of the formation, representation, and organization of concepts have been central to the field of cognitive psychology over the past several decades (for a more thorough review, see [14]). In this review, several of the key questions to emerge from these investigations will be addressed. For example, one area of intense scrutiny in cognitive psychology has been the relation between conceptual knowledge and visual perception, and the extent to which these two processes share common mechanisms (e.g. [5]). Another active area of research has been the organization

and structure of semantic networks (e.g. [19]). For many years, investigations of these and related topics were largely conducted using classic behavioral methods, such as the examination of measurements of speed and accuracy in normal subjects, occasionally augmented by quantitative models of these phenomena and observations in patients with neurological impairments. However, the past 15 years has seen a resurgence of interest in the area of semantic memory, driven in part by the development of functional neuroimaging methods such as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI), which have been deployed to address some of these central questions about conceptual knowledge. In this review, I examine some of the contributions that functional neuroimaging has made to our understanding of semantic memory.

2. Organization of conceptual knowledge

2.1. Modality-specificity

Several of the early attempts to use functional neuroimaging to study semantic memory focused on the question of whether words and pictures are interpreted by a common semantic system. This question has its roots in the seminal work of Allan Paivio (e.g. [74]) describing a dual-code theory of mental representations, and it has been a central question in the study of semantic memory (e.g. [96]) ever since. In neuropsychological investigations of

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semantic memory impairments, striking dissociations have been noted between visual and verbal input modalities. For example, patients with optic aphasia are unable to name visually-presented objects; one hypothesis of this deficit is a disconnection between a visual-modality semantic store and a verbal-modality semantic store (e.g. [7]).

In one of the first PET cognitive activation studies, Petersen and colleagues examined differences between semantic retrieval with visual or auditory input [78]. Subjects either heard or saw concrete nouns (e.g. apple) and were instructed to generate an action word (e.g. eat) that was associated with each noun. Compared to a baseline word repetition task, semantic retrieval was associated with increased blood flow in the left inferior frontal gyrus (LIFG) for both visual and auditory presentations. Based on the similarity of activation across modalities, the authors concluded that prefrontal cortex activity reflects amodal semantic processing. Subsequent studies reached similar conclusions when comparing visual and verbal semantic processing [76,107]. For example, Vandenberghe and colleagues [107] reported that both words and pictures activated a common semantic system that was distributed throughout inferior temporal and frontal cortex. Few areas were uniquely activated by only pictures (left posterior inferior temporal sulcus) or only words (left anterior middle temporal gyrus and left inferior frontal sulcus). These studies provide evidence for a distributed semantic system that is shared by visual and verbal modalities.

2.2. Attribute-specificity

Evidence for a common semantic system for words (both auditory and visual) and pictures does not imply that there is a single semantic system. Many cognitive models have described conceptual knowledge representations that are composed of distinct parts. For example, Allport [1] described semantic memory (i.e. word meaning) as a distributed pattern across distinct attribute domains (e.g. visual elements, action-oriented elements, tactile elements, etc.). One must be clear to distinguish these attributes, which may be tied to a specific modality, from the input and output modalities that are used to access semantic memory (as described above). Throughout this review, the term "attribute" is used to describe the type of knowledge (e.g. knowledge about what an object looks like versus knowledge about what an object does) whereas the term "modality" is used to describe the form in which it is accessed (e.g. picture versus word).

The distinction between *visual* and *functional* attributes is the most common and perhaps also the most coarse division of semantic memory in the literature. Research in several diverse areas, from language acquisition (e.g. [37,70]) to object categorization (e.g. [87]) to language dysfunction (e.g. [111]), indicates that semantic knowledge may be usefully divided into visual attributes and functional attributes. Given that precedent, it was somewhat surprising when an early PET study failed to find evidence for a dissociation between visual and functional semantic knowledge [107]: similarity judgments either based on "meaning" (i.e. functional knowledge; e.g. coat goes with glove, not sock) or based on real-life size (i.e. visual knowledge; e.g. chisel goes with banana, not kite) activated temporal and frontal cortex. Apart from this study, neuroimaging studies have largely supported the visual/functional distinction. For example, Martin and colleagues [63] asked subjects to view line drawings of common objects and to report either an associated color or an action word. Analysis of the PET data collected during each task revealed common regions of activation in prefrontal cortex but distinct areas of activation in posterior areas. Specifically, color generation was associated with activity in ventral temporal cortex bilaterally, while action generation was associated with activity in the left middle temporal gyrus and Broca's area. Since this seminal study, a number of other investigators have reported neuroanatomical dissociations between visual and functional attributes [10,68,100], or between abstract and concrete words, which, by definition, differ with regard to visual knowledge [6,22] (but see [56]). The next two sections describe some of the principle neuroimaging findings relating to visual and functional semantic knowledge.

2.2.1. Visual semantic knowledge

One interpretation of the studies reviewed above is that our knowledge about the visual attributes of an object is represented differently from our knowledge of nonvisual attributes. This conjecture is related to a central debate in cognitive science about the extent to which any type of conceptual knowledge relies on perceptual representations, as opposed to propositional, amodal representations (for a review, see [5]). In recent years, cognitive neuroscientists have weighed in on this debate using functional neuroimaging to examine the relation between visual semantic knowledge and visual representations. One line of inquiry has focused on the task of explicit mental imagery, and the relationship between processes and neural systems supporting imagery and those supporting perception. Numerous neuroimaging studies have found activation in visual cortex during mental imagery (e.g. [17–40,86]), in extrastriate and occasionally primary visual areas (for a more in depth review, see [59]). We have taken a slightly different approach recently [53], in which we examined activation in visual association cortex during a property verification task (e.g. does a camel have a hump?). With no explicit imagery instructions, we observed activation in visual association cortex (i.e. left fusiform gyrus) only under conditions in which conceptual knowledge was required (i.e. not when the nature of the foils allowed for word association strength to be sufficient to make a correct response); this pattern indicates a specific reliance of conceptual knowledge on perceptual representations.

If one believes that knowledge of visual attributes depends on visual representations, then one might logically ask whether divisions that have been observed in visual perception exist in our representations of visual knowledge.

For example, it is well known that regions of cortex are specialized for form perception, color perception, and motion perception. Recently, investigators have used functional neuroimaging to probe for similar distinctions within semantic knowledge. In the remainder of this section, evidence for distinctions between visual attributes is reviewed.

2.2.1.1. Color.　When Martin and colleagues [63] reported activation of ventral temporal regions during retrieval of color knowledge, they noted the proximity of this region to areas involved in color perception. A subsequent study in which color knowledge and color perception were examined in the same group of subjects confirmed that color knowledge retrieval activated regions of ventral temporal cortex 2-3 cm anterior to regions active during color perception [16]. Unlike other regions activated during semantic retrieval tasks (e.g. inferior frontal gyrus), activation of left or bilateral ventral temporal cortex may be relatively specific to retrieval of color knowledge (e.g. in contrast to size knowledge, as discussed below [55]).

2.2.1.2. Size.　An early neuroimaging study that addressed retrieval of size knowledge found no differences between size judgments and function judgments [107]. This result is particularly interesting because several other studies have revealed strong evidence for dissociations between visual attributes and functional attributes, as reviewed above. An intriguing hypothesis to emerge from this finding is that knowledge of size is distinct from knowledge of other visual attributes, such as color, which is routinely dissociated from functional knowledge (e.g. [63]). The notion that size is distinct from other visual attributes has been suggested by some investigators, based in consideration of dissociations observed in patients with selective semantic memory deficits [20,92,94]. This hypothesis was explicitly tested in a recent PET study which found that size judgments, relative to color or sound judgments, activated medial parietal structures [55]. A speculative interpretation of these data is that knowledge of size depends, in part, on brain regions that subserve spatial processing, because determinations of size require determinations of location.

2.2.1.3. Form.　The evidence about the neural basis for knowledge of object form is somewhat indirect. Martin and colleagues [64] recently argued that regions of ventral temporal cortex, including the fusiform gyrus, are tuned to specific features of object form, based in part on evidence from fMRI studies that this region of cortex is organized by object category (e.g. [50,51]). However, these studies are quite different from other studies of attribute-specific knowledge because subjects were not required to retrieve information about form from memory. Consistent with their claims, Thompson-Schill and colleagues [100] found increased activity in the left fusiform gyrus when subjects were asked to answer questions about visual attributes of objects. Most of these questions were about form, although no direct comparison was made between knowledge of form and knowledge of other visual attributes. Some studies of patients with brain damage are suggestive of dissociations between color and form [66], but to date no neuroimaging studies have systematically made this comparison.

2.2.1.4. Motion.　As they did with form, Martin and colleagues [64] proposed that regions of lateral temporal cortex, specifically the left middle temporal gyrus, are tuned to features of object motion. One source of evidence for this hypothesis comes from studies using the action generation task, such as the one described above [63]. In this study, and in other studies of retrieval of action knowledge (e.g. [109,112]), activation was observed in the left middle temporal gyrus, anterior to the region associated with motion perception. Because of the coincidence of these locations, this posterior activation during action generation has been attributed to retrieval of motion knowledge (action generation is also associated with anterior activation, which is discussed below.) Kable and colleagues [52] examined the relationship between motion and action more directly, by examining fMRI signal changes in regions of lateral temporal cortex that respond to motion perception (human MT/MST) while subjects made semantic judgments about actions depicted in static pictures. Retrieving knowledge about actions, relative to objects, was associated with bilateral increases in activity in lateral temporal cortex. Similarly, Decety and colleagues [25,90] have reported increased activation in lateral temporal cortex in subjects who are imagining actions or who are observing semantically meaningful actions, and Kourtzi and Kanwisher [60] found that the response in these regions was greater during passive viewing of static photographs that implied motion (such as a photographs of a running athlete) than during passive viewing of similar photographs that did not imply motion (such as an athlete at rest).

2.2.1.5. Summary.　The notion that semantic memory, like perception, can be subdivided into types of visual information—color, size, form, and motion—is a relatively new idea, and the preceding review illustrates that we are still at the early stages of developing a clear account of the neural bases of visual semantic knowledge. At this stage the following conclusions can be made only tentatively, as many of the direct tests of these statements await further investigation: left or bilateral ventral temporal cortex appears to be involved in retrieval of knowledge of color and form, left lateral temporal cortex in knowledge of motion, and parietal cortex in knowledge of size.

2.2.2. Functional semantic knowledge

When the term "functional knowledge" has been used in the past, it often has been defined by exclusion. For example, the term has been used by some to denote any abstract property that is not physically defined (e.g. [93]); this type of definition has led some researchers to abandon the

term "functional" in favor of an equally nondescriptive term "nonvisual" (e.g. [100]). In contrast, the term has been used by others to denote an attribute that is physically defined, but by motor properties (e.g. how the object is manipulated) rather than sensory properties (e.g. [30,110]). It is this latter sense of functional knowledge that has been most clearly addressed by neuroimaging studies.

If one considers the ubiquitous action generation task to require the retrieval of functional knowledge, then there are numerous investigations that bear on the question of the relation of function and motor processing. Petersen and colleagues [78] first reported activation in left prefrontal cortex associated with retrieval of action words; this locus of activation appeared to be consistent with reports of verb retrieval deficits associated with left prefrontal lesions (for a review, see [35]). When Martin and colleagues [63] compared action generation and color generation, they found activation in this region during both tasks, which is inconsistent with the hypothesis that action generation is linked to motor cortex; however, few of the objects used in that experiment were actually manipulable, so it is possible that neither task was tapping motor representations. Subsequent support of the motor hypothesis of action knowledge was provided by Grafton and colleagues [43], who reported increased activation of left premotor cortex during retrieval of actions associated with tools. Grossman and colleagues [45] reported increased prefrontal activity (and lateral temporal activity) during semantic processing of verbs of motion (relative to verbs of cognition). Differences within premotor cortex have even been observed for actions that involve legs (e.g. walking) versus those that involve the face (e.g. talking) using EEG recordings [83]. Taken together with the results described above, these studies indicated that knowledge of actions is related to both motor systems and motion perception systems.

Just as studies of visual imagery are relevant to questions about visual semantic knowledge, so too are studies of motor imagery relevant to questions about functional semantic knowledge, insofar as functional semantic knowledge includes knowledge of action. Left premotor cortex is activated during imagined grasping [26,42] and during other imagined hand movements [99]. These findings parallel reports of neurons in monkey premotor cortex that are involved in the recognition of motor actions [85].

2.2.3. Summary
The evidence reviewed above is consistent with the following claims about the representation of semantic memory. First, semantic memory is not a unitary, undifferentiated system; rather, it is a collection of systems that are functionally and anatomically distinct. Second, semantic memory is not amodal: each attribute-specific system is tied to a sensorimotor modality (e.g. vision) and even to a specific property within that modality (e.g. color). Information about each feature of a concept is stored within the processing streams that were active during the acquisition of that feature. These findings are problematic for many current theories of semantic memory which represent concepts with amodal symbols [32,47,48,84] (for a review, see [95]) but are consistent with theories of sensorimotor representations of semantic memory (e.g. [1]). However, perhaps critically, results of neuroimaging studies also suggest a distinction between semantic processing and sensorimotor processing: studies which have directly compared semantic retrieval and perception have consistently found an anterior shift in activation during semantic processing (e.g. [16]). This systematic and often-overlooked shift ultimately may be quite important for theoretical accounts of the organization and representation of conceptual knowledge.

2.3. Category-specificity

Much of the evidence reviewed above has been used to support the hypothesized subdivision of semantic memory according to sensorimotor properties. A very different hypothesis has been championed by Caramazza and colleagues (e.g. [13]), largely on the basis of neuropsychological dissociations: a substantial body of data is consistent with the hypothesis that semantic memory is subdivided by taxonomic category. According to some accounts of this theory, evolutionary pressures produced categorically-organized brain systems that are dedicated to perceptually and conceptually processing certain classes of objects, such as animals, plants, and tools [13] (see also [36]). Although most of the evidence for this account comes from studies of patients with category-selective knowledge deficits, the interpretation of these deficits in not unequivocal (for a sample of the theoretical accounts of these deficits, see [12,49,91]).

Most of the neuroimaging studies that examine category-specific differences have used word retrieval tasks (e.g. verbal fluency, picture naming). Mummery and colleagues compared PET activation while subjects named exemplars of living (vegetables, fruits, land animals, sea animals) and nonliving (toys, clothes, tools, weapons) categories [69]; they reported increased activation in anteromedial temporal cortex for living things relative to nonliving things, and increased activation in left posterior temporal cortex for nonliving things relative to living things. Martin and colleagues [65] measured PET activity while subjects named pictures of animals and tools, and they reported differences between these two categories. Specifically, animal-naming was uniquely associated with activation of left medial occipital cortex, whereas tool-naming was uniquely associated with activation of left premotor and middle temporal cortex; both animal and tool naming activated regions of ventral temporal cortex (i.e. fusiform gyrus) bilaterally and left prefrontal cortex. In a subsequent fMRI study, this group reported multiple, small category-specific sites (for animals, tools, faces, and houses) in ventral temporal cortex that were likely not evident in their earlier PET study due to the limitations in spatial resolution [15]. Spitzer and colleagues [97,98] also reported small regions of category-specific

activity in frontal and temporo-parietal cortex during covert naming of natural (animals) and man-made (furniture and small household items) things. Although there were no consistent areas of category-specific activation across subjects, consistent activation was observed in one subject on two scanning dates. These findings were taken as evidence for category-specific semantic representations that are highly variable across subjects as a result of different life histories (and therefore different cortical maps). Damasio and colleagues [23,41] reported category-specific PET activation in the left hemisphere during naming of people (temporal pole), animals (middle portion of inferior temporal gyrus and medial occipital cortex), and tools (posterior portion of inferior temporal gyrus and premotor cortex). A similar category-specific organization was observed in patients with lesions to these regions [23]; however, these patients had anomia (i.e. word retrieval deficits) rather than semantic knowledge deficits. Thus, the evidence for category-specific representations in studies of verbal fluency and picture naming may reflect principles of lexical organization rather than semantic organization.

A few neuroimaging studies have examined category-specific differences with nonverbal tasks. Perani and colleagues [75,76] compared PET activation during same-different judgments about animals and tools. In one study they reported that tool judgments activated left frontal cortex (although not the same premotor region as reported elsewhere) but animal judgments were associated with no consistent locus of activation [75]. In a subsequent study, they identified common regions of activation for both pictures and words: across modalities, tool judgments were associated with middle temporal activation whereas animal judgments were associated with left fusiform gyrus activation [76]. Although this study might be seen as an improvement over strictly verbal studies, the extent to which semantic knowledge was required for these tasks is not known (e.g. their word task required matching two stimuli presented in different fonts, which is arguably non-semantic).

Only one experiment to date has directly contrasted category-specific and attribute-specific hypotheses [68]. In this PET study, subjects had to identify which of two words was more similar to a third target word on the basis of either perceptual (i.e. color) or functional (i.e. typical location) information; the three words were either living things (e.g. animals, vegetables, fruits) or nonliving things (e.g. musical instruments, vehicles, tools). With this fully crossed design, it was possible to compare the relative effects of category and attribute in a single experiment. Both category-specific effects and attribute-specific effects were observed; however, in contrast to some of the word retrieval studies described above (e.g. [65,69]), no regions were selectively activated during semantic judgments about living things relative to nonliving things. Based on this finding, the authors concluded that attribute-specific distinctions were more prominent neurally than category-specific distinctions.

When Warrington and colleagues initially proposed the idea that semantic knowledge was stored in modality congruent channels, they further claimed that the relative importance of information contained in these channels would vary across items. That is, one's knowledge of an object will typically comprise both visual and functional attributes, although not in equal proportions for all categories of objects. This further assumption, which is crucial for accounting for neuropsychological data with this theory, explains category-specific effects as an emergent property of interactive, attribute-specific systems (for a computational demonstration of this principle, see [30]). One explanation of category-specific activation in neuroimaging studies is that these differences reflect the differential weighting of visual and functional knowledge across categories (e.g. [65]).

Thompson-Schill and colleagues [100] sought physiological evidence for the assumptions that are necessary to produce emergent category-specificity in an attribute-specific semantic system. Specifically, we examined the prediction that an interactive, attribute-specific system (e.g. [30]) would yield the following pattern of results: for living things, retrieval of visual or non-visual information would require activation of visual representations, because of the disproportionate weighting of visual information in the representations of living things. For non-living things, no such dependence on visual knowledge should occur, and visual representations should therefore only be activated when explicitly required for the task (i.e. when answering questions about visual features). In other words, activation in areas involved in visual knowledge retrieval should be present during judgments about visual *and* non-visual attributes of living things but only during judgments about visual attributes of non-living things. This pattern was observed in the left fusiform gyrus [100], a region which has been linked to visual knowledge retrieval (as described above; e.g. [22]). These results lend credence to claims (e.g. [65]) that category-specific activations actually reflect attribute-specific representations (for a different interpretation of these data, see [11]).

In summary, although there are reports of category-specific activation in neuroimaging studies, the interpretation of these findings is somewhat controversial. First, the extent to which category-specific activations reveal the organization of semantic representations, as opposed to lexical (including phonological and orthographic) representations is unknown because most of the studies of category-specificity have been verbal. Second, it is not clear whether category-specific activations during semantic processing would be indicative of category-specific representations, given the potential for emergent category-specificity from attribute-specific representations. Those caveats aside, the most consistent category-specific findings have been activation of medial occipital cortex in response to animals and activation of lateral temporal and premotor cortex in response to tools; there may be other category-specific differences throughout
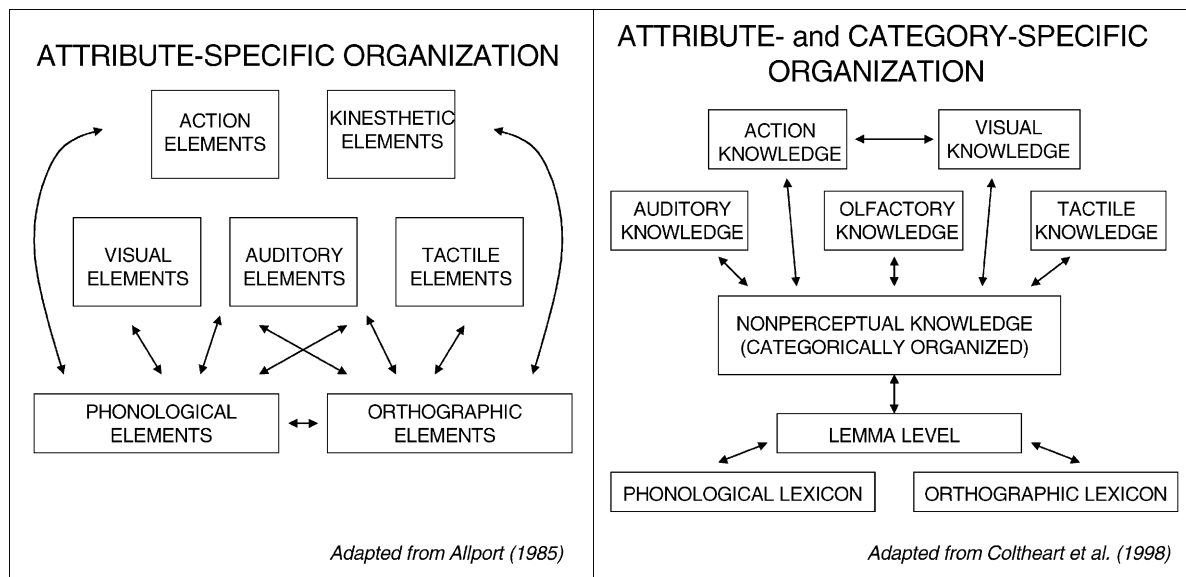
Fig. 1. Two distributed models of attribute-specific semantic knowledge. The figure on the left is adapted from Allport [1]. The figure on the right is adapted from Coltheart et al. [20]. Note that the latter model includes the addition of a nonperceptual knowledge system intermediate to sensorimotor representations and linguistics representations that is organized categorically.

temporal cortex, although these locations have not thus far been reliable across studies.

Finally, it is worth noting that evidence for category-specific representations does not necessarily refute the hypothesis that there are attribute-specific representations (and vice versa); it is possible that the organization of semantic representations has more than one governing principle. Coltheart and colleagues [20] have proposed that semantic knowledge is distributed across both sensorimotor systems which are not categorically organized and a nonperceptual system which is categorically organized; the relationship of a putative nonperceptual system to verbal knowledge may be critical for understanding the emergence of a categorically-structured representation. The fundamental difference between this distributed model of semantic knowledge and that of Allport [1] is the addition of this nonperceptual representation as an intermediary between perceptual (and motor) knowledge and language (see Fig. 1). The relationship of semantic knowledge to language, and the extent to which category-specific representations exist in either or both, should be the subject of future research.

3. Retrieval and selection of conceptual knowledge

The preceding discussion of the organization of semantic memory illustrated many types of specificity which have been observed in neuroimaging studies of semantic processing: modality-specificity, attribute-specificity, and category-specificity. Across all of these different studies, in addition to various activations that were specific to some feature of the task, two regions tended to be consistently activated irrespective of modality, attribute, or category: left

prefrontal cortex and ventral temporal cortex. For example, these regions were activated during semantic processing of both pictures and words [107], during generation of both actions and colors [63], and during picture naming of both animals and tools [65]. Thus, left prefrontal cortex and left (or bilateral) ventral temporal cortex are two promising candidate regions for a general-purpose semantic system (if one exists) for either the storage or retrieval of semantic knowledge.

The left inferior frontal gyrus (LIFG) was activated during semantic retrieval conditions in one of the first functional neuroimaging studies [78], and investigations of the role of this region in semantic processing have been central to discussion of the neural bases of conceptual knowledge ever since. Since this initial report, increased activity in LIFG has been replicated many times, not only during the verb generation task [63], but also during color generation [63], semantic classification [27,33,54], and semantic monitoring [28]. In a review of eight semantic retrieval studies, Buckner and Tulving [8] suggested that the activations related to semantic processing cluster at or near Brodmann's areas 44 and 45 in LIFG, although more recently, anterior and ventral regions of LIFG (Brodmann's area 47) have also been associated with semantic processing [80]. One ongoing area of investigation is whether there is a functional distinction between anterior and posterior divisions of LIFG with regard to their roles in semantic processing. Several early reports argued that anterior portions of LIFG play a differential role in semantic retrieval whereas posterior portions of LIFG are specialized for phonological processing (e.g. [80,81]). However, subsequent investigations that have examined phonological processing using nonwords (so that there is not concurrent semantic processing that may conflict

with phonological task demands) have reported comparable patterns of activation in anterior and posterior LIFG during semantic and phonological processing [4,38]. The precise nature of the differences between these two divisions, to the extent that functional differences exist, is still an open question. For the remainder of this section, LIFG will be used to refer to the region more generally, without specific reference to either anterior or posterior divisions.

One hypothesis for the role of LIFG in these various semantic processing tasks is that activity in this region reflects retrieval of semantic knowledge [106]. However, it is also likely that these tasks have in common other, non-semantic mechanisms that may be responsible for the observed prefrontal activity. Thompson-Schill and colleagues have proposed that LIFG is necessary for the selection of semantic information from competing alternatives and not semantic retrieval per se [101,102,104]. This hypothesis was motivated in part by the observation that naming pictures and making semantic comparisons do not consistently lead to LIFG activation, despite the prima facie involvement of semantic knowledge in these tasks (e.g. [112]), and in part by the absence of converging evidence from lesion studies for the necessity of LIFG for semantic retrieval. For example, Price and colleagues [82] described a patient with LIFG damage who was able to make semantic similarity judgments; a PET study of this patient revealed temporal, not frontal, activation associated with semantic processing.

We directly tested the hypothesis that LIFG is engaged by the selection of semantic knowledge from competing alternatives in three tasks: verb generation, object classification, and semantic comparison [101]. We selected three tasks that previously were used in neuroimaging studies: two which were associated with LIFG activity (verb generation and object classification) and one which was not (semantic comparison). We modified each task in order to manipulate selection demands, and then identified brain regions in which fMRI activity was modulated by these manipulations. Across all tasks, we found more activity in LIFG during the high selection condition than during the low selection condition (see Fig. 2, top panel); we subsequently demonstrated the necessity of LIFG for selection in a study of patients with lesions to this region (see Fig. 2, bottom panel), in which we showed a correlation between damage to posterior LIFG and selection-related errors on a verb generation task [104]. A recent study using a modified version of our verb generation task demonstrated that activity in LIFG reflects selection demands and not response conflict [3].

Theoretically, demands for selection that occur in a given task are orthogonal to demands for semantic retrieval. However, in most of the research on semantic processing, selection and retrieval have been confounded. Nearly all of the semantic retrieval tasks that have been studied (e.g. verb generation) have high demands for selection; notably, the few tasks that have lesser demands for selection (e.g. semantic comparisons) have not produced reliable increases in LIFG activity. Systematic manipulation of the demands
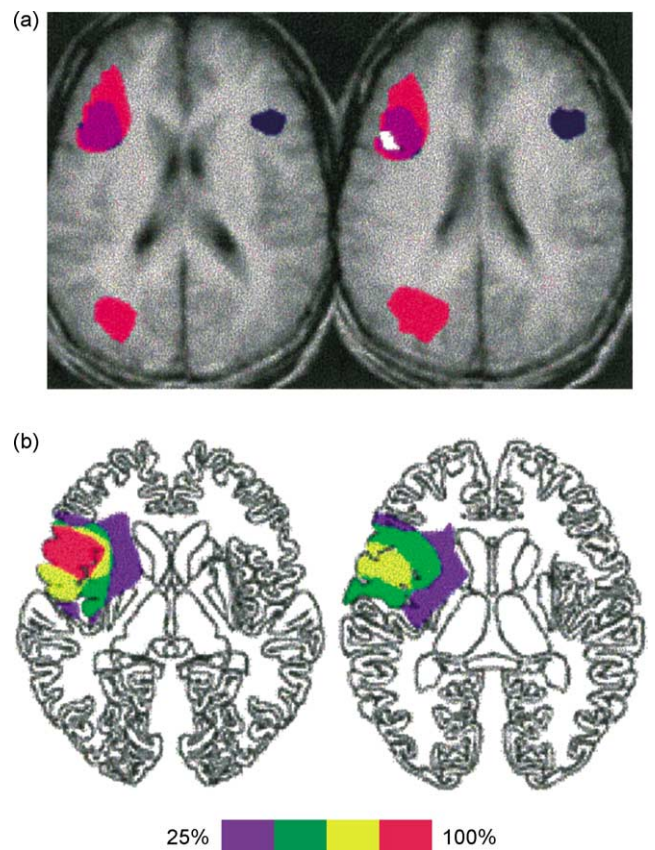

Fig. 2. The top panel indicates regions of selection-dependent activity in each of three semantic tasks (shown by different colors) and common to all three tasks (shown in white). Selection-dependent activity was observed in LIFG (pictured here) and anterior cingulate across all tasks. The bottom panel indicates lesion locations of patients who exhibited impairments on a high-selection verb generation task but normal performance on a low-selection verb generation task; the correlation between extent of damage in posterior LIFG and selection-related errors was 0.95 (adapted from [104]).

for selection (without a confounded manipulation of semantic retrieval) should result in the modulation of LIFG activity. In practice, it has proven difficult to unequivocally vary retrieval and selection demands independently. For example, Thompson-Schill and colleagues [101] compared global similarity judgments of three items with global similarity judgments of five items; we argued that this manipulation, which had no effect on LIFG activity, affected retrieval demands but not selection demands, in contrast to the clear effects of independent selection manipulations on LIFG activity. However, one might reasonably object to our assertion that our selection manipulation did not also affect retrieval demands, and vice versa (e.g. the high selection task may have required subjects to retrieve more detailed information about the items). Similarly, Wagner and colleagues [108] compared semantic judgments of strongly and weakly associated word pairs (e.g. candle-flame versus candle-halo); they argued that this manipulation, which modulated LIFG activity, affected retrieval demands but not selection demands. Again, one might disagree with the authors' claim
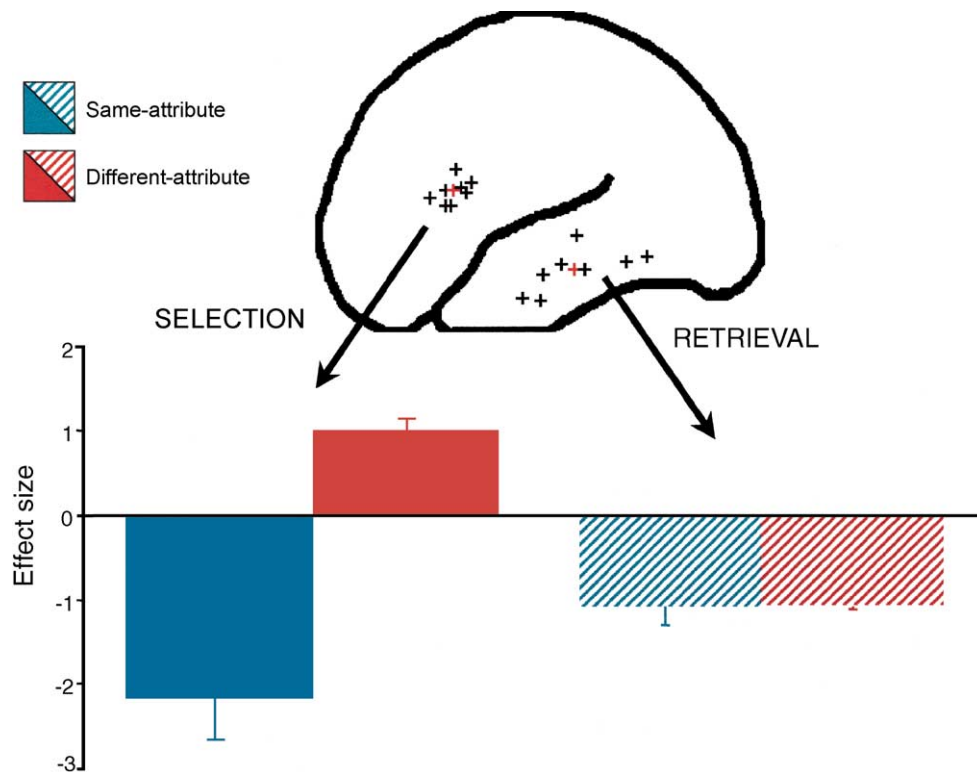
Fig. 3. Increased activity was observed in all subjects during covert word generation (compared to silent reading) in LIFG and left temporal cortex (collateral sulcus). The black crosses indicate the local maximum of activation for each subject in each region, projected on the lateral surface of the left hemisphere; the red cross indicates the average location of activation. The bar graph indicates the magnitude of the difference in activation between the first and second presentation of an item (negative numbers indicate less activation on the second presentation). In every subject, there was a decrease in activity relative to unprimed items in left temporal cortex during both same-attribute and different-attribute conditions. In contrast, there was a *decrease* in activity relative to unprimed items in the LIFG during same-attribute conditions, but an *increase* in the LIFG during different-attribute conditions (adapted from [102]).

that selection demands are not also affected by the manipulation of associative strength (e.g. weakly associated pairs have both related and unrelated features that are in competition).

These studies [101,108] illustrate the difficulty of teasing apart selection demands and retrieval demands. In a subsequent study, we took a different tactic to demonstrate that selection, and not retrieval, drives activity in LIFG. We used a word generation task with a repetition manipulation in order to dissociate the effects of selection and retrieval on prefrontal and temporal cortex [102]. By varying the type of attribute that subjects were asked to retrieve on each presentation of an item in a word generation task (i.e. same attribute on each presentation or different attributes), we were able to distinguish semantic retrieval demands from repetition demands. We found that left temporal cortex was sensitive to the effects of repetition of semantic retrieval whereas LIFG was sensitive to the effects of competition (see Fig. 3). This double dissociation observed here provides compelling evidence as to different functions that left prefrontal and left temporal cortex have in semantic memory.

Several other hypotheses have recently been proposed to account for LIFG activity that is observed during many semantic processing tasks. One alternative proposal is that

the LIFG is involved in temporary maintenance of semantic attributes in working memory [34]. Another alternative proposal is that LIFG reflects "controlled semantic retrieval" [108]. There are a number of similarities and differences between these hypotheses and the selection hypothesis discussed in detail above (for a more thorough discussion, see [2]). One key difference is that the selection mechanism proposed by Thompson-Schill and colleagues (see also [3,31]) is a potentially general purpose mechanism that is not specific to semantic processing, whereas proposals of semantic working memory or controlled semantic retrieval are clearly specific to semantic retrieval. One reason to favor a more general account is that numerous lines of evidence suggest that prefrontal cortex is not organized by stimulus content or domain but rather by processing type (for reviews of this literature, see [21,73]). Although many of these studies have compared visual and spatial forms of working memory, we have reported a similar lack of material-specificity in LIFG in a comparison of semantic and phonological processing [4].

Empirically, prefrontal cortex has been linked to context-sensitive responding in a variety of non-semantic domains, such as the ability to identify a color type instead

of reading a word (i.e. the Stroop task [77]), or even the ability to maintain fixation instead of making a saccade to a target (i.e. the anti-saccade task [46]). Recent theorizing about the role of prefrontal cortex on these tasks has frequently invoked mechanisms similar to the idea of selection described above. Cohen and Servan-Schreiber [18] argued that PFC enables context-sensitive responses, particularly when a response other than the prepotent one must be selected. A recent investigation of fMRI activity during a modified Stroop task revealed that different regions of PFC respond to different types of selection: the authors distinguished between response selection and non-response selection, and linked the latter to LIFG [67]. Kimberg and Farah [57] characterized the role of PFC in cognition as mediating the selection of action by the weighting of information in working memory. When the contents of working memory overwhelmingly support one action, then demands on PFC are low; demands on PFC will be high in any task that requires selection among competing sources of information in working memory to guide a response. Several recent working memory studies critiqued a widely-held opinion that dorsolateral prefrontal cortex is involved in the maintenance of information over delays by providing evidence that regions of prefrontal cortex subserve the selection of competing information from working memory [88,89]. We recently tested the idea that selection and maintenance can be dissociated in a study of memory deficits in brain-damaged patients, and argued that selection from working memory is an LIFG function [103]. Norman and Shallice [72] proposed that prefrontal cortex supports a supervisory attentional system that permits the modulation of routine processing (i.e. contention scheduling) by activating or inhibiting other representations; in more recent work, Shallice and colleagues have argued that left prefrontal cortex is involved in the selection of semantic attributes as a way of "sculpting" the response space through the processes of selection and inhibition [31]. Together, these studies support the hypothesis that selection of information from competing alternatives is a general function of prefrontal cortex; various theoretical accounts converge on the idea that prefrontal cortex functions to bias, filter, or modulate posterior representations of information in certain contexts or situations.

In summary, despite the preponderance of semantic memory tasks that are associated with activation in LIFG across different modalities, attributes, and categories, it appears unlikely that LIFG is the locus of a general purpose semantic processing or retrieval mechanism. As mentioned above, the remaining candidate would seem to be ventral temporal cortex. Like LIFG, ventral temporal cortex is activated in nearly all studies of semantic processing, seemingly regardless of task factors such as modality or stimulus category. In contrast to LIFG, activity in this region appears to be sensitive to retrieval demands and not competition or selection demands [102]. While ventral temporal cortex does appear to be involved in the storage and retrieval of semantic knowledge, it appears to be highly structured (although variable across subjects). As reviewed above, multiple category-specific sites have been reported throughout the ventral region of the posterior temporal lobes, often bilaterally [15]. Based on these and related data, Martin and colleagues have proposed that ventral temporal cortex is organized according to clusters of object features [51,62]. Thus, neither LIFG nor ventral temporal cortex seem a likely site for a general semantic retrieval mechanism, leading one to question whether such a mechanism exists.

4. Conclusions and future directions

The search for the neuroanatomical locus of semantic memory has simultaneously led us nowhere and everywhere. There is no compelling evidence that any one brain region plays a dedicated and privileged role in the representation or retrieval of all sorts of semantic knowledge. Prefrontal cortex (specifically, LIFG) is likely to be involved in a more general purpose selection mechanism that may be useful but that is not necessary for semantic retrieval. No other part of cortex is consistently activated across all semantic retrieval tasks. Rather, the neuroimaging studies reviewed here suggest a large, distributed network of semantic representations that are organized, at a minimum, by attribute, and perhaps additionally by category. These networks include extensive regions of ventral (form and color knowledge) and lateral (motion knowledge) temporal cortex, parietal cortex (size knowledge), and premotor cortex (manipulation knowledge). Other areas, such as more anterior regions of temporal cortex, may be involved in the representation of nonperceptual (e.g. verbal) conceptual knowledge, perhaps in some categorically-organized fashion. Crucially, there is no evidence for some common, amodal semantic system that would serve to integrate or combine information across all of these different systems; this suggests that the coherence of conceptual knowledge across different attributes and modalities reflects interactions across a highly distributed system.

Numerous questions still await additional exploration to further develop theories about the representation and organization of semantic memory and the neural systems that support these processes. A nonexhaustive list of remaining issues includes: (1) What is the relation of semantic knowledge to language? For example, is a putative "nonperceptual knowledge system" [20] better viewed as a conceptual or a linguistic system? (2) What is the relation of attribute-specific semantic knowledge to perception (and motor) systems? Many studies have reported attribute-specific activation in regions that are *near* the regions that support perceptual (or motor) processing of that attribute. Consistently, these semantic regions are more anterior than their primary sensorimotor counterparts (e.g. [63]). Does this anterior shift represent a process of abstraction away from original sensory features? (3) Are category-specific representations limited to abstract

or symbolic linguistic systems or do they also exist in non-linguistic, conceptual knowledge systems? (4) What is functional knowledge? What is the relation of functional knowledge to motion and manipulation, and are there other types of functional information that are not readily explained by these sensorimotor systems (e.g. [9])? (5) Why do most studies of attribute-specific semantic processing report unilateral (left hemisphere) activation when the original sensorimotor encoding of these attributes is most likely a result of bilateral processing? What is the role of the right hemisphere in semantic processing? (6) How automatic is activation of attribute-specific conceptual knowledge, or how subject is it to manipulation by task demands (e.g. [44])? Does the automaticity of activation vary between different semantic attributes or categories, or some interaction between the two? (7) What is the origin of subsystems of semantic knowledge? What are the effects of early experience (or deprivation) on the resulting organization and representation of semantic information?

Finally, a cautionary note: this review is not meant to be an exhaustive account of the extensive literature of semantic memory. In writing this summary, I have largely resisted the urge (with an occasional exception) to include studies of semantic memory that make use of methods other than functional neuroimaging, such as investigations using brain-damaged patients, ERP recordings, or computational modeling to address important questions about the structure of semantic knowledge. To do these areas justice would fall beyond the scope of this special issue on neuroimaging of memory.[1] Rather, this review was intended to provide a snapshot of the current state of theorizing about semantic memory, insofar as it has been guided by the emergence of functional neuroimaging as a method for observing dynamic changes in the normal brain. These neuroimaging techniques are widely lauded for their ability to localize with fine spatial resolution physiological changes correlated with cognitive processing. In this review, I have tried to demonstrate that beyond simply localizing processes related to semantic memory, functional neuroimaging studies have provided us with some answers (and many more questions) about the representation, organization, and retrieval of semantic knowledge.

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