

Lateral Inferotemporal Cortex Maintains Conceptual–Semantic Representations in Verbal Working Memory

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Abstract

■ Verbal working memory, that is, the temporary maintenance of linguistic information in an activated state, is typically assumed to rely on phonological representations. Recent evidence from behavioral, neuropsychological, and electrophysiological studies, however, suggests that conceptual–semantic representations may also be maintained in an activated state. We developed a new semantic working memory task that involves the maintenance of a novel conceptual combination. Functional magnetic resonance imaging data acquired during the maintenance of conceptual combinations, relative to an

item recognition task without the possibility of conceptual combination, demonstrate increased activation in the posterior left middle and inferior temporal gyri (known to be involved in conceptual representations) and left inferior frontal gyrus (known to be involved in semantic control processes). We suggest that this temporo-frontal system supports maintenance of conceptual information in working memory, with the frontal regions controlling the sustained activation of heteromodal conceptual representations in the inferior temporal cortex. ■

INTRODUCTION

Working memory (WM) is a cognitive system responsible for the temporary maintenance and manipulation of behaviorally relevant information. Within this system, verbal WM is the subset of mechanisms dealing with spoken or written linguistic information. The most prominent theory of WM, the multicomponent model (e.g., Baddeley, 2003; Baddeley & Logie, 1999), postulates that the short-term maintenance of verbal information relies exclusively on phonological information, that is, on the rehearsal of the sound structure of the verbal material. This system for verbal WM maintenance consists of a capacity-limited short-term store for phonological representations and a subvocal articulatory rehearsal system that continuously refreshes the decaying contents of the passive store.

In contrast to this postulate, numerous findings suggest that verbal WM can maintain lexical and semantic information as well. It has long been known that short-term memory for words is better than for pronounceable nonwords (Schweickert, 1993; Hulme, Maughan, & Brown, 1991; Brener, 1940) and that high-frequency

words are better remembered than low-frequency words (Roodenrys, Hulme, & Lethbridge, 2002; Hulme et al., 1997; Roodenrys, Hulme, & Alban, 1994). These findings suggest that, in addition to phonological codes, information about the *lexical* status and about the organization of word representations in the mental lexicon influences verbal WM. Similarly, lists of concrete words are better recalled from WM than lists of abstract words (Bourassa & Besner, 1994), suggesting that *conceptual–semantic* information also contributes to verbal WM. This is also supported by neuropsychological studies showing that patients can be selectively impaired either on phonological or semantic WM tasks (e.g., Martin & Romani, 1994; Martin, Shelton, & Yafee, 1994).

The involvement of nonphonological representations in verbal WM is consistent with procedural models of WM (e.g., Crowder, 1993) that argue against the existence of special-purpose modules dedicated to the short-term storage of specific types of information, such as the phonological store. Procedural models, on the contrary, postulate that the same brain systems involved in perceptual processing and the primary analysis of the to-be-maintained materials are involved in the short-term maintenance of these stimuli (Fuster, 1995; Crowder, 1993; Monsell, 1984). For example, in neurophysiological studies of monkeys, color-selective neurons of the inferotemporal cortex are involved in the active maintenance of that color in delayed matching-to-sample tasks (Fuster &

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Jervey, 1981; see Ranganath, DeGutis, & D'Esposito, 2004; Druzgal & D'Esposito, 2001; Courtney, Ungerleider, Keil, & Haxby, 1997, for converging evidence from human neuroimaging). The procedural model of WM has been further articulated by Ruchkin, Grafman, Cameron, and Berndt (2003). Relying primarily on evidence from electrophysiological studies, these authors claim that posterior brain systems involved in language processing provide the representational basis for verbal WM, and that prefrontal attentional mechanisms maintain posterior language representations at an activated level during a brief delay (see also Miller & D'Esposito, 2005; Curtis & D'Esposito, 2003).

To summarize, the proposal that conceptual–semantic representations can be maintained in verbal WM receives support from behavioral and recent electrophysiological studies. In addition, the hypothesized neural mechanism, that is, the prefrontally controlled activation of conceptual–semantic representations in the posterior cortex in the absence of language input (Ruchkin et al., 2003), is consistent with the neurophysiological studies cited above. However, the proposal of interest has not been directly tested in neuroimaging experiments that focus on conceptual–semantic aspects of language. Three recent brain imaging studies aimed to identify mechanisms of semantic WM. The results, however, are mixed. Martin, Wu, Freedman, Jackson, and Lesch (2003) compared delayed synonym judgments with delayed rhyme judgments, and found no activation differences. Shivde and Thompson-Schill (2004), however, report increased activation for maintenance of a single word in a delayed synonym task relative to a phonological task, in predefined regions of interest in the inferior frontal gyrus and in the middle temporal gyrus. A further study focused on the role of categorical information in verbal WM representations using a task in which participants continuously judged category relatedness between words maintained in memory and a list of subsequently presented words (Crosson et al., 1999). During the performance of this task, posterior left inferior temporal and anterior left inferior frontal regions were activated. These activations, however, did not differ reliably from activity elicited in a phonological task. In addition, this task does not specifically map the neural correlates associated with the retention of semantic concepts in WM, but rather the continuous activation and comparison of higher-level semantic information (i.e., category membership).

One possible reason why previous research has not provided stronger evidence for the maintenance of conceptual–semantic representations in WM is that the tasks used in these studies have not required the maintenance of sufficiently rich semantic representations. Judging whether a probe word is a synonym of a target word, or an instance of a target category, may require accessing only a limited portion of the words' semantic representation. To provide a more semantically demanding task, in the present study we presented participants

novel conceptual combinations, such as “tomato-not-ripe,” which participants had to briefly maintain and then decide whether a probe word named an emergent property of the combination, such as “green.” Correctly responding to such probes requires one to perform some semantic computations on the constituent words—“not,” “ripe,” and “tomato”—and use the composite to answer the probe question. Presumably, participants will create the composite during encoding, and be motivated to maintain it in an active state during the retention interval, rather than maintaining it in phonological form and reperforming the semantic computations at retrieval. Indeed, some of us have recently provided behavioral (priming) evidence that the semantic computations in question are performed on-line as the constituent words are presented (Swinney, Love, Walenski, & Smith, 2007). Thus, this semantic WM task required the semantic composition of the three memory words and maps brain regions involved in retaining the emergent meaning in WM over a delay interval of 7.5 sec in order to answer the probe question (Figure 1). Importantly, the emergent properties used as probe words were carefully pretested in order to assure that they were not directly related in a semantic-associative way with any of the three words in the memory set.

Brain regions specific to semantic WM maintenance are hypothesized to be located in the left temporal and left frontal cortex. With respect to the temporal lobe, it is well known that left posterior temporal regions (often subsumed under the label Wernicke's area) are involved in semantic aspects of sentence comprehension, such as integrating distinct lexical items into semantic propositions and concepts (e.g., Friederici, Ruschemeyer, Hahne, & Fiebach, 2003; Hillis et al., 2001). Left anterior inferior frontal areas have been associated with strategic or controlled processes operating upon semantic knowledge (e.g., Poldrack et al., 1999; Fiez, 1997) and with a semantic WM circuit for current task performance (Gabrieli,

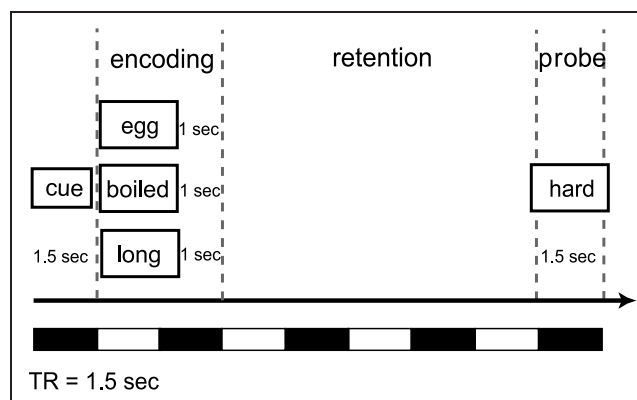


Figure 1. Working memory paradigm. A schematic of the order of events in experimental trials of the semantic WM task and the item recognition task. Overall trial length was 21 sec, that is, 14 images of TR = 1.5 sec. (Repetition time is displayed by black and white boxes at the bottom of the figure.)

Poldrack, & Desmond, 1998). We therefore hypothesized that temporal and inferior frontal regions of the left hemisphere should be more strongly activated for semantic WM relative to nonsemantic verbal WM rehearsal.

METHODS

Participants

Twelve native speakers of German (6 women; mean age = 25 years) participated after giving informed consent. All participants were undergraduate students at the University of Leipzig, had normal or corrected-to-normal vision, were without known history of psychiatric or neurological diseases, and were right-handed according to the Edinburgh Handedness Inventory (Oldfield, 1971). Data from two further participants were excluded from the analysis due to excessive head motion.

Materials and Procedure

Each WM trial consisted of a word triplet that had to be maintained, followed by a probe word. Word triplets were presented visually (1 word/sec) in light gray letters on a black background. The probe word was presented for 500 msec after a 7.5-sec retention interval (Figure 1). Responses were registered during a period of 2.5 sec following probe word onset. The response period was followed by 7.5 sec intertrial interval. Forty items were presented per condition in pseudorandom sequence. The functional magnetic resonance (fMRI) experiment was conducted in an event-related single-trial design (Burock, Buckner, Woldorff, Rosen, & Dale, 1998). Each trial was preceded by a 1.5-sec one-letter cue indicating which task had to be performed. For the semantic WM task, items were constructed such that each triplet formed a relatively novel conceptual combination (e.g., “tomato not ripe”), which had associated with it an emergent property (“green”). Items were selected from a larger pool based on pretesting. During pretesting, independent participants ($n = 15$; mean age = 24.9 years; 8 women) freely produced up to four associates for each memory and probe word in the item pool. No items were included in which there were direct semantic associations produced among words in the memory set or between memory and probe words. A second group

($n = 13$; mean age = 25.2 years; 5 women) was asked to freely generate up to three properties that came to their mind when reading each word triplet. The items selected to be positive probes in the fMRI study were those with a high rate of spontaneous productions. Care was taken to ensure that word triplets did not consist of short sentences. Words had between one and three syllables; word triplets varied in length between four and eight syllables.

To control for the possibility that participants, nonetheless, also retained items based on phonological and lexical codes rather than solely through conceptual–semantics, a second WM task was used. In this task, participants were presented with three unrelated words in the encoding phase, one of which could appear as a probe in the test phase (i.e., a classical item recognition task that involved maintenance based on lexical and phonological but not conceptual–semantic codes). The items for this task were chosen such as to discourage the possibility of conceptual combination. Word triplets for the item recognition control task consisted of either three nouns or of three adjectives or noun/adjective (e.g., see Table 1), noun/past participle or noun/adverb adjective combinations. The absolute number of words from the open and the closed class in the item set for the item recognition task was matched to the semantic WM task. The word stimuli in the item recognition task condition were also matched in length to those of the semantic WM condition [mean number of letters per item: semantic task, 18.15; item recognition task, 18; control task (see next paragraph), 18.15; $F(2, 117) = 0.025$, $p > .95$]. For the yes/no decisions in the two WM conditions, on half the trials the probe word was exchanged for an unrelated word (in the case of the semantic condition) or a word not included in the memory set (in the item recognition task).

In addition, a perceptual–motor control task without memory demands was administered, controlling for the perceptual and motor components of the WM tasks. Control task items consisted of three strings of repeated letters (see Table 1). Participants were instructed to not memorize the letters. After the delay period (during which participants were instructed to not actively maintain the three letter strings), participants were presented with a probe and judged whether or not there was an additional space between the letters, which was the case

Table 1. Example Stimuli

Task	Memory Set	Probe Word	Response
Perceptual–motor control task	XXXX XXXXX XXX	X X X X	yes
Item recognition task	Glas Zweig Meer (glass branch sea)	Zweig (branch)	yes
Semantic working memory task	Ei lange gekocht (egg boiled long)	hart (hard)	yes
	Tomate nicht reif (tomato not ripe)	gelb (yellow)	no

in 50% of the trials (Table 1). Half of the letter strings were presented in upper case and half in lower case. Letter strings were matched in length between the three tasks on an item-for-item basis.

fMRI Data Acquisition and Analysis

Hemodynamic responses were measured using a Bruker 30/100 Medspec 3-Tesla scanner. Twenty-one sagittal slices (5.1 mm thickness, 1 mm gap) were acquired using a BOLD-sensitive gradient-echo, echo-planar imaging sequence (repetition time/TR = 1.5 sec; echo time/TE = 30 msec; acquisition bandwidth = 100 kHz; field of view = 192 mm; data matrix = 64×64 ; resulting in-plane resolution = 3×3 mm). T1-weighted modified driven equilibrium Fourier transform (MDEFT) structural images were obtained for coregistration with previously acquired whole-head 3-D MDEFT brain scans. All analyses were carried out with the LIPSIA software package (Lohmann et al., 2001). Preprocessing involved a two-dimensional movement correction with two translational and one rotational parameter, using the linear correlation coefficient as a matching metric and applying Powell's optimization method to find the best match. A temporal interpolation correcting for slice acquisition time differences, baseline correction, and spatial smoothing (Gaussian kernel of 9 mm full width at half maximum [FWHM]) were applied. Subject-specific statistics were conducted in native space. For group analyses, resulting contrast images were linearly normalized into Talairach and Tournoux (1988) space, resampling voxels to $2 \times 2 \times 2$ mm. Statistical modeling consisted of an individual fixed effects model for each participant followed by a group analysis treating participants as random effects. Design matrices were generated using a synthetic hemodynamic response function (Friston et al., 1998; Josephs, Turner, & Friston, 1997). The model equation was convolved with a Gaussian kernel of dispersion of 4 sec FWHM. Each trial phase (i.e., encoding, retention, retrieval) of each condition was modeled with an individual vector of onsets. A more detailed description of how trial phases were modeled, in two different analyses, is given with the description of the results. During parameter estimation, low-frequency signal components were treated as confounds. For each participant, contrasts were calculated based on linear combinations of parameter estimates of the general linear model representing the retention period of the WM tasks. For group analyses, individual contrast images were submitted to a one-sample *t* test, testing at each voxel whether contrast values reliably differ from zero. Statistical parametric maps were thresholded at $p < .001$ (uncorrected at the voxel level). To protect against false-positive results, only clusters are reported whose size is significant at $p < .05$ after correction for multiple comparisons according to the theory of Gaussian random fields (i.e., that have $k > 110$ voxels of size $2 \times 2 \times 2$ mm; Kiebel, Poline, Friston, Holmes, & Worsley, 1999; Worsley

et al., 1996). This restricts significant clusters to a size of at least 880 mm³.

For an additional parametric analysis of the influence of behavioral difficulty on brain activation, contrast images representing the comparison of semantic WM retention versus the item recognition task were modeled as a single covariate, and each participant's difference in accuracy and response time between the semantic WM task and the item recognition task, normalized by the group mean, were introduced as regressors. Activation results are displayed on a brain from the Max Planck Institute's database chosen on the basis of its clear and representative anatomy of the left inferior frontal gyrus, which has been used for display in previous language-related studies.

RESULTS

Behavioral Data

All three tasks (perceptual-motor control, item recognition task, and semantic WM) were performed without great difficulties by the participants. This was reflected in the high percentage of correct responses [control task: 97.5% (*SEM* = 0.92); item recognition task: 98.5% (*SEM* = 0.57); semantic WM: 95.4% (*SEM* = 0.86)]. However, accuracy did differ between the three conditions [$F(2, 33) = 4, p < .05$] as participants gave significantly fewer correct answers in the semantic WM than the item recognition task [$t(11) = 4.1, p < .002$], whereas the item recognition task did not differ significantly from the control task [$t(11) = -.96, p = .36$]. Response times also varied significantly between conditions [$F(2, 33) = 5, p < .05$; control task: 770 msec (*SEM* = 41.6); item recognition task: 854 msec (*SEM* = 46.5); semantic WM: 984 msec (*SEM* = 54.7)]. The control task was performed significantly faster than both WM conditions [both $t(11) > 3.5, p < .005$], and the item recognition task was performed faster than the semantic WM task [$t(11) = 5.5, p < .001$].

Functional Imaging Data

fMRI data representing activation from the retention period of the two WM tasks were analyzed in two steps. First, brain activation during the retention period of the item recognition task was compared to the perceptual-motor control task, so as to demonstrate that the present paradigm, indeed, elicited brain activation as typically reported for verbal WM tasks. For this analysis, the three component periods of a WM trial—encoding, retention, and retrieval—and the corresponding periods of the case judgment control task were modeled as epochs of length 3 sec (encoding), 7.5 sec (retention), and 1.5 sec (retrieval). More specifically, these epochs were modeled by convolving boxcar functions of the specified lengths with a canonical hemodynamic response function. This approach has been used repeatedly to

map retention period activity in the brain (e.g., Courtney, Petit, Maisog, Ungerleider, & Haxby, 1998), but is prone to a possible confound with encoding or retrieval activity due to colinearity between covariates (e.g., Zarahn, Aguirre, & D'Esposito, 1997). For the first stage of our data analysis, we chose this approach because it has the greatest possible power for detecting activity related to WM maintenance. As Figure 2 demonstrates, maintenance of words based on phonological and lexical, but not conceptual–semantic codes in the item recognition task, elicits activation in a predominantly left hemispheric system of brain regions, including the posterior inferior frontal gyrus (Broca's area), the premotor cortex, and the temporo-parietal junction area, as well as the medial premotor cortex and the right cerebellum. These activation effects are as expected for a verbal WM task that relies primarily on the rehearsal of phonological information (e.g., Smith & Jonides, 1997, 1998, 1999).

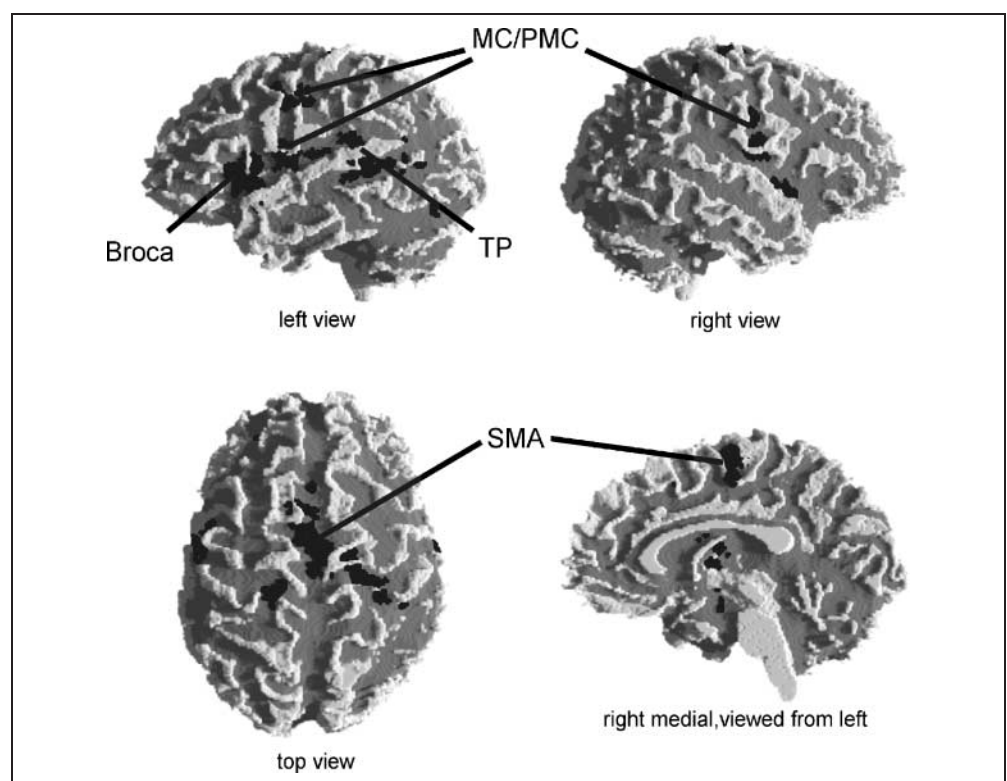
In order to identify significant activation differences between the retention period of the semantic WM task and the item recognition control task, we then conducted a second independent analysis of the same dataset. In this analysis, we used a different strategy to assess fMRI signals attributable to the retention period of delayed response tasks (Postle, Zarahn, & D'Esposito, 2000; Zarahn et al., 1997). Encoding and retrieval period activity was modeled as before. Retention period activity was represented by a single impulse response function convolved with a canonical hemodynamic response function that was placed in the middle of the retention pe-

riod, that is, at the third of five acquired images. This approach is more conservative, as fewer observations contribute to retention period activity and part of the retention period is now implicitly treated as baseline. However, this approach reduces the likelihood of a statistical confound between retention period activity and encoding or retrieval period activity (Zarahn et al., 1997); activity detected using this approach has a greater likelihood of actually reflecting retention-related brain activation.

As Figure 3 demonstrates, the only area that was significantly more active for semantic WM relative to the item recognition task is in the posterior inferior temporal lobe [BA 37; $t(11) = 7.04, p < .001$; size = 154 voxels; corrected cluster-level significance $p = .015$; $x = -51, y = -46, z = -5$]. More specifically, this activation cluster has an activation peak in the left inferior temporal sulcus and extends both into the middle temporal gyrus and the inferior temporal gyrus, and will be referred to as MTG/ITG in what follows. Post hoc analyses of MTG/ITG activity did not differ significantly between the item recognition task and the control task [$t(11) = 1.3, p = .23$]. Furthermore, MTG/ITG activity was significantly greater during the retention of semantic information, both compared to the control task [$t(11) = 4.4, p = .001$] and to the item recognition task [$t(11) = 6.2, p < .0001$; one-way analysis of variance with factor task: $F(2, 33) = 5.3, p = .01$].

Previous studies of semantic WM primarily focused on the left inferior prefrontal cortex by using predefined

Figure 2. Brain activation during the item recognition task. Brain activation for the retention period of the item recognition task relative to the perceptual–motor control task. Brain activation was rendered onto a white matter segmentation in which sulci were filled, to facilitate the display of activation in the depth of the sulci. For purposes of display, the statistical map was thresholded at $Z > 3.09$ ($p < .001$, uncorrected). Broca = Broca's area; MC/PMC = motor cortex and premotor cortex; SMA = supplementary motor area; TP = temporo-parietal region. Activity in the right cerebellum is not visible.



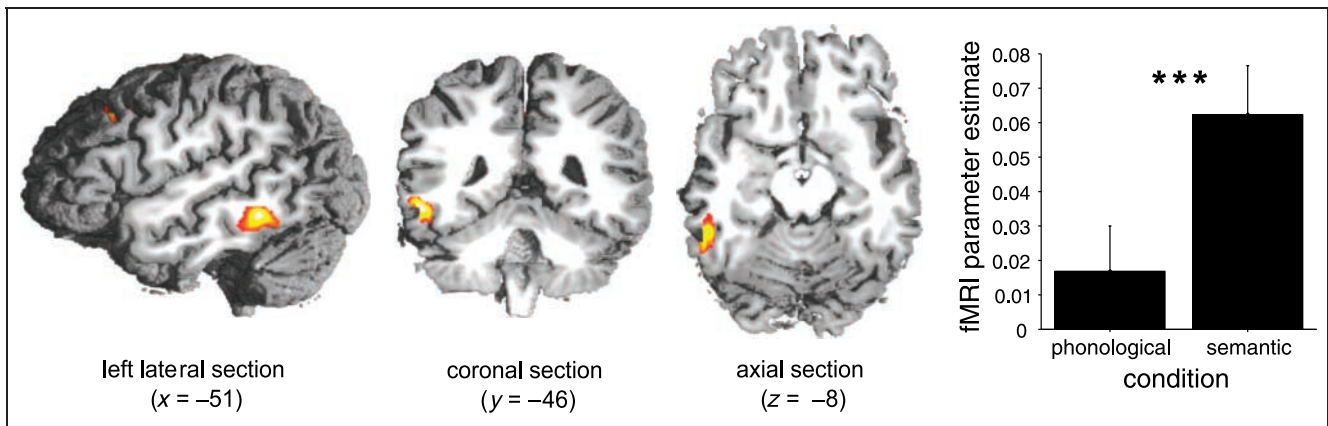


Figure 3. Semantic WM effect. Brain activation for the maintenance of conceptual–semantic representations (“semantic”), relative to the maintenance period of the item recognition task (“phonological”). For purposes of display, the statistical map was thresholded at $Z > 3.09$ ($p < .001$, uncorrected). Right panel: Brain activation, displayed using the parameter estimates (beta values) of the general linear model, for retention during the phonological (i.e., item recognition) and semantic WM conditions relative to the appropriate trial period of the control task. Activation displayed here reflects an average of all voxels in the activated cluster. Error bars show the standard error of the mean. *** $p < .001$.

Figure 5. Phonological relative to semantic maintenance activity. Brain activation elicited for the maintenance period of the item recognition task relative to maintenance in the semantic WM task. For purposes of display, the statistical map was thresholded at $Z > 3.09$ ($p < .001$, uncorrected). STSh = superior temporal sulcus, horizontal branch; CS = cingulate sulcus.

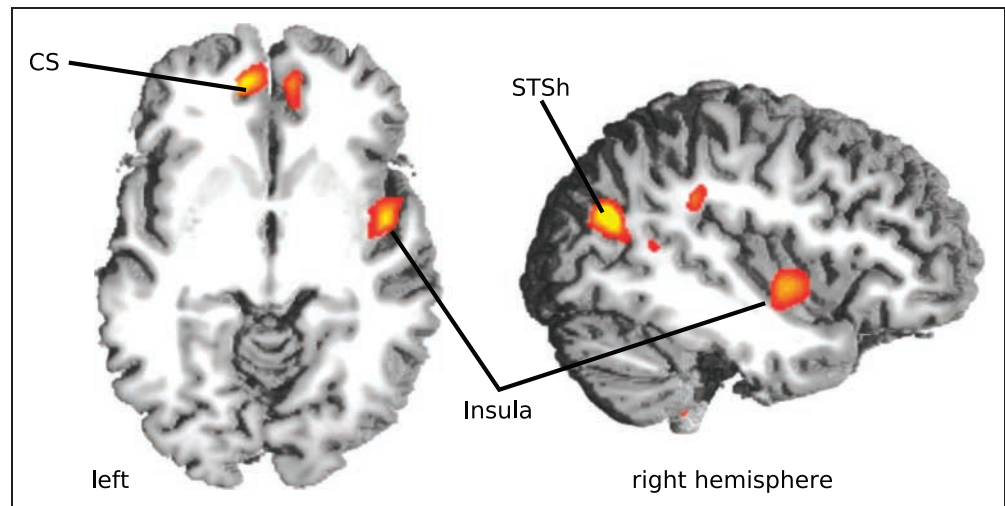
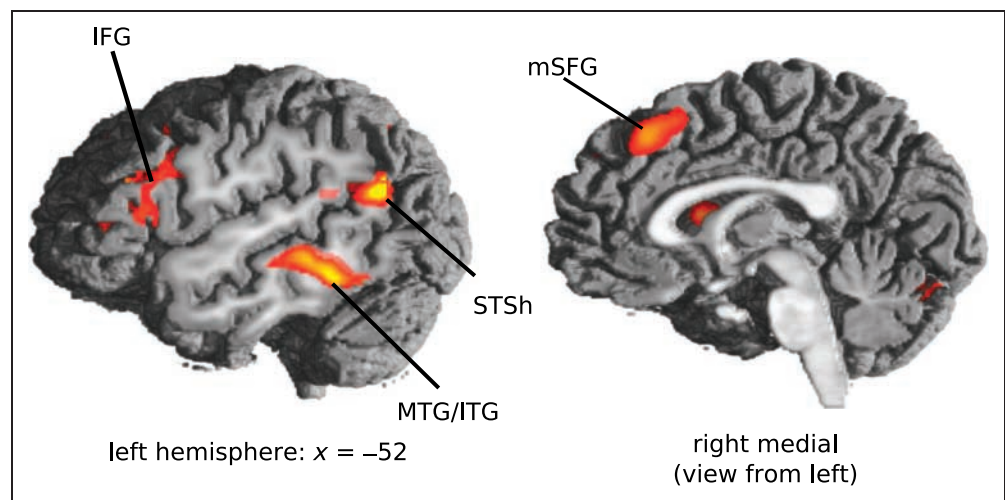


Figure 6. Retention period \times Task interaction. The interaction of retention period (i.e., early vs. late retention period) with task (i.e., semantic WM vs. item recognition task) results in brain regions that show a greater activation increase for semantic WM, relative to the item recognition task, in the early than in the late retention period. For purposes of display, the statistical map was thresholded at $Z > 3.09$ ($p < .001$, uncorrected). Note that activity in the right caudate head, which is visible in the right panel, did not pass the cluster size criterion for significance. STSh = superior temporal sulcus, horizontal branch; MTG/ITG = middle and inferior temporal gyrus; mSFG = medial superior frontal gyrus; IFG = inferior frontal gyrus.



regions of interest (ROIs; cf. Shivde & Thompson-Schill, 2004; Martin et al., 2003). As these studies indeed detected increased activation specific to semantic WM, we also examined ROIs in the left inferior prefrontal cortex (see Figure 4A). ROIs were spheres of radius 2 mm that were centered around the coordinates given in the following. Martin et al. (2003), based on reported activation from a study by Thompson-Schill, D'Esposito, Aguirre, and Farah (1997), probed an area in the left posterior prefrontal cortex that lies in the precentral sulcus, close to the end of the inferior frontal sulcus (Talairach coordinates: $x = -44, y = 9, z = 31$). In this ROI, we observed greater retention-based activity during semantic WM than during the item recognition task [$t(11) = 2.7, p < .05$; Figure 4B]. Three further ROIs were tested, which were positioned in the pars opercularis ($x = -50, y = 15, z = 18$), pars triangularis ($x = -48, y = 27, z = 10$), and pars orbitalis ($x = -44, y = 31, z = -6$) of the left inferior frontal gyrus (cf. Figure 4A). Increased activity for semantic WM relative to the item recognition task was also seen in the pars opercularis [BA 44; $t(11) = 3.2, p < .01$; Figure 4C] and the pars orbitalis [BA 47; $t(11) = 2.2, p < .05$; Figure 4E], but not in the triangular portion of the inferior frontal gyrus [BA 45; $t(11) = 1.3, p = .24$; Figure 4D].

The reverse contrast, that is, identifying retention period activity for the item recognition task relative to semantic WM maintenance, resulted in increased activity in the right insula, the right posterior horizontal branch of the superior temporal sulcus, and the anterior cingulate sulcus bilaterally (Figure 5; Table 2). During en-

coding, more distributed activation was observed for the item recognition task relative to semantic WM, whereas no differential activation was seen for semantic WM relative to the item recognition task. During the retrieval period, there were selectively increased activations both for the item recognition task and for the semantic WM task. These activations are listed in Table 2, but not discussed in detail, as the focus of the present study is on the analysis of maintenance-related activation for semantic WM. However, given that there was no specific activation increase for the semantic WM task during the encoding period—although we assume that additional semantic processes are triggered during encoding—we speculate that these semantic processes may be slightly delayed relative to the onset of rehearsal in the item recognition task. This would predict an increased level of semantic activation at the beginning of the retention period. As analysis of the retention period reported above focused on a single image acquired between 3 and 4.5 sec, we conducted a third analysis in which early and late retention period (i.e., the first 3 sec and the last 3 sec of the retention period) are modeled separately. In this analysis, we observe significantly greater task effects (i.e., semantic WM > item recognition task) during the early as compared to the late retention period. This result is best characterized by considering the interaction of retention period (early vs. late) with task (semantic WM vs. item recognition task) (Figure 6 and Table 3). A significant interaction is observed in the left posterior superior temporal sulcus, the left posterior

Figure 4. Region-of-interest analysis of semantic WM effects. (A) Display of a priori defined ROIs and the peak of the MTG/ITG region rendered onto the lateral surface of a template brain. MTG/ITG = posterior middle and inferior temporal gyrus; PCS/IFS = junction of the inferior frontal and precentral sulci (coordinates derived from Martin et al., 2003); IFG = inferior frontal gyrus; op = pars opercularis; tri = pars triangularis; orb = pars orbitalis. The PCS/IFS ROI was projected laterally by about 1.5 cm; the three inferior frontal ROIs were projected laterally by about 1 cm for better visualization. (B–E) Brain activation for semantic and phonological (i.e., item recognition) WM (see the legend of Figure 3 for more details). * $p < .05$; ** $p < .01$.

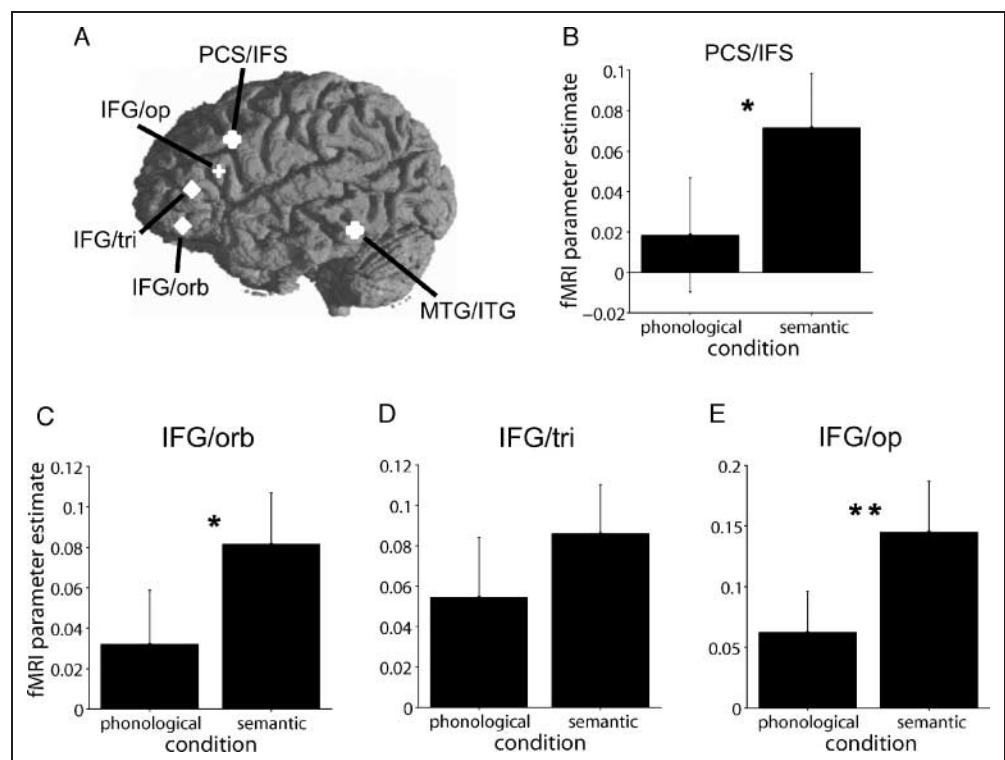


Table 2. Activation Results

Brain Region	Hemisphere	BA	Cluster Size (voxels)	t_{max} (df = 11)	Talairach Coordinates		
					x	y	z
<i>Retention Period: Semantic WM > Item Recognition Task</i>							
Middle and inferior temporal gyrus (MTG/ITG)	L	37	154*	7.04	-51	-46	-5
<i>Retention Period: Item Recognition Task > Semantic WM</i>							
Insula	R		159*	5.53	42	-4	0
Superior temporal sulcus (posterior horizontal branch)	R	39/19	154*	8.16	44	-66	23
Anterior cingulate sulcus	L/R	32/10	140*	5.33	10	49	3
<i>Encoding Period: Semantic WM > Item Recognition Task</i>							
-							
<i>Encoding Period: Item Recognition Task > Semantic WM</i>							
Parieto-occipital sulcus	L	7/19	138*	5.49	-13	-76	33
Basal occipito-temporal cortex	L	19	1683***	12.71	-42	-69	10
	R	18/19	967***	9.48	34	-77	14
Intraparietal sulcus/superior parietal lobe	L	7	136*	6.93	-29	-40	45
Posterior medial parietal cortex	L	7	168*	8.15	-11	-56	51
	L	7/5	195**	6.74	-11	-42	47
Perisylvian cortex (insula, planum temporale, superior temporal gyrus, inferior parietal lobe, inferior frontal gyrus)	R	7	566***	6.96	20	-69	37
	L	22/42/44/45	2087***	8.57	-47	-34	17
Supplementary motor area	R	22/40/42	2174***	8.79	36	-31	20
	L/R	6	145*	7.25	-2	-9	53
<i>Retrieval Period: Semantic WM > Item Recognition Task</i>							
Inferior frontal gyrus	L	44/45	726***	8.38	-47	13	9
Medial superior frontal gyrus	L	8/9	444***	8.13	-9	37	35
Caudate nucleus	L		135*	5.1	-8	-1	12
<i>Retrieval Period: Item Recognition Task > Semantic WM</i>							
Lateral occipito-temporal cortex	R	18/19	267***	5.46	32	-77	22
Parieto-occipital sulcus	L	7/19	276***	7.18	-15	-70	39
Fusiform gyrus/parahippocampal gyrus	R	37	150*	5.82	28	-48	0
Posterior cingulate gyrus	L/R	31	262***	14.73	-1	-30	43
Planum temporale	L	22/42	125*	5.41	-53	-32	17
Anterior cingulate sulcus	R	32	205**	10.67	10	49	3

p Values for the cluster-level significance are corrected for multiple comparisons (Kiebel et al., 1999; Worsley et al., 1996).

* $p < .05$.

** $p < .01$.

*** $p < .001$.

inferior and middle temporal gyrus, the medial superior frontal gyrus, the inferior frontal gyrus and sulcus, the globus pallidus of the basal ganglia, as well as in the right cerebellum. Each of these areas showed a greater task effect (i.e., semantic WM – item recognition task contrast) during the early retention period than during the late retention period [all $t(11) > 5.4$, $p < .0005$; paired two-sample t tests]. As we have demonstrated in the analyses reported above, only two of these regions, ITG/MTG and the left inferior prefrontal cortex, show sustained retention period activation.

Given that the semantic WM condition was behaviorally more difficult than the item recognition task, it could be argued that the observed MTG/ITG activity for semantic WM may reflect generally increased task difficulty. This is unlikely because task difficulty is typically reflected in prefrontal activations such as in the anterior cingulate cortex (e.g., Paus, Koski, Caramanos, & Westbury, 1998; Barch et al., 1997). To more convincingly rule out this alternative account of increased MTG/ITG activity in the present semantic WM task, we examined the correlation between behavioral difficulty and MTG/ITG retention period activation across participants. If MTG/ITG activity for semantic WM is due to increased task difficulty, there should be a positive correlation across individuals between their brain activation in this area and the difficulty they experienced in the task. More specifically, to the degree that the difference in response accuracies between the item recognition task and semantic WM (i.e., item recognition – semantic condition) increases, there should be an increase in retention-based activation for semantic WM relative to the item recognition task in this brain area (i.e., semantic – item recognition). This, however, was not the case. Condition effects on response accuracy and activation increase during retention are uncorrelated [$r = .05$, $t(10) = 0.146$, $p = .887$]. Response time (RT) differences (i.e., semantic WM – item recognition task) were

also uncorrelated with the difference in retention-based activation between the two conditions [$r = -.23$, $t(10) = -0.76$, $p = .46$]. In addition, the MTG/ITG activation difference during encoding or retrieval was also not correlated with behavioral difficulty; for encoding period activity [accuracy: $r = .26$, $t(10) = 0.84$, $p = .42$; RT: $r = .05$, $t(10) = 0.147$, $p = .886$]; for retrieval period activity [accuracy: $r = -.008$, $t(10) = -0.02$, $p = .98$; RT: $r = .45$, $t(10) = 1.6$, $p = .15$]. Whole-brain group analyses that used differences in individual performance (accuracy as well as RT) as additional regressors furthermore demonstrated that there is no other area that tracks performance difficulty in the comparison of the semantic WM and the item recognition task, in any of the three trial periods.

Finally, given that previous studies (e.g., Crosson et al., 1999) report basal ganglia activity during semantic WM and given that the specific combination of spatial smoothing and cluster size thresholds chosen for the analyses reported so far may be insufficient to detect focused activation in the basal ganglia, we reanalyzed our data with a spatial smoothing kernel of 3 mm FWHM and reduced statistical thresholds ($p < .005$; >5 voxels). In this analysis, increased activity for semantic WM relative to the item recognition task was observed in the heads of the caudate nuclei bilaterally (left: $x = -7$, $y = 13$, $z = 3$; $Z_{\max} = 3.11$, 16 voxels; right: $x = 10$, $y = 13$, $z = 11$; $Z_{\max} = 3.09$, 12 voxels). No other basal ganglia structure showed effects of semantic WM.

DISCUSSION

The present fMRI study examined the neural bases of maintaining conceptual–semantic representations in WM, using a new paradigm that requires maintaining a relatively novel conceptual combination, and then determining whether a probe names an emergent property

Table 3. Activation Results, Retention Period (i.e., Early vs. Late Retention Period) \times Task (Semantic WM vs. Item Recognition Task)

Brain Region	Hemisphere	BA	Cluster Size		Talairach Coordinates		
			(voxels)	t_{\max} ($df = 11$)	x	y	z
Superior temporal sulcus (posterior)	L	39	139**	6.68	-49	-62	21
Middle and inferior temporal gyrus	L	21	304***	6.63	-54	-39	0
Inferior frontal gyrus and sulcus, middle frontal gyrus	L	8/44/45/47	403***	7.85	-46	29	20
Medial superior frontal gyrus	L/R	6/8	205**	5.61	2	29	43
Basal ganglia, globus pallidus	L		143**	5.64	-18	1	8
Cerebellum	R		434***	5.67	26	-72	-31

p Values for the cluster-level significance are corrected for multiple comparisons (Kiebel et al., 1999; Worsley et al., 1996).

** $p < .01$.

*** $p < .001$.

of that combination. This new task was contrasted with a classical item recognition task that involves the maintenance of lexical and phonological codes of semantically unrelated words. As expected, the item recognition task elicited retention-related activation in brain regions involved in the phonological loop, namely, Broca's area, motor and premotor cortex, the cerebellum, and the lateral temporo-parietal region (cf. Smith & Jonides, 1997, 1998). Relative to the semantic WM task, phonologically based retention more strongly activated the right insula and the right posterior-most superior temporal sulcus. By analogy to studies of the processing of sentence melody (prosodic processing; e.g., Meyer, Alter, Friederici, Lohmann, & von Cramon, 2002), we suggest that these right hemispheric activations may reflect the additional utilization of a prosody-based strategy for rehearsing phonological items. This is possible as the word triplets have different lengths (i.e., between four and eight syllables), and the phonological rehearsal of these triplets therefore follows a rhythmic pattern. Some researchers have suggested that prosodic patterns may form a basic mechanism for holding sequences of auditory items in memory (Frazier, Carlson, & Clifton, 2006; Reeves, Schmauder, & Morris, 2000; Sturges & Martin, 1974).

Crucially, the retention of unrelated words in the classical WM task did not tax the phonological loop system more than did the semantic WM condition. This is important as it suggests that the presence of a single conceptual combination (in the semantic WM condition) did not reduce the overall verbal WM load, as might be expected if the combination replaced the phonological representation. Rather, the brain activation results suggest the parallel retention of both a phonological representation of the memory set and the emergent semantic concept in the semantic WM condition; this dual storage may be a strategy to deal with incorrect probe items, in which case subjects may have to reconsider the original word list to generate a correct decision.

Our main result, however, is the observation that the semantic WM task elicits increased retention-related activation in the left posterior inferior/middle temporal cortex and in the left inferior prefrontal cortex. These results are consistent with previous studies of semantic WM (Shivde & Thompson-Schill, 2004; Crosson et al., 1999), and allow us to interpret earlier findings more narrowly as retention-related activity. Our finding of posterior inferior temporal activation for semantic WM maintenance has important implications for models of verbal WM, which will be discussed below. The additional observation that semantic WM activity in the MTG/ITG is stronger during the early than during the late portion of the retention period is compatible with semantic WM as a continuously decaying activation of semantic representations. However, this observation may also result from a greater demand on MTG/ITG processing during semantic computations that may still be on-

going during the early retention period. This alternative account might be explored in future studies by varying the duration of the retention period, which would make it possible to estimate the exact time course of the hemodynamic response elicited in the MTG/ITG. This may provide further insight into the contribution of this brain region to semantic relative to nonsemantic WM demands.

Performance Differences between Semantic WM and the Item Recognition Task

The behavioral performance data indicate that the semantic WM task was more difficult than the item recognition task. This finding contrasts with the assumption that the additional availability of conceptual-semantic information should support the maintenance of verbal information in WM. However, we assume that this difference in performance difficulty does not primarily stem from the retention period of the current tasks. The brain regions identified for semantic WM maintenance relative to the item recognition task are not typically influenced by behavioral difficulty (Paus et al., 1998; Barch et al., 1997), and were shown to be unaffected by behavioral difficulty in the present study. For these reasons, we believe that behavioral difficulty primarily stems from the retrieval period of the task, where judging whether the probe word represents an emergent property of a novel concept may be more difficult than judging whether the probe word was part of the memory set. This assumption receives support from the observation of a medial frontal activation for semantic WM relative to the item recognition task during the retrieval period, as this region (in particular BA 8) is known to be involved in the effortful monitoring of ongoing processing, and more specifically may be related to decision uncertainty and prereponse conflict (Ridderinkhof, Ullsperger, Crone, & Nieuwenhuis, 2004), components that are likely to be present in the decision stage of the current semantic WM task.

The Time Course of Semantic Working Memory

In addition to demonstrating the involvement of the MTG/ITG region in the maintenance of conceptual-semantic information, the present results also provide some evidence concerning the time course of semantic components of verbal WM. Our analyses indicate that the involvement of semantic systems has a slightly slower time course than the recruitment of other components of the verbal WM system. During the encoding period of the semantic WM task, there was no evidence of an involvement of additional semantic processing systems. However, during the first seconds of the retention period, a fronto-temporal semantic system was engaged, more strongly than during later portions of the retention period. This

system encompassed Wernicke's area, the MTG/ITG region, and left inferior frontal regions known to be involved in semantic retrieval processes (e.g., Bookheimer, 2002). In addition, a superior anteromedial prefrontal region is also recruited that is known to be involved in the monitoring of ongoing processing (Ridderinkhof et al., 2004). In the present task, medial prefrontal activation may be related to the assessment of the fit between the emergent semantic concepts and the presented word list. We tentatively suggest that lateral prefrontal and temporal involvement may be mostly automatic, induced by the semantics of the stimulus list, whereas the medial prefrontal involvement may be task-induced. This suggestion needs to be tested empirically.

Semantic Working Memory and Models of Language

The posterior inferior temporal region identified here as a neural correlate of semantic WM maintenance is well known from neural and cognitive studies of language processing. According to Hickok and Poeppel (2004), for example, this area is involved in the transformation of sound-based language codes into modality-independent meaning representations. More specifically, these authors propose that acoustic-phonetic processing is carried out in superior temporal brain regions and then interfaces with conceptual representations in the left posterior inferior temporal cortex. In line with this proposal, transcortical sensory aphasia, a neurolinguistic syndrome often associated with lesions in this region (Damasio, 1991), is characterized by auditory comprehension deficits and semantic paraphasias during language production (Kertesz, Sheppard, & MacKenzie, 1982). A similar proposal was made by Binder et al. (2000), who suggest a dorsal-to-ventral organization of the temporal lobe for speech perception. According to this model, information proceeds from the processing of basic auditory information in more dorsal temporal areas toward more semantic processing in middle and inferior temporal regions. Given that the inferior temporal lobe is the heteromodal association cortex, it is likely that orthographic processing of visually presented words converges onto inferior temporal regions in an analogous way (e.g., Price, 2000).

The middle and inferior temporal cortex is also implicated in object naming (e.g., Ojemann, 1983) and in meta-linguistic semantic tasks. For example, it was demonstrated that the posterior inferotemporal cortex is activated during semantic tasks that require knowledge about visual features of objects (e.g., Vandenberghe, Price, Wise, Josephs, & Frackowiak, 1996). Such findings suggest that the semantic concepts that were maintained in WM during the present study may be based on or include sensory information related to concrete objects. Models of semantic object representations in

the brain (e.g., Martin, Ungerleider, & Haxby, 2000) postulate that different attributes of objects (such as color or form) are represented in distinct brain areas that are related to the sensory processing of these features. Most items of the semantic WM condition do elicit sensory-relevant states (i.e., taste, color, form, or haptic; see the examples in Table 1). We therefore speculate that semantic WM involves the sustained activation of separable neural components representing distinct aspects of the relevant semantic representation.

The inferotemporal cortex is anatomically linked to the left inferior frontal cortex (e.g., Petrides & Pandya, 2002; Ungerleider, Gaffan, & Pelak, 1989), and the left inferior frontal cortex is also strongly associated with language processing. The posterior inferior frontal cortex (i.e., the pars opercularis) has been related to phonological and syntactic processing, whereas more anterior regions (i.e., pars triangularis and pars orbitalis) are associated with semantic processing (Bookheimer, 2002; Friederici, 2002). Critically, inferior frontal areas are not only involved in the on-line processing of language, but also when maintaining phonological, syntactic, and semantic information in the service of the on-line build-up of syntactic and semantic relations in a given sentence (cf. Friederici, 2002, for a detailed review). However, these regions have also been implicated in the effortful retrieval of stored phonological and semantic knowledge (e.g., Wagner, Bunge, & Badre, 2004) as well as in certain aspects of executive functions, particularly the selection of one alternative from a set of competing alternatives (e.g., Thompson-Schill et al., 1997). In the present study, the semantic WM condition did recruit both anterior and posterior regions of the left inferior prefrontal cortex tested in the ROI analysis. This observation is consistent with data from metalinguistic semantic tasks (e.g., Devlin, Mathhews, & Rushworth, 2003; Gold & Buckner, 2002). The clearly increased involvement of the posterior inferior frontal cortex in the semantic WM condition relative to the predominantly phonological retention processes of the item recognition task is unexpected, as this region is most robustly associated with phonological and syntactic processes (e.g., Bookheimer, 2002). This may indicate that phonological and/or syntactic processes may have been recruited to support semantic WM mechanisms. Alternatively, this result may also be taken to call into question the clear spatial separation of prefrontal language mechanisms and more domain-general cognitive control processes attributed to the posterior dorsolateral prefrontal cortex (e.g., Brass, Derrfuss, Forstmann, & von Cramon, 2005).

The specific role of the caudate nucleus in semantic WM is open. Caudate head activity was seen in an experiment similar to the present one, although without WM component. Word-picture pairs were shown that represent features of an object whose semantic representation, according to the authors, is activated by the pair (e.g., "candle," "cake" > "birthday"; Kraut et al.,

2002). Across studies, however, caudate activity is typically seen under conditions involving effortful processing such as similarity judgments on degraded stimuli (Grossman et al., 2002) or bilingual language control (Crinion et al., 2006). For this reason, it was proposed that the caudate generally supports controlled processing, rather than language-specific processes (Friederici, 2006).

Neural Mechanisms of Semantic Working Memory

Proponents of the multicomponent model of WM posit that the short-term retention of verbal information relies exclusively on phonological information (e.g., Baddeley & Logie, 1999; Hulme et al., 1997), and argue that semantic effects reported in behavioral studies stem from long-term memory processes at encoding and retrieval. However, Haarmann and Usher (2001) could eliminate semantic WM effects by inserting a distracter task between the encoding phase and the retrieval phase, a finding that is not consistent with the long-term memory account of semantic WM effects. In addition, Ruchkin et al. (1999, 2003) report event-related potential (ERP) effects of lexical status, word frequency, and word concreteness during the retention period of a verbal WM task. Furthermore, Cameron, Haarmann, Grafman, and Ruchkin (2005) report semantic priming effects on the N400 ERP component for incidental probes related to the words of the memory list, during the retention period of a verbal WM task. Finding a reduction in an ERP component sensitive to semantic context effects suggests that the processing of the incidental probe is facilitated by the sustained activation of the semantic representations of the memory set, lending support to the notion of sustained activation of conceptual–semantic representations during the short-term maintenance of words in WM. The present findings support these electrophysiological studies and suggest that conceptual–semantic information can be maintained in WM during a brief retention period.

Relative to earlier studies of lexical and semantic WM, the present study allows us to specify more confidently the posterior inferior temporal and inferior frontal areas as supporting the maintenance of semantic concepts in an activated state. Crucially, this semantic WM activation is not driven by behavioral difficulty, but rather reflects a specific neuroanatomical correlate of the retention (and possibly manipulation) of conceptual–semantic information in WM. In analogy to neurophysiological and human neuroimaging studies of visual WM (Miller & D’Esposito, 2005; Curtis & D’Esposito, 2003; Fuster, 1995), we suggest that semantic WM relies on the sustained activation of conceptual–semantic representations in the posterior inferior temporal lobe, driven by top–down signals emanating from the left inferior prefrontal cortex. A recent study by Fiebach, Rissman, and D’Esposito (2006) supports this suggestion by demonstrating that a closely located, slightly more anterior inferotemporal brain region

is functionally coupled with the left prefrontal cortex during the maintenance of words, but not during that of pseudowords. Our suggestion differs from earlier proposals in that it does not restrict semantic WM to the prefrontal cortex. For example, Haarmann and Usher (2001) hold, based on computational modeling work, that conceptual–semantic representations are maintained in a limited-capacity system in the prefrontal cortex. This prefrontal semantic WM consists of activated long-term memory representations that are *transmitted from* posterior cortices *to* the prefrontal semantic store. The present data, in contrast, indicate a sustained activation of posterior semantic representations, most likely under the control of the prefrontal cortex. Although the present study demonstrates the additional involvement of the MTG/ITG region for the maintenance of semantic concepts, it cannot specify the exact nature of the semantic representation that is kept active. The robust activation observed for the semantic condition may be taken to suggest a high semantic WM load, which might imply that the semantic representation itself is an integration of several representational nodes of the semantic system (e.g., “green” and “tomato”) or of several sensory features of a semantic concept (e.g., color, form; cf. Martin et al., 2000), posing a heavy burden on WM maintenance systems. Previous fMRI studies demonstrated brain activation even during the maintenance of single words (e.g., Shivde & Thompson-Schill, 2004), so it appears possible to assume that the sustained activation of a single semantic concept generates a robust neural signature. Future studies employing techniques such as semantic priming may help to specify the nature of semantic concepts retained in semantic WM.

The hypothesis of a frontally guided activation of inferotemporal semantic representations, as developed here, is consistent with models of prefrontal cortex function (Miller & Cohen, 2001; Petrides, 1996) and with procedural models of WM (e.g., Ruchkin et al., 2003; Crowder, 1993). These models suggest that WM does not involve cortical mechanisms exclusively dedicated to the maintenance of specific types of information, but rather involves sustained activation of cortical representations that are involved in the perceptual processing of the to-be-maintained materials. An analogous theoretical position was developed based on neurophysiological studies of WM in monkeys, where WM is described as activated long-term memory (“active memory”; Fuster, 1995). In analogy to neurocognitive models of language, this procedural, or active, memory model suggests a dorsal-to-ventral recruitment of temporal lobe representations for verbal WM, with lexical–semantic WM mediated by middle temporal regions, and conceptual–semantic WM mediated by more ventral regions of the inferior temporal cortex.

To summarize, we report an fMRI study using a novel conceptual–semantic WM task, in which participants maintain emergent semantic concepts over a retention

period. We demonstrate that a region in the left posterior inferior temporal cortex and left inferior prefrontal regions are more strongly activated during semantic maintenance than during an item recognition task involving phonology- and lexicality-based, but not conceptual-semantic, maintenance. On the one hand, these results demonstrate a contribution of conceptual-semantic representations to the successful maintenance of linguistic information in verbal WM. Importantly, this semantic contribution is not restricted to the encoding and retrieval periods, as was claimed before, but is also effective during retention. In addition, our results indicate that semantic WM is not supported by a special-purpose semantic WM component, but rather by the sustained activation of temporal brain regions involved in semantic processing of linguistic information.

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REFERENCES

- Baddeley, A. (2003). Working memory: Looking back and looking forward. *Nature Reviews: Neuroscience*, 4, 829–839.
- Baddeley, A. D., & Logie, R. H. (1999). Working memory: The multiple-component model. In A. Miyake & P. Shah (Eds.), *Models of working memory: Mechanisms of active maintenance and executive control* (pp. 28–61). Cambridge: Cambridge University Press.
- Barch, D. M., Braver, T. S., Nystrom, L. E., Forman, S. D., Noll, D. C., & Cohen, J. D. (1997). Dissociating working memory from task difficulty in human prefrontal cortex. *Neuropsychologia*, 35, 1373–1380.
- Binder, J. R., Frost, J. A., Hammeke, T. A., Bellgowan, P. S., Springer, J. A., Kaufman, J. N., et al. (2000). Human temporal lobe activation by speech and nonspeech sounds. *Cerebral Cortex*, 10, 512–528.
- Bookheimer, S. (2002). Functional MRI of language: New approaches to understanding the cortical organization of semantic processing. *Annual Review of Neuroscience*, 25, 151–188.
- Bourassa, D. C., & Besner, D. (1994). Beyond the articulatory loop: A semantic contribution to serial order recall of subspan lists. *Psychonomic Bulletin & Review*, 1, 122–125.
- Brass, M., Derrfuss, J., Forstmann, B., & von Cramon, D. Y. (2005). The role of the inferior frontal junction area in cognitive control. *Trends in Cognitive Sciences*, 9, 314–316.
- Brener, R. (1940). An experimental investigation of memory span. *Journal of Experimental Psychology*, 26, 467–482.
- Burock, M. A., Buckner, R. L., Woldorff, M. G., Rosen, B. R., & Dale, A. M. (1998). Randomized event-related experimental designs allow for extremely rapid presentation rates using functional MRI. *NeuroReport*, 9, 3735–3739.
- Cameron, K. A., Haarmann, H. J., Grafman, J., & Ruchkin, D. S. (2005). Long-term memory is the representational basis for semantic verbal short-term memory. *Psychophysiology*, 42, 643–653.
- Courtney, S. M., Petit, L., Maisog, J. M., Ungerleider, L. G., & Haxby, J. V. (1998). An area specialized for spatial working memory in human frontal cortex. *Science*, 279, 1347–1351.
- Courtney, S. M., Ungerleider, L. G., Keil, K., & Haxby, J. V. (1997). Transient and sustained activity in a distributed neural system for human working memory. *Nature*, 386, 608–611.
- Crinion, J., Turner, R., Grogan, A., Hanakawa, T., Noppeney, U., Devlin, J. T., et al. (2006). Language control in the bilingual brain. *Science*, 312, 1537–1540.
- Crosson, B., Rao, S. M., Woodley, S. J., Rosen, A. C., Bobholz, J. A., Mayer, A., et al. (1999). Mapping of semantic, phonological, and orthographic verbal working memory in normal adults with functional magnetic resonance imaging. *Neuropsychology*, 13, 171–187.
- Crowder, R. G. (1993). Short-term memory: Where do we stand? *Memory & Cognition*, 21, 142–145.
- Curtis, C. E., & D'Esposito, M. (2003). Persistent activity in the prefrontal cortex during working memory. *Trends in Cognitive Sciences*, 7, 415–423.
- Damasio, H. (1991). Neuroanatomical correlates of the aphasias. In M. T. Sarno (Ed.), *Acquired aphasias* (pp. 45–71). San Diego, CA: Academic Press.
- Devlin, J. T., Mathhews, P. M., & Rushworth, M. F. S. (2003). Semantic processing in the left inferior prefrontal cortex: A combined functional magnetic resonance imaging and transcranial magnetic stimulation study. *Journal of Cognitive Neuroscience*, 15, 71–84.
- Druzgal, T. J., & D'Esposito, M. (2001). Activity in fusiform face area modulated as a function of working memory load. *Brain Research, Cognitive Brain Research*, 10, 355–364.
- Fiebach, C. J., Rissman, J., & D'Esposito, M. (2006). Modulation of inferotemporal cortex activation during verbal working memory maintenance. *Neuron*, 51, 251–261.
- Fiez, J. A. (1997). Phonology, semantics, and the role of the left inferior prefrontal cortex. *Human Brain Mapping*, 5, 79–83.
- Frazier, L., Carlson, K., & Clifton, C. (2006). Prosodic phrasing is central to language comprehension. *Trends in Cognitive Sciences*, 10, 244–249.
- Friederici, A. D. (2002). Towards a neural basis of auditory sentence processing. *Trends in Cognitive Sciences*, 6, 78–84.
- Friederici, A. D. (2006). What's in control of language? *Nature Neuroscience*, 9, 991–992.
- Friederici, A. D., Ruschemeyer, S. A., Hahne, A., & Fiebach, C. J. (2003). The role of left inferior frontal and superior temporal cortex in sentence comprehension: Localizing syntactic and semantic processes. *Cerebral Cortex*, 13, 170–177.
- Friston, K. J., Fletcher, P., Josephs, O., Holmes, A., Rugg, M. D., & Turner, R. (1998). Event-related fMRI: Characterizing differential responses. *Neuroimage*, 7, 30–40.
- Fuster, J. M. (1995). *Memory in the cerebral cortex*. Cambridge: MIT Press.
- Fuster, J. M., & Jervey, J. P. (1981). Inferotemporal neurons distinguish and retain behaviorally relevant features of visual stimuli. *Science*, 212, 952–955.
- Gabrieli, J. D., Poldrack, R. A., & Desmond, J. E. (1998). The role of left prefrontal cortex in language and memory. *Proceedings of the National Academy of Sciences, U.S.A.*, 95, 906–913.

- Gold, B. T., & Buckner, R. L. (2002). Common prefrontal regions coactivate with dissociable posterior regions during controlled semantic and phonological tasks. *Neuron*, *35*, 803–812.
- Grossman, M., Smith, E. E., Koenig, P., Glosser, G., DeVita, C., Moore, P., et al. (2002). The neural basis for categorization in semantic memory. *Neuroimage*, *17*, 1549–1561.
- Haarmann, H. J., & Usher, M. (2001). Maintenance of semantic information in capacity-limited item short-term memory. *Psychonomic Bulletin & Review*, *8*, 568–578.
- Hickok, G., & Poeppel, D. (2004). Dorsal and ventral streams: A framework for understanding aspects of the functional anatomy of language. *Cognition*, *92*, 67–99.
- Hillis, A. E., Wityk, R. J., Tuffiash, E., Beauchamp, N. J., Jacobs, M. A., Barker, P. B., et al. (2001). Hypoperfusion of Wernicke's area predicts severity of semantic deficit in acute aphasia. *Annals of Neurology*, *50*, 561–566.
- Hulme, C., Maughan, S., & Brown, G. D. A. (1991). Memory for familiar and unfamiliar words: Evidence for a long-term memory contribution to short-term memory span. *Journal of Memory and Language*, *30*, 685–701.
- Hulme, C., Roodenrys, S., Schweickert, R., Brown, G. D. A., Martin, S., & Stuart, G. (1997). Word-frequency effects on short-term memory tasks: Evidence for a redintegration process in immediate recall. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *23*, 1217–1232.
- Josephs, O., Turner, R., & Friston, K. J. (1997). Event-related fMRI. *Human Brain Mapping*, *5*, 243–248.
- Kertesz, A., Sheppard, A., & MacKenzie, R. (1982). Localization in transcortical sensory aphasia. *Archives of Neurology*, *39*, 475–478.
- Kiebel, S. J., Poline, J. B., Friston, K. J., Holmes, A. P., & Worsley, K. J. (1999). Robust smoothness estimation in statistical parametric maps using standardized residuals from the general linear model. *Neuroimage*, *10*, 756–766.
- Kraut, M., Kremen, S., Moo, L. R., Segal, J. B., Calhoun, V., & Hart, J. (2002). Object activation in semantic memory from visual multimodal feature input. *Journal of Cognitive Neuroscience*, *4*, 37–47.
- Lohmann, G., Muller, K., Bosch, V., Mentzel, H., Hessler, S., Chen, L., et al. (2001). LIPSIA—A new software system for the evaluation of functional magnetic resonance images of the human brain. *Computing Medical Imaging Graph*, *25*, 449–457.
- Martin, A., Ungerleider, L. G., & Haxby, J. V. (2000). Category specificity and the brain: The sensory/motor model of semantic representations of objects. In M. S. Gazzaniga (Ed.), *The cognitive neurosciences* (pp. 1023–1036). Cambridge: MIT Press.
- Martin, R. C., & Romani, C. (1994). Verbal working memory and sentence comprehension: A multiple-components view. *Neuropsychology*, *8*, 506–523.
- Martin, R. C., Shelton, J. R., & Yafee, L. S. (1994). Language processing and working memory: Evidence for separate phonological and semantic capacities. *Journal of Memory and Language*, *33*, 83–111.
- Martin, R. C., Wu, D., Freedman, M., Jackson, E. F., & Lesch, M. (2003). An event-related fMRI investigation of phonological versus semantic short-term memory. *Journal of Neurolinguistics*, *16*, 341–360.
- Meyer, M., Alter, K., Friederici, A. D., Lohmann, G., & von Cramon, D. Y. (2002). fMRI reveals brain regions mediating slow prosodic modulations in spoken sentences. *Human Brain Mapping*, *17*, 73–88.
- Miller, B. T., & D'Esposito, M. (2005). Searching for “the top” in top-down control. *Neuron*, *48*, 535–538.
- Miller, E. K., & Cohen, J. D. (2001). An integrative theory of prefrontal cortex function. *Annual Review of Neuroscience*, *24*, 167–202.
- Monsell, S. (1984). Components of working memory underlying verbal skill: A “distributed capacities” view. In H. Bouma & D. G. Bouwhuis (Eds.), *Attention and performance: X. Control of language processes* (pp. 327–250). Hillsdale, NJ: Erlbaum.
- Ojemann, G. A. (1983). Brain organization for language from the perspective of electrical stimulation mapping. *Behavioral and Brain Sciences*, *6*, 189–230.
- Oldfield, R. C. (1971). The assessment and analysis of handedness: The Edinburgh Inventory. *Neuropsychologia*, *9*, 97–113.
- Paus, T., Koski, L., Caramanos, Z., & Westbury, C. (1998). Regional differences in the effects of task difficulty and motor output on blood flow response in the human anterior cingulate cortex: A review of 107 PET activation studies. *NeuroReport*, *9*, R37–R47.
- Petrides, M. (1996). Specialized systems for the processing of mnemonic information within the primate frontal cortex. *Philosophical Transactions of the Royal Society of London, Series B, Biological Sciences*, *351*, 1455–1461.
- Petrides, M., & Pandya, D. N. (2002). Association pathways of the prefrontal cortex and functional observations. In D. T. Stuss & R. T. Knight (Eds.), *Principles of frontal lobe function* (pp. 31–50). Oxford: Oxford University Press.
- Poldrack, R. A., Wagner, A. D., Prull, M. W., Desmond, J. E., Glover, G. H., & Gabrieli, J. D. (1999). Functional specialization for semantic and phonological processing in the left inferior prefrontal cortex. *Neuroimage*, *10*, 15–35.
- Postle, B. R., Zarahn, E., & D'Esposito, M. (2000). Using event-related fMRI to assess delay-period activity during performance of spatial and nonspatial working memory tasks. *Brain Research, Brain Research Protocol*, *5*, 57–66.
- Price, C. J. (2000). The anatomy of language: Contributions from functional neuroimaging. *Journal of Anatomy*, *197*, 335–359.
- Ranganath, C., DeGutis, J., & D'Esposito, M. (2004). Category-specific modulation of inferior temporal activity during working memory encoding and maintenance. *Cognitive Brain Research*, *20*, 37–45.
- Reeves, C., Schmauder, A. R., & Morris, R. K. (2000). Stress grouping improves performance on an immediate serial list recall task. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *26*, 1638–1654.
- Ridderinkhof, K. R., Ullsperger, M., Crone, E. A., & Nieuwenhuis, S. (2004). The role of the medial frontal cortex in cognitive control. *Science*, *306*, 443–447.
- Roodenrys, S., Hulme, C., & Alban, J. (1994). Effects of word frequency and age of acquisition on short-term memory span. *Memory & Cognition*, *22*, 695–701.
- Roodenrys, S., Hulme, C., & Lethbridge, A. (2002). Word-frequency and phonological-neighborhood effects on verbal short-term memory. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *28*, 1019–1034.
- Ruchkin, D. S., Berndt, R. S., Johnson, J., Grafman, J., Ritter, W., & Canoune, H. L. (1999). Lexical contributions to retention of verbal information in working memory: Event-related brain potential evidence. *Journal of Memory and Language*, *41*, 345–364.
- Ruchkin, D. S., Grafman, J., Cameron, K., & Berndt, R. S. (2003). Working memory retention systems: A state of activated long-term memory. *Behavioural Brain Science*, *26*, 709–728.

- Schweickert, R. (1993). A multinomial processing tree model for degradation and reintegration in immediate serial recall. *Memory & Cognition*, *21*, 168–175.
- Shivde, G., & Thompson-Schill, S. L. (2004). Dissociating semantic and phonological maintenance using fMRI. *Cognitive, Affective, & Behavioral Neuroscience*, *4*, 10–19.
- Smith, E. E., & Jonides, J. (1997). Working memory: A view from neuroimaging. *Cognitive Psychology*, *33*, 5–42.
- Smith, E. E., & Jonides, J. (1998). Neuroimaging analyses of human working memory. *Proceedings of the National Academy of Sciences, U.S.A.*, *95*, 12061–12068.
- Smith, E. E., & Jonides, J. (1999). Storage and executive processing in the frontal lobes. *Science*, *283*, 1657–1661.
- Sturges, P. T., & Martin, J. G. (1974). Rhythmic structure in auditory pattern perception and immediate memory. *Journal of Experimental Psychology*, *102*, 377–383.
- Swinney, D., Love, T., Walenski, M., & Smith, E. E. (2007). Conceptual combination during sentence comprehension: Evidence for compositional processes. *Psychological Science*, *18*, 397–400.
- Talairach, J., & Tournoux, P. (1988). *Co-planar stereotaxic atlas of the human brain*. Stuttgart: Georg Thieme Verlag.
- Thompson-Schill, S. L., D'Esposito, M., Aguirre, G., & Farah, M. J. (1997). Role of left prefrontal cortex in retrieval of semantic knowledge: A re-evaluation. *Proceedings of the National Academy of Sciences, U.S.A.*, *94*, 14792–14797.
- Ungerleider, L. G., Gaffan, D., & Pelak, V. S. (1989). Projections from inferior temporal cortex to prefrontal cortex via the uncinate fascicle in rhesus monkey. *Experimental Brain Research*, *76*, 473–484.
- Vandenberghe, R., Price, C., Wise, R., Josephs, O., & Frackowiak, R. S. (1996). Functional anatomy of a common semantic system for words and pictures. *Nature*, *383*, 254–256.
- Wagner, A. D., Bunge, S. A., & Badre, D. (2004). Cognitive control, semantic memory, and priming: Contributions from prefrontal cortex. In M. S. Gazzaniga (Ed.), *The cognitive neurosciences* (3rd ed., pp. 709–725). Cambridge: MIT Press.
- Worsley, K. J., Marrett, S., Neelin, P., Vandal, A. C., Friston, K. J., & Evans, A. C. (1996). A unified statistical approach for determining significant signals in images of cerebral activation. *Human Brain Mapping*, *4*, 58–73.
- Zarahn, E., Aguirre, G., & D'Esposito, M. (1997). A trial-based experimental design for fMRI. *Neuroimage*, *6*, 122–138.