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# CORTICAL CELL ASSEMBLIES FOR LEXICAL AND CATEGORY-SPECIFIC SEMANTIC PROCESSING AS REVEALED BY FMRI CLUSTER ANALYSIS

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**CORTICAL CELL ASSEMBLIES FOR LEXICAL AND CATEGORY-SPECIFIC SEMANTIC PROCESSING AS REVEALED BY FMRI CLUSTER ANALYSIS**

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7 **DISTRIBUTED CELL ASSEMBLIES FOR GENERAL LEXICAL AND CATEGORY-**  
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## Abstract

Here, we ask whether frontotemporal cortex is functionally dissociated into distributed lexical and category-specific semantic networks. To this end, fMRI activation patterns elicited during the processing of words from different semantic categories were categorized using *k*-means cluster algorithms. Results showed a distributed pattern of inferiorfrontal, superiortemporal and fusiform activation shared by different word categories. This shared activation contrasted with patterns of category-specific semantic activation in widely distributed neural systems. Clustering revealed congruent functional specificity of focal area activations in frontal and temporal cortex, thus suggesting a correspondence between functional partitionings of frontocentral mirror neuron systems and that of inferiortemporal lexical and semantic circuits. Action words related to the face, arms and legs specifically activated the motor system in a somatotopic manner, whereas form-related words activated prefrontal areas. Similar functional specificity was evident in temporal cortex, where a different semantic topography emerged for form- and action-related words. Results were replicated in a separate data set, therefore recommending fMRI cluster analysis as a reliable method for scrutinizing the brain basis of lexical, semantic and conceptual systems in humans. **As focal modules do not explain the distributed character of functionally specific clusters and their distinct topographies are at variance with general distributed processing accounts, the functionally-homogenous distributed clusters specific to semantic types are best explained by specifically-distributed cortical circuits which, similar to Hebbian cell assemblies, represent functional units with specific roles in cognitive processing, especially in lexical and semantic access.**

## CATEGORY-SPECIFIC SEMANTIC CIRCUITS

## Introduction

The quest for the ultimate processes and representations that form the basis of conceptual thought has been a main motivation for the advent of neurocognitive imaging. Active areas, however, only allow for limited conclusions on the differential orchestration of brain networks in cognitive tasks. Especially, neuroimaging work so far has not yet provided a definitive answer to the fundamental question of what kinds of representations and processing units in the brain form the critical building blocks of thought. Two main proposals had been formulated: the local modular position, according to which specific focal brain centers, single cardinal or 'grandmother' cells in the extreme, represent an object, person, word or concept (Barlow 1972; Geschwind 1970; Hubel 1995), and the distributed holistic view positing that learning in a homogenous network leads to interference patterns and fully distributed representations of cognitive entities (Elman, et al. 1996; Lashley 1950; McClelland and Rumelhart 1985). Since cognitive neuroimaging provided evidence for both local specificity and wide distributedness of brain processes of thought, this discussion is still ongoing.

Discussions of global vs. locally-specific processing systems have recently been focusing on cortical regions relevant for sensorimotor and conceptual binding (Barsalou 2008; Patterson, et al. 2007; Pulvermüller 1999). In frontocentral cortex, the Mirror Neuron (MN) system is critical for mental processes ranging from binding of information about action execution and perception of the same actions to the recognition of goals and intentions and the processing of words, sentences and their meaning (Gallese and Lakoff 2005; Olivier, et al. 2007; Pulvermüller 2005; Rizzolatti and Craighero 2004; Rizzolatti and Wolpert 2005). In humans, this binding is attributable to a great extent to the inferiorfrontal premotor cortex homologue to macaque area F5, but more recently, additional MN systems in dorsolateral premotor cortex, prefrontal and parietal cortex, possibly with more specific function, have

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been discovered (Fogassi, et al. 2005; Hauk, et al. 2004; Nelissen, et al. 2005). To what degree these different sections of the MN system carry the same or dissociable functions, especially in cognitive domains such as language and conceptual processing, is largely open. The question about functional specificity or more general responsiveness also arises for cortical areas that contribute to the binding of semantic information to words, signs and symbols. A unitary semantic binding area was proposed in inferiorfrontal cortex (Bookheimer 2002), temporal pole (Patterson, et al. 2006), anterior-superiortemporal gyrus (Scott and Johnsrude 2003) and more posterior inferiortemporal cortex (Price 2000). As these areas may contribute to category-specific semantic and conceptual processes (Martin and Chao 2001), it once again appears crucial to clarify whether one or all of them have a homogeneous function in linguistic, semantic and conceptual processing or whether their contribution is specific to certain categories of knowledge. A further possibility is that some of these frontal and temporal areas carry a general role in symbol processing while other areas engage in category-specific semantic processing.

We here address the question of functional specificity vs. more general responsiveness in local or widely distributed systems using cluster analysis of the activation signatures of small brain loci as they emerged during processing of different types of semantic and conceptual information. **We focus on *conceptual* information systematically linked to words. We call this specific type of conceptual knowledge *semantic* as it is critical for defining word meaning** (see also Lambon Ralph and Patterson 2008; Patterson, et al. 2007).

In order to address functional specificity and segregation one can, in principle, use classic methods such as statistical parametric mapping. However, as the number of relevant parametric contrasts increases rapidly with the number  $m$  of conditions, this approach is cumbersome. Cluster analysis offers an alternative, which does not require any *a priori*

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grouping of data into sub-categories, and which can separate specific from global brain activity. In a data driven manner, cluster analysis creates natural groupings according to the specificity or more general activation of voxels (Baune, et al. 1999; Golland, et al. 2008; Simon, et al. 2004). The main principle of the *k*-means clustering algorithm applied in the present study is that it minimizes the variance within clusters while at the same time maximizing variance between them. Therefore, the method classifies voxels into the same cluster if they exhibit homogeneous function and are maximally segregated functionally from those in other partitions. As the voxels belonging to the same cluster therefore show the same functional activation pattern across conditions, we will say they have the same *functional signature*. Critically, the clustering algorithm is not influenced by spatial proximity in the brain and can, therefore, reveal local and distributed neuronal systems with similar function in the very same way.

To monitor conceptual and linguistic processes, words of different semantic types were presented and subjects were asked to read them to understand their meaning. An advantage of word stimuli lies in the possibility to match them for perceptual properties (for example their length), familiarity and other important psychological features, so that these factors do not act as confounds in the investigation of category-specific processes. Some words included in the present study were semantically related to visual information (color words, e.g. “green”, and form/shape words, e.g. “square”) and others related to actions (face-, arm-, and leg-related words, e.g. “lick”, “pick”, “kick”). Results of a range of studies had provided evidence for both globally distributed and locally specific cortical activation to words and concepts. Written language generally activated a distributed frontotemporal network spread out over fusiform (the so-called “visual word for area”, McCandliss, et al. 2003) and inferiorfrontal gyrus (containing the human homologue of mirror neuron area F5,

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Rizzolatti and Craighero 2004). Action words semantically related to the face, arms and legs specifically sparked single foci in motor and premotor areas (e.g., Hauk, et al. 2004) and words related to visual information ignited different parts of the temporal lobe (e.g., Martin and Chao 2001). For identifying brain voxels with the same functional characteristics, we used *k*-means cluster analysis of fMRI data (Simon, et al. 2004). **The underlying assumption was that voxels within one functionally coherent cluster** include neuronal elements from the same type of cortical circuit. To test the reliability of the functional clustering, the experiment was performed twice, in different subjects.

## Materials and Methods

### *Subjects*

21 young monolingual right-handed healthy native speakers of English (11 males) participated in the experiments. They were, on average, 24.5 years old (SD = 5.3), with an average laterality quotient of 87.1 (SD = 15.4, Oldfield 1971). Twelve subjects participated in Experiment 1 and nine in Experiment 2; subgroups did not differ in age or laterality. All participants were paid for their participation and had signed an informed consent form prior to testing. Ethics approval had been obtained from the Local Research Ethics Committee, Cambridge.

### *Stimuli and experimental design*

250 words semantically related to actions and visual features of objects were used as stimuli along with 250 strings of hash marks matched pair-wise in length to the words. In addition, 100 null events during which a fixation cross was displayed were included. The word stimuli were submitted to extensive testing for psycholinguistic properties before the

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experiment (psycholinguistic evaluation procedures as in Hauk and Pulvermüller 2004; Pulvermüller, et al. 1999). Meticulous investigation of stimulus features revealed that 50 words were semantically related to arm or hand actions, 50 to foot or leg actions and 50 to actions to which the muscles of the mouth, face or articulators mainly contribute. 50 words referred to colour and 50 to form or shape information. The action word groups were precisely matched to each other in word length, frequency, imageability, semantic relationship to visual and action information and number of ambiguous items. The visually-related word groups were matched for the same variables. Visually-related words were more common than action words (word form frequency 508 vs. 265 occurrences in the CELEX database, Baayen, et al. 1995). Stimuli from the five semantic word categories, arm, colour, face, form and leg, and control items were each presented for 100 ms with a stimulus onset asynchrony between two consecutive items of 2.5 s, so that stimulus presentation and scanner trigger were out of phase by ~500 ms. Each stimulus word was presented once to each subject. Two pseudo-randomized stimulus sequences were alternated between subjects. Subjects were instructed to attend to all stimuli flashed on the screen and to silently read the words.

*Imaging methods*

Subjects were scanned in a 3T Bruker MR system using a head coil. Echo planar imaging (EPI) sequence parameters were TR = 3.02 s, TE = 27 ms, flip angle = 90 degrees. The functional images consisted of 21 slices covering the whole brain (slice thickness 4 mm, inter-slice distance 1 mm, field-of-view 25 cm, in plane resolution 128\*128). Imaging data were processed using SPM99 software (Wellcome Department of Cognitive Neurology, London, UK).

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Images were corrected for slice timing, and then realigned to the first image using sinc interpolation. Phase maps were used to correct for inaccuracies resulting from inhomogeneities in the magnetic field (Cusack, et al. 2003; Jezzard and Balaban 1995). Any non-brain parts were removed from the T1-weighted structural images using a surface model approach (“skull-stripping”) (Smith 2002). The EPI images were co-registered to these skull-stripped structural T1-images using a mutual information co-registration procedure (Maes, et al. 1997). The structural MRI was normalized to the 152-subject T1 template of the Montreal Neurological Institute (MNI). The resulting transformation parameters were applied to the co-registered EPI images. During the spatial normalization process, images were resampled with a spatial resolution of  $2*2*2\text{ mm}^3$ . Finally, all normalized images were spatially smoothed with a 12 mm full-width half-maximum Gaussian kernel, globally normalized, and single-subject statistical contrasts were computed using the general linear model (Friston, et al. 1998). **The choice of the smoothing parameter was motivated by earlier work on category-specific brain activation (e.g., Hauk, et al. 2004; Pulvermüller, et al. 2006) and aimed at reducing the effect of inter-subject variability.** Low-frequency noise was removed applying a high-pass filter with time constant 60 s. Group data were analyzed with random-effects analyses. To control for low-level visual activation, all word category-induced activation was considered relative to the visual control condition, where hash mark strings matched in lengths to the written words were presented. For statistical analysis, the SPM99 canonical haemodynamic response function (HRF) was used to model the activation time course to each event type. Stereotaxic coordinates for voxels with maximal  $z$ -values within activation clusters are reported in Talairach space (Talairach and Tournoux 1988).

*Data analysis*

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7 Random-effects  $t$ -tests were performed for each voxel to test the hypothesis that  
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9 activation was present at a given brain locus in a given condition. Activation effects given as  
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11  $t$ -values for all brain voxels found active at a criterion of  $p < 0.005$  (uncorrected) in one or  
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13 more of the conditions were analyzed using  $k$ -means clustering. This relatively lenient  
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15 threshold was chosen to minimize the likelihood of misses. It was expected that any random  
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17 result of clustering would fail the replication test (see Reliability Check below). Activation of  
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19 each voxel was plotted in five-dimensional space, each dimension being defined by one of the  
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21 five conditions.  
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26 The two phase algorithm started with random seeds for  $k$  cluster centroids. Data points  
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28 were first partitioned by assigning them to the cluster with the nearest centroid. After all data  
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30 points had been assigned to clusters, centroids were updated. These phases were iterated until  
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32 no data points were reassigned to different clusters in consecutive runs. As clustering is  
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34 sensitive to starting conditions, the entire procedure was repeated 100 times using different  
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36 random seeds to calculate centroids. From the 100 solutions, the best clustering was selected  
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38 using a criterion value calculated as the between-cluster (explained) variance divided by the  
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40 within-cluster (unexplained) variance.  
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45 As the *a priori* hypothesis immanent to this study was that there is at least one type of  
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47 distributed cell assembly for each semantic type plus at least one additional type for the  
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49 processing of words as signs or spoken/written “word forms” (cf. de Saussure 1916), the  
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51 number  $k$  of clusters was set to 6. To ascertain that this choice of  $k$  was in the range  
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53 appropriate for explaining the maximum explainable variance in the present data set, we  
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55 calculated the explained effect size ( $t$  values) for increasing numbers of  $k$  (starting at  $k=1$ ).  
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58 The average and maximal  $t$  values obtained for each  $k$  are plotted in Figure 1 (top). It can be  
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seen that there was an increase of explained effect size up to a number of clusters of 6. This further endorses the choice of  $k = 6$  for the main analyses.

The specificity of clusters was evaluated using the measure of *normalized cluster entropy*, or NCE. Intuitively, cluster entropy is the specificity of a cluster to one stimulus condition. NCE is derived for each cluster  $i$  through the proportion  $p_{ij}$  of the effect size for the  $j^{\text{th}}$  of  $m$  conditions,

$$\text{NCE}_i = - \sum_{j=1}^m p_{ij} \ln p_{ij} / \ln m$$

Large entropy values imply nonspecific activation, i.e. similar activation values to different semantic categories. Small entropy values imply order and thus category-specific activation. Specific clusters were so selective that their normalized effect size was always greater than 50% for their “best activator” condition, so that less than 50% of their aggregated effect was accounted for by all other conditions taken together. Nonspecific clusters showed more balanced activation over conditions.

*Reliability check*

To check the reliability of the method, we determined whether the clustering of data obtained from Experiments 1 and 2 led to similar clustering. To this end, the Rand index (Rand 1971) was calculated. The Rand index provides a measure of agreement between two pairs of cluster analyses  $CA1$  and  $CA2$ . It is defined as

$$\text{Rand index} = (a + d) / (a + b + c + d)$$

where  $a$  is the number of voxel pairs clustered in the same partition in both  $CA1$  and  $CA2$ ,  $b$  the number of voxel pairs clustered in the same partition in  $CA1$  but in different ones in  $CA2$ ,  $c$  the voxel pair number in different partitions in  $CA1$  but in the same in  $CA2$ , and  $d$  the

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number of voxel pairs assigned to different partitions in both analyses. The Rand index ranges between 0 and 1; a Rand index  $> 0.5$  indicates good correspondence between two classifications. Rand indexes were calculated for the two optimal cluster analyses for Experiment 1 and 2 and were also calculated for 9 additional pairs of clusterings obtained after random assignment of subjects to experiments.

## Results

Cluster analysis revealed six clusters of voxels, each characterized by a specific activation signature to semantic word categories (Figure 1, Table 1). Importantly, all of these clusters were distributed, consisting of five to 43 local cluster components in different lobes of the cortex. These “foci” each included between 1 and 1147 voxels; foci  $\geq 50$  voxels were considered in detail. Two of the six distributed clusters were active to different degrees to a range of semantic word categories (non-specific clusters 1 and 2, see Figure 1B-C). In contrast, four distributed clusters had a preferred semantic-category condition activating them, as over 50% of their aggregate effect could be explained by the effect of one semantic category alone, the *best activator* category (specific clusters 3-6, Figure 1B-C, Table 1, columns H, J). In fact, best activator categories accounted for 75-90% of the aggregate effect captured by three out of the four specific clusters (Table 1H). Most of the aggregate effect obtained in the two experiments (rank numbers 1-3, Table 1F) was explained by two semantic-category specific clusters and one nonspecific cluster. In Experiment 1, specific (nonspecific) clusters accounted for 64% (34%) of the metabolic changes and the respective numbers for Experiment 2 were 63% (33%, Table 1E).

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It was surprising that all distributed clusters included local clusters in different cortical lobes, especially in frontal and temporal cortex (Table 2). These foci in different lobes but belonging to the same distributed cluster thus showed the same selectivity to word categories, i.e. the same functional signature. Nonspecific cluster 1 consisted of strong left-hemispheric inferiorfrontal triangular-opercular and inferiortemporal fusiform, along with some right-inferiorfrontal activation, whereas nonspecific cluster 2 **was distributed over** perisylvian left-inferior-prefrontal and middle-temporal areas. Cluster 3 specifically active to face action concepts also showed a left-inferiorfrontal distribution extending into postcentral gyrus along with left-inferiortemporal and right-inferiorfrontal areas. Cluster 4 specifically active to arm words had a strong bihemispheric component with local clusters in bilateral precentral cortex, where arm motor and premotor cortex are situated, extending into postcentral gyrus on the right. Left-inferiortemporal and right-inferiorfrontal activation were also seen. Leg words sparked an assembly of local clusters distributed over left and right dorsal pre- and postcentral cortex, where leg motor and premotor cortex is situated, left-frontodorsal supplementary motor cortex, left-middletemporal gyrus, hippocampus, parahippocampus and temporooccipital lingual gyrus (cluster 5). The most widely distributed activation was seen for cluster 6 specific to words related to form concepts. They activated a network of local clusters in bilateral inferiorfrontal and lateral-pre- and -postcentral cortex along with left-dorsolateral prefrontal, supplementary-motor, inferiortemporal and parietotemporooccipital areas.

--- Please insert Figure 1-2 and Table 1-2 about here ---

Cluster analysis results from Experiment 1 agreed well with those from Experiment 2, as demonstrated by a Rand index of 0.8696. Nine additional pairs of cluster analyses (performed on the same data sets with different random assignments of subjects to groups)

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yielded Rand indexes ranging between 0.6174 and 0.8696 (average = 0.7888). This proves replicability of cluster analysis results.

Most of the local clusters making up a distributed cluster in one analysis had a homologue in the analysis of the other experiment (Table 2). 27 of the larger foci ( $\geq 50$  voxels) in each analysis directly matched with a focus in the other analysis (there were sometimes two focal homologues to one larger focus, see Table 2). In addition to the 27 replicated focal clusters, Experiment 1 revealed three “idiosyncratic” foci not matched by analyses of Experiment 2. Experiment 2 gave rise to 13 idiosyncratic foci; some of these additional foci may be related to the smaller sample size ( $n = 9$ ) of that study, leading to increased opportunity to reflect inter-individual variation. Among the overall 70 larger foci ( $\geq 50$  voxels) in both studies taken together, there were 54 matches and 16 mismatches. The number of voxels in these matching foci was 23,823 (90.8 %) and that in idiosyncratic ones was 2,415 (9.2 %). These numbers confirm good replicability of results. Replicability is further proven by the visual similarity of the cortical distributions of the six distributed clusters (Figure 2).

## Discussion

Cluster analysis of fMRI activation identified six functionally distinct distributed sets of cortical foci. Four of these distributed clusters were specifically activated by one semantic word category, suggesting that, in these cases, the foci comprised by the distributed clusters related to word-induced semantic or conceptual processes. Two clusters were activated in a nonspecific manner, to all word kinds under study, suggesting a relationship to general mechanisms of word processing. Remarkably, all clusters were widely dispersed and included

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7 activation foci in both left frontocentral and temporal cortex. As all clusters showed specific  
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9 cortical distribution and most of them signified one semantic word type, these data indicate  
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11 topographical and functional specificity of distributed cortical networks involved in semantic  
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13 processing. **Focal modules do not explain the distributed character of functionally**  
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15 **specific clusters and general distributed processing accounts face difficulties accounting**  
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17 **for the topographical specificity of the individual clusters.** The distributed clusters are best  
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19 explained by distributed cortical circuits which, similar to Hebb's construct of cell assemblies  
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21 (Braitenberg 1978; Hebb 1949; Milner 1996), form functional units with a specific role in  
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23 cognitive processing, especially in semantic access. Similar to the observed clusters, these  
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25 neuronal circuits had been proposed to be distributed but also specific in their distribution and  
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27 function (Pulvermüller 1992; Pulvermüller 1999). As distributed circuits appear to connect  
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29 neurons in frontocentral areas controlling actions with neurons in temporal areas receiving  
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31 auditory and visual information, this organization provides a mechanism for multimodal  
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33 response characteristics as they are found in memory cells (Fuster 1997; Fuster and Alexander  
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35 1971) and action-related mirror neurons (Gallese, et al. 1996; Rizzolatti and Craighero 2004).  
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42 We will now turn to a detailed discussion of the cortical organisation of functional  
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44 clusters revealed and confirmed by our experiments and their possible roles in cognitive  
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46 processing. Results will be related to theories of semantic and conceptual brain systems and  
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48 the question whether the distributed clusters and their local foci might index functional  
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50 contributions or possibly epiphenomenal activation will be addressed in the light of  
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52 neuropsychological and TMS studies. A final paragraph offers conclusions on the nature of  
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54 cognitive representations in the brain.  
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*Clusters signify general linguistic and specific conceptual processes*

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Two of the distributed clusters, clusters 1 and 2, were nonspecific as voxels became active for a range of word types. These clusters' local activations in left inferiorfrontal, middle-temporal and fusiform gyrus, may reflect links between motor, acoustic and visual representations of spoken and written words and possibly modality-nonspecific processing of such abstract "word forms". We here use the term "word form" in the sense of "words as written or spoken signs" and distinguish word form from meaning adopting a distinction well-established in language science (de Saussure 1916). Although both nonspecific clusters included superior- and inferiortemporal along with inferiorfrontal foci, the relative size of the temporal foci was different. The superiortemporal foci were pronounced in cluster 2 (> 100 adjacent voxels), whereas the inferiortemporal ones were smaller. The substantial foci included posterior superiortemporal sulcus, which is known to respond specifically to vowels (coordinates (-64/-22/-2), Uppenkamp, et al. 2006), individual speech sounds ((-60/-20/-2), Pulvermüller, et al. 2006) and spoken words ((-48/-27/-5), Shtyrov, et al. 2008). In contrast, cluster 1 was characterized by substantial foci (including > 200 voxels) in left-inferiortemporal and -fusiform cortex, which included a locus possibly contributing to visual word form processing ((-42/-57/-15), McCandliss, et al. 2003). These distributional differences suggest that cluster 1 is more closely related to visual word form processing, whereas cluster 2 plays a greater role in phonological and spoken word processing. As only visual stimuli were used in the current experiments, these suggestions must however await further experimental confirmation.

Critically, the majority of clusters were specific and responded primarily to one semantic word type. Four clusters showed most of their effect size in response to one semantic category of words. Words referring to face (Cluster 3), arm (4), leg (5) and form (6) each activated a replicable and specific set of foci. The foci in the motor/premotor system indexing

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semantic relationship of action words to different parts of the body are each part of a distributed cluster also including specific temporal areas. Temporal foci may index circuits activated by the visual perception of actions to which the words refer and/or target areas of specific temporal projections from the sensorimotor cortex.

Whereas action word categories were matched for a range of psycholinguistic variables, visually-related words had higher word frequencies than action words. The absence of a separate cluster for color words in the present results may reflect the relatively high frequency of this word group, which may be the reason for the reduced brain response (Chee, et al. 2003; Fiebach, et al. 2002; Hauk, et al. 2008b). A further reason for the absence of a separate cluster for color words may be the spatial vicinity of relevant circuits to cluster 5.

**Previous studies indicated that color words activate inferior temporal fusiform and parahippocampal gyri (Pulvermüller and Hauk 2006; Simmons, et al. 2007), which are** close to the temporal foci of cluster 5. As common words elicit *less* brain activity than rare ones (Chee, et al. 2003; Fiebach, et al. 2002; Hauk, et al. 2008b), the more widespread activation compared with all other clusters elicited by the form-word cluster 6 cannot be due to word frequency. It appears more plausible that form word cluster 6 reflects sensorimotor semantic aspects of form words and concepts. Note that words semantically related to visual shapes (“square”, “round”) are related to the motor system, too, as observing shapes is usually accompanied by specific eye movement patterns tracing the shape. The frontoparietal and temporal circuits included in the form word cluster may provide a basis for such cross-modal binding of action and perception-related semantic information. **Similar mechanisms for cross-modal information linkage may underpin the processing of abstract words** (Binder, et al. 2005; Pexman, et al. 2007a; Pexman, et al. 2007b; Pulvermüller 2008)

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In inferiorfrontal cortex, foci that indexed general word-form processing were sandwiched in-between areas that responded specifically to semantic categories (Figures 2, 3), a precentral focus of the cluster specific to shape words (-36/21/8) and a precentral focus of that to face words (-49/11/16). Similarly, inferior- and middle temporal foci contributing to word form processing (-42/-44/-19, -53/-49/-1) were surrounded by category-specific activations. The motor-premotor region was dominated by semantic somatotopy (Aziz-Zadeh, et al. 2006; Boulenger, et al. 2009; Buccino, et al. 2001; Hauk, et al. 2004; Pulvermüller, et al. 2001) with face, arm and leg word activation foci at inferiorlateral (-49/11/16), dorsolateral (-32/-5/52) and dorsal sites (-19/-21/61). A different semantic map was seen in the temporal cortex and the hippocampal formation where an anterior-to-posterior order emerged for foci included in specific clusters for leg words (-29/-7/-15), shape words (-32/-28/-17), and face and arm words (-51/-50/3 and -49/-51/-9).

*Distributed neuronal circuits for different types of cognitive processes*

These results offer answers to critical questions about the specificity of cortical area activations in linguistic, semantic and conceptual processing. The observed pattern of local functional alteration between general word processing circuits and category-specific ones adds to the evidence about the functional parcellation of the left-inferiorfrontal cortex (Bookheimer 2002). However, while confirming a role of anterior inferiorfrontal cortex to category-specific semantic processing, they also suggest a similar role, but for different categories, of posterior inferiorfrontal and motor/premotor cortex. In between category-specific semantic activations, the data suggest a “layer” for lexical or more general semantic computations (Figure 3).

## CATEGORY-SPECIFIC SEMANTIC CIRCUITS

As general language regions and category-specific conceptual-semantic foci reside side-by-side in inferiorfrontal cortex, this area can be seen to unite a general language processor operating on MNs (Rizzolatti and Arbib 1998) and more specific MN circuits involved in understanding subtypes of action words and concepts (Pulvermüller 2005). The semantic map uncovered in temporal cortex adds to previous evidence about category-specificity in this region (Martin and Chao 2001), as a wider variety of words and concepts, including face-, arm-, leg- and form-related ones, elicited specific activations in this brain part. The general word-related activations together with the category-specific semantic ones in temporal areas now offer a solution of the controversy about the posterior inferiortemporal cortex and its relationship to processing of either visual word form or semantics (e.g., McCandliss, et al. 2003; Price and Devlin 2003). Both possibilities seem to be correct, but, however, for different closely adjacent areas.

--- Please insert Figure 3 about here ---

*Category-specificity explains most of the neurometabolic effect*

Table 1 shows that about two thirds of the aggregated effect in neurometabolic activation was accounted for by specific clusters, therefore demonstrating the predominance of category-specific brain activation over nonspecific responsiveness to lexical items. The clear and reproducible category-differences obtained from concept groups pre-selected for specific semantic features might provide a hint why earlier neuroimaging studies failed to find category-specificity in brain activation (Devlin, et al. 2002). This may be due to the natural heterogeneity of the stimulus categories and the lack of behavioral control of semantic variables. In our view, control of variance in physical and psychological features of the stimulus set is important for obtaining category effects (Penolazzi, et al. 2007; Pulvermüller

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1999). The present data suggest that the lion's share of brain activation in word-elicited conceptual/semantic thought is category-specific. Therefore, studies of nonspecific brain activation to words averaging over semantic categories may miss out on these critical effects.

*Category-specific semantic activation clusters and the effect of lesions and TMS*

The present results from a metabolic imaging study show that topographically specific cortical clusters become active when words with different meaning are being processed. They also *suggest* that circuits with different distributions contribute to, and form the basis of, semantic processing. Although it is well-established in cognitive neuroscience that action-perception systems in the brain play a critical role in semantic and conceptual processing (e.g., Barsalou 2008; Hoenig, et al. 2008; Kemmerer and Gonzalez-Castillo 2008; Martin 2007; Olivier, et al. 2007; Pulvermüller 1996; Pulvermüller 2005; Rizzolatti and Craighero 2004; Warrington and Shallice 1984), it is important to point to the limits of any functional imaging study, which can show correlated activation but not a causal role of such activation. Some effort has been spent to extend the range of conclusions from fMRI work, for example by looking at priming and category-specificity of word frequency effects (Gold, et al. 2006; Hauk, et al. 2008a; Wheatley, et al. 2005). However, for finding out whether the activated distributed circuits represent a *necessary* brain basis of semantic processing, or rather a basis for epiphenomenal processes not related to semantics (see, e.g., Oliveri, et al. 2004), it is necessary to consider complementary methods, especially TMS and lesion studies.

Previous patient work revealed double dissociations in support of category-specific semantic processing (Daniele, et al. 1994; Warrington and Shallice 1984). **Especially the double dissociation in the processing of animal and tool knowledge (e.g., Buxbaum and Saffran 2002) and in processing object-nouns and action verbs (e.g., Neininger and**

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**Pulvermüller 2003) provide strong evidence that the cortical systems necessary for processing visually-based conceptual-perceptual knowledge and action knowledge differ. In addition,** recent studies showed that motor cortex degeneration in Motor Neuron Disease leads to a specific impairment of action words and concepts (Bak, et al. 2001; Bak, et al. 2006), frontoparietal lesion associated with apraxia degrades object utilization knowledge more strongly than other conceptual aspects of object understanding (Buxbaum and Saffran 2002), focal lesion in the motor cortex selectively impairs action word processing (e.g., Neiningen and Pulvermüller 2003) and Parkinson's disease is also accompanied by a specific deficit in processing action verbs (Boulenger, et al. 2008). **Although these studies are consistent with the notion of distributed semantic circuits with distinct topographies (for discussion, see Neiningen and Pulvermüller 2003), they address relatively large semantic and conceptual domains (animal/tool, object/action, noun/verb), whereas the present study focused on more fine-grained distinctions (e.g., action subtypes). However, neuropsychological work also showed that the areas found active for the more fine-grained semantic subcategories play a critical role in their processing.** TMS to hand and foot motor cortex respectively influenced the processing of hand- and leg-related words, **yielding a double dissociation in processing these categories (Pulvermüller, et al. 2005) - and, vice versa, action language processing affected motor system activation and behavior (Boulenger, et al. 2006; Buccino, et al. 2005). Also object color and form knowledge was found to dissociate after lesion in anterior temporal areas, consistent with differential functional activation (Miceli, et al. 2001; Pulvermüller and Hauk 2006). These results further support a critical functional role of category-specific circuits in semantic processing and in part validate the functional clusters. Still, as this study revealed for the first time that category-specific distributed clusters are each composed of several foci**

## CATEGORY-SPECIFIC SEMANTIC CIRCUITS

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7 **with similar functionality, it is evident that lesion and TMS evidence is not available for**  
8 **the full set of foci.** Future neuropsychological work is necessary to clarify whether the  
9 different foci included in the distributed clusters each play a critical role in semantic  
10 processing.  
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*Specific distribution of semantic circuits*

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21 The present results neither support a nonspecific holistic network approach according  
22 to which cognitive processes freely use distributed cortical resources, nor does it bolster a  
23 modular localist framework according to which semantics or concepts are bound to a single  
24 local site. Instead, the present results support what one may want to call “*specific*  
25 *distributionalism*”: Semantic and conceptual processes specific to categories of knowledge  
26 are carried by scattered neuronal circuits with specific cortical distributions in the brain.  
27 Accordingly, the cortical binding **devices** for word-related conceptual information are  
28 distributed semantic circuits spread out over specific areas in different cortical lobes. It is  
29 possible that these conceptual representations are linked into word processing circuits at one  
30 critical location, a unitary centre for semantics. However, the present data indicate that the  
31 entirety of the frontotemporal perisylvian cortex, the distributed cluster array for (**spoken and**  
32 **visual**) word form circuits (i.e., Clusters 1 and 2), is available for semantic linkage between  
33 words and concepts. This conclusion is consistent with neuroimaging work arguing for a role  
34 in semantic linkage for both temporal (Price 2000) and inferior-prefrontal cortex (Bookheimer  
35 2002). In addition, studies of degenerative brain diseases characterized by semantic deficits  
36 for action and object processing and caused by degradation of either inferiorfrontal (Bak, et al.  
37 2001) or temporal systems (Patterson, et al. 2007) further suggest the possibility of multiple  
38 semantic links between words and concepts. Our present results indicate that the areas of  
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## CATEGORY-SPECIFIC SEMANTIC CIRCUITS

general lexical and/or semantic processing are, in both inferiorfrontal and temporal cortex, localized in-between areas specifically processing semantic categories.

*Summary*

We here report evidence for scattered cortical circuits with specific distribution, which are either selectively activated by individual semantic word categories or show non-selective activation to words of different kinds. These results refute strong versions of both local modular and distributed holistic proposals of lexical and semantic processing and enforce proposals according to which distributed neuronal assemblies with specific and partly overlapping topographies carry language, concepts, and thought.

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For Peer Review

## CATEGORY-SPECIFIC SEMANTIC CIRCUITS

## TABLES

<i>A</i>	<i>B</i>	<i>C</i>	<i>D</i>	<i>E</i>	<i>F</i>	<i>G</i>	<i>H</i>	<i>I</i>	<i>J</i>
# Clust.	# <i>local</i> <i>clust.</i>	# <i>voxel</i>	Avg. <i>effect</i> <i>size</i> [ <i>t</i> ]	Overall <i>variance</i> <i>explained</i> [%]	Rank	Norm. <i>cluster</i> <i>entropy</i>	% <i>effect</i> <i>size, best</i> <i>activator</i> <i>condition</i>	% <i>effect</i> <i>size, 2<sup>nd</sup></i> <i>best</i>	Specificity/ <i>Best activator</i> <i>condition</i>
Experiment 1 (n=12)									
1	6	916	2.44	20	2	.86	31.01	30.92	nonspecific
2	9	1060	1.54	14	4	.62	45.99	43.06	nonspecific
3	16	2957	0.82	22	1	.32	85.01	9.75	face
4	14	1830	0.72	12	5	.30	87.24	8.34	arm
5	20	1437	0.80	10	6	.57	65.63	25.41	leg
6	19	3016	0.73	20	2	.25	90.94	3.32	form
Experiment 2 (n=9)									
1	5	1053	2.416	17	3	.93	31.01	28.28	nonspecific
2	15	1633	1.479	16	4	.75	41.80	37.06	nonspecific
3	17	4156	0.710	20	1	.49	76.97	7.92	face
4	21	2110	0.630	9	6	.54	75.25	10.86	arm
5	43	3685	0.635	16	4	.71	53.45	30.88	leg
6	25	4127	0.653	18	2	.46	79.10	11.48	form

Table 1: Summary of cluster analysis performed on data from Experiments 1 and 2. For each of the distributed partitions are listed (*A*) its ID number, (*B*) the number of local clusters it consisted of, (*C*) the number of its voxels, (*D*) the effect size averaged over stimulus categories, and (*E*) the percentage of the haemodynamic variance explained. (*F*) A rank index for the amount of explained variance (“rank 1” means “cluster explains most of the variance”, “rank 2” means “second most” etc.) is followed by (*G*) normalised cluster entropy, (*H*, *I*) percentage of the aggregated effect size of each cluster attributable to the most active and second most active semantic category, (*J*) specificity/non-specificity of the cluster and, for specific clusters, the best activator condition. Clusters for which maximally active categories explained more than 50% of their aggregated effect sizes were considered specific. 2 specific and 1 nonspecific clusters explain most of the variation in the data (*F*, *J*).

## CATEGORY-SPECIFIC SEMANTIC CIRCUITS

<i>Experiment 1</i>			<i>Experiment 2</i>		
	n	x / y / z	n	x / y / z	Local clusters
Cluster 1 (nonspecific - frontofusiform)			Cluster 1 (nonspecific – frontofusiform)		
L-F, triangular, opercular	595	-47/22/15	581	-49/22/16	L-F, opercular, precentral
L-T, inf., fusiform	207	-42/-44/-19	441	-45/-46/-14	L-T, inf., mid., fusiform
Cluster 2 (nonspecific - perisylvian)			Cluster 2 (nonspecific - perisylvian)		
L-F, triangular, orbital	873	-45/20/8	1226	-46/18/13	L-F, triangular, orbital
L-T, mid.	127	-53/-49/-1	288	-50/-50/-6	L-T, mid., inf.
Cluster 3 (face)			Cluster 3 (face)		
L-F, opercular, precentral	809	-49/11/16	912	-50/9/10	L-F, opercular, precentral
L-P, sup., postcentral	142	-32/-38/58	659	-38/-34/51	L-FP, pre-, postcentral
L-P, inf., postcentral	243	-44/-29/40			
L-T, mid., inf., fusiform	712	-51/-50/-3	826	-49/-50/-4	L-T, mid., inf., fusiform
R-F, triangular, opercular	710	48/22/10	866	49/21/8	R-F, triangular, opercular
Cluster 4 (arm)			Cluster 4 (arm)		
L-F, precentral	383	-32/-5/52	574	-34/-10/50	L-FP, pre-, postcentral
L-T, inf., mid.	89	-49/-51/-9	20*	-52/-52/-9	L-T, inf.
R-FP, pre-, postcentral	730	27/-17/56	181	36/-8/48	R-F, precentral
			813	7/-8/58	R-FP, pre-, postcentral
R-F, triangular	93	37/21/13	124	38/19/12	R-F, triangular, insular
Cluster 5 (leg)			Cluster 5 (leg)		
L-FP, pre-, postcentral	417	-19/-29/61	1017	-20/-26/57	L-FP, pre-, postcentral
LR-F, suppl. motor	417	0/3/56	180	0/2/58	LR-F, suppl. Motor
			167	-4/20/48	LR-F, suppl. Motor
L-T, hippocampus, parah.	237	-29/-7/-15	980	-35/-8/-11	L-T, sup., hippocampal
L-TO, lingual	69	-12/-43/-6	65	-11/-38/-10	L-TO, lingual, parah.
R-F, precentral	57	28/-19/60	181	38/-17/53	R-FP, pre-, postcentral
Cluster 6 (form)			Cluster 6 (form)		
L-F, triangular, insular	1147	-36/21/8	1051	-39/26/2	L-F, triangular, insular
L-FP, pre-, postcentral	261	-46/6/42	352	-50/-3/38	L-FP, pre-, postcentral
LR-F, suppl. motor	328	-4/20/52	166	-2/20/56	LR-F, suppl. Motor
LR-F, suppl. motor	82	1/-10/61	144	0/-14/61	LR-F, suppl. Motor
L-T, inf., fusiform	418	-32/-28/-17	987	-28/-19/-16	L-T, inf., fusiform
L-TOP	247	-33/-67/22	540	-28/-66/38	L-TOP
R-FP, pre-, postcentral	420	32/-26/53	198	38/-31/52	R-P, postcentral, mid

Table 2: Major foci of distributed clusters and their replication. For both experiments, the 6 distributed clusters are decomposed into their largest local clusters (50 voxel cut-off; \*exception). For each local cluster, its cortical gyrus/sulcus, the number of active voxels and the Talairach coordinate of its voxel with maximal effect size are listed. Replicated local clusters are shown. Standard abbreviations are used (L, R – left, right hemisphere, F – frontal, P – parietal, T – temporal, O – occipital, inf. – inferior, med. – medial, mid. – middle, parah. – parahippocampus, sup. - superior, suppl. – supplementary).

## FIGURE CAPTIONS

Figure 1: (A) Effect size explained as a function of the number  $k$  of clusters. Maximal and average effect size explained by all clusters are given as  $t$  values. Note the plateau at 6 clusters indicating that further adding clusters will not increase the variance explained. (B, C) Effect size ( $t$  values) explained by 5 different semantic word categories for each of 6 clusters. Two nonspecific clusters (1, 2; in orange and brown) can be distinguished from specific clusters, which predominantly explain variance from one semantic word category (3 in cyan – face-related words, 4 in dark purple – arm related words, 5 in yellow – leg-related words, 6 in blue – shape words). Figure parts (B) and (C) present data from Experiments 1 and 2, respectively.

Figure 2: Specifically distributed functionally coherent sets of foci as revealed by the distribution of voxels belonging to 6 distributed clusters obtained from Experiments 1 (left) and 2 (right). Neuronal assemblies revealed by two non-specific clusters (top, in orange and brown) include foci in inferiorfrontal, middle- and inferiortemporal cortex. Clusters specific to semantic categories shown in cyan, purple, yellow and blue have an even wider specific distribution. Similarity of clusters on the left and right proves excellent replicability.

Figure 3: All 6 distributed clusters obtained from Experiments 1 (left) and 2 (right) reveal functional segregation of general lexical and/or semantic processes on the one hand (brown and orange clusters) and category-specific semantic processes in frontocentral mirror neuron systems and in temporal cortex (all other colours).

CATEGORY-SPECIFIC SEMANTIC CIRCUITS

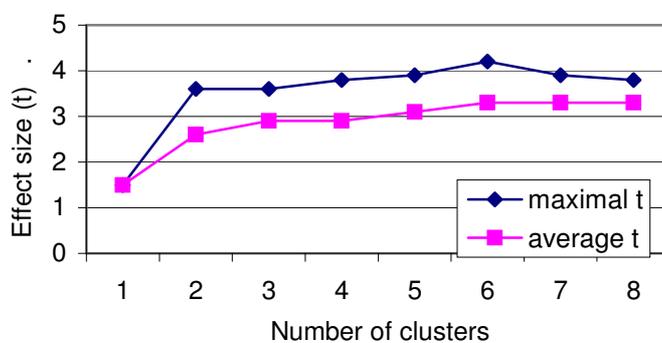


Figure 1A

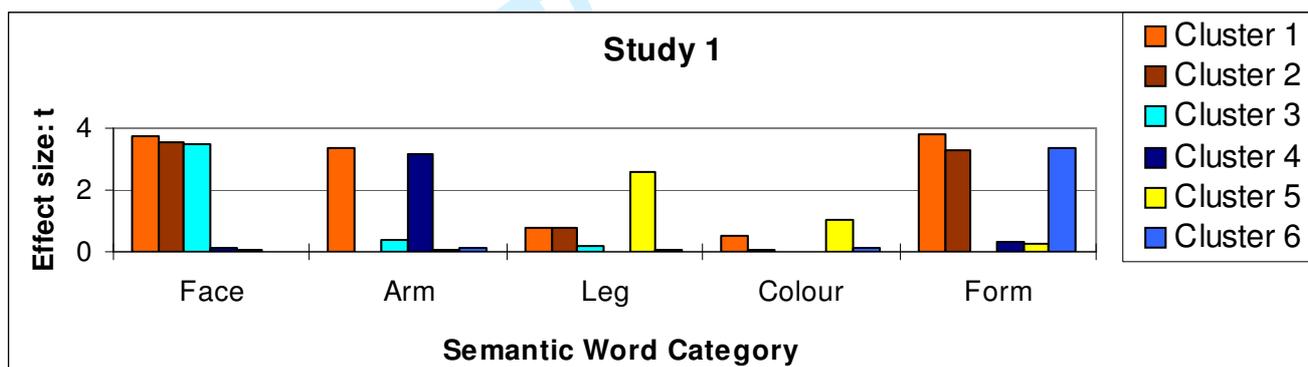


Figure 1B

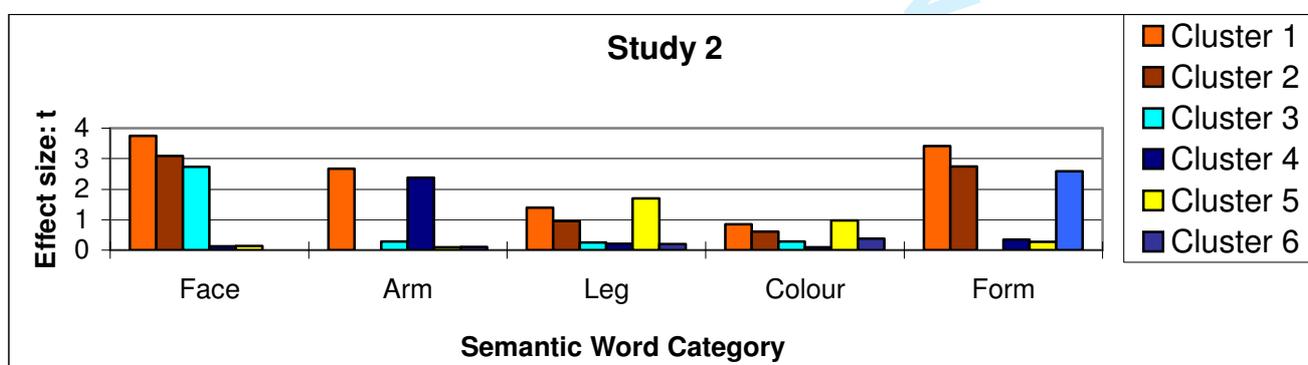


Figure 1C

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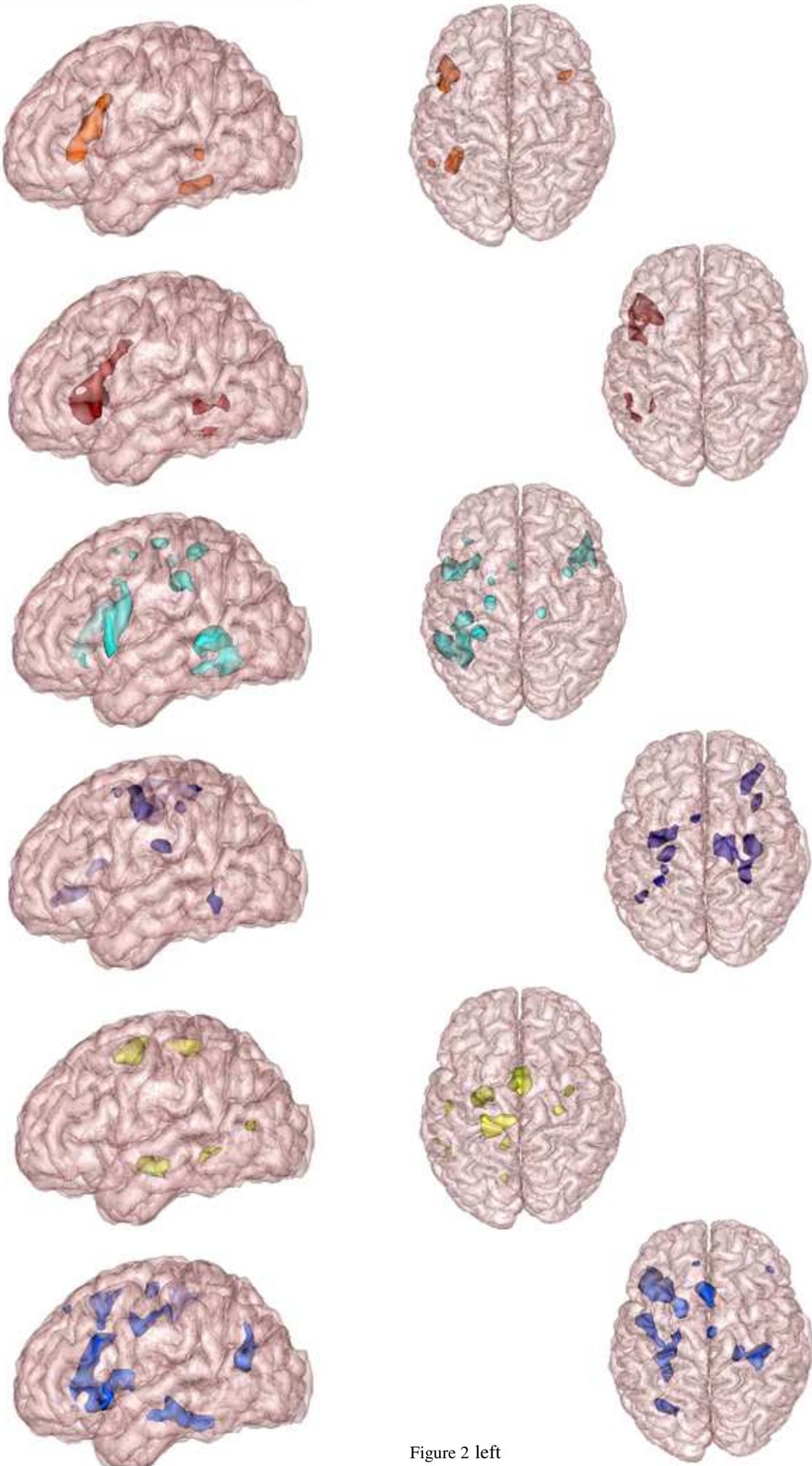
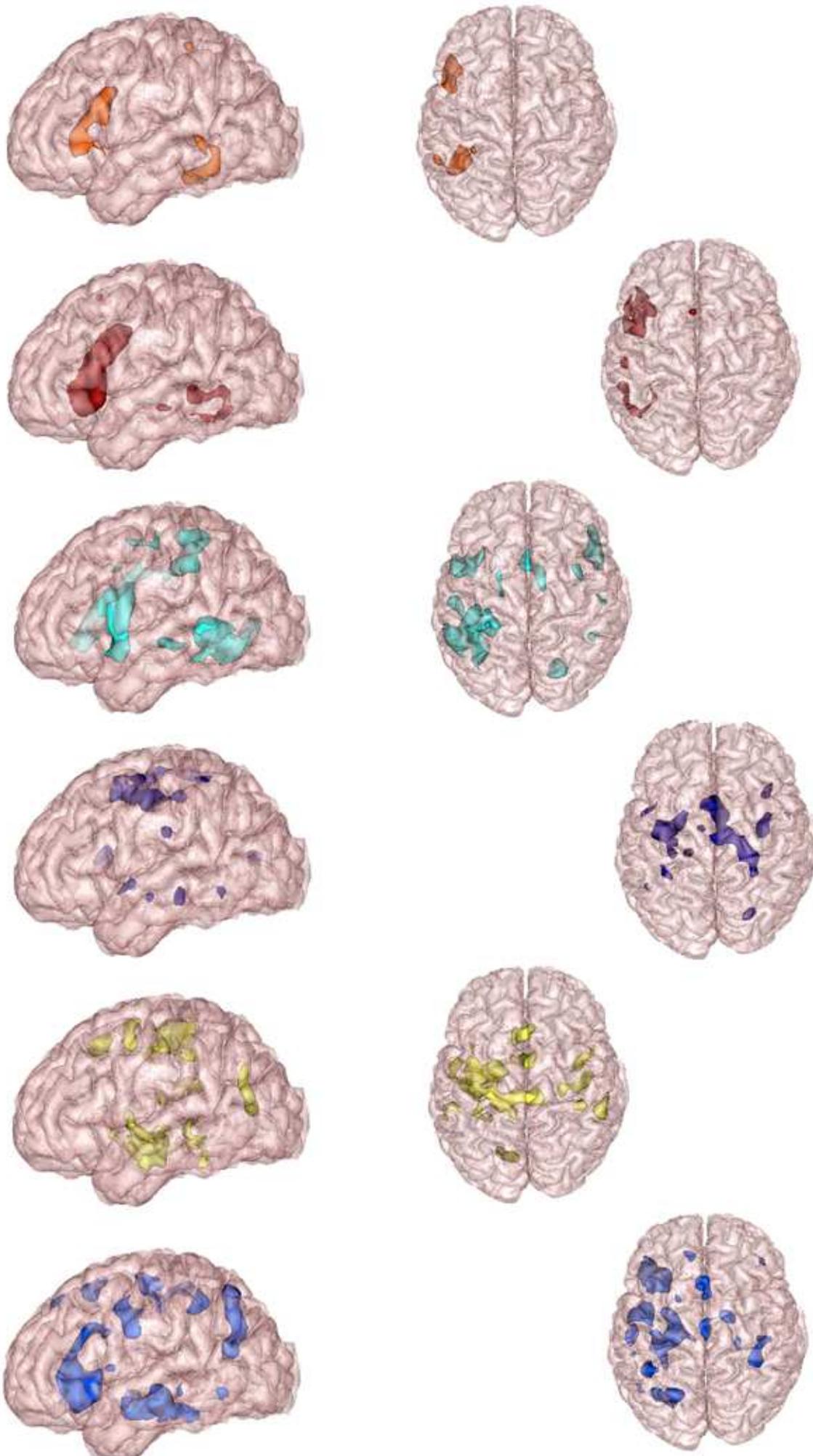


Figure 2 left

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Fig 2 right  
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CATEGORY-SPECIFIC SEMANTIC CIRCUITS

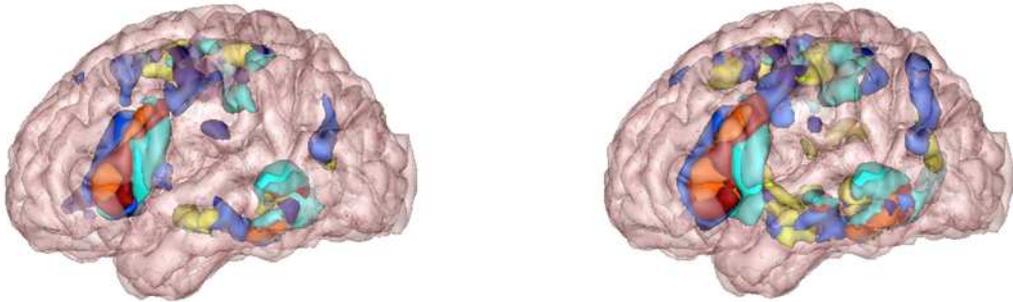


Figure 3

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