Functional magnetic resonance imaging of category-specific cortical activation: evidence for semantic maps

Manfred Spitzer a,*, Udo Kischka b, Friedemann Gückel c, Matthias E. Bellemann d, Thomas Kammer e, Soraya Seyyedi a, Matthias Weisbrod a, Andreas Schwartz f, Gunnar Brix d

a Psychiatrische Universitätsklinik, Ulm, Germany
b Rehabklinik Rheinfelden, Rheinfelden, Switzerland
c Institut für Klinische Radiologie, Klinikum Mannheim, Klinische Fakultät II der Universität Heidelberg, Heidelberg, Germany
d Forschungsschwerpunkt Radiologische Diagnostik und Therapie, Deutsches Krebsforschungszentrum (dkfz), Heidelberg, Germany
e Max-Planck-Institut für biologische Kybernetik, Tübingen, Germany
f Neurologische Klinik, Klinikum Mannheim, Klinische Fakultät II der Universität Heidelberg, Heidelberg, Germany

Accepted 6 May 1997

Abstract

Functional magnetic resonance imaging (fMRI) was used to examine the pattern of cortical activity during a picture naming task. Subjects (n = 12) had to covertly name either animals or furniture items. Functional scanning was performed using a conventional 1.5-Tesla whole-body MRI system. Images obtained during naming the two categories were compared using a non-parametric test. The study revealed evidence for domain-specific lexical regions in left middle, right middle and inferior frontal areas, as well as in superior and middle temporal areas. The results corroborate neuropsychological data and demonstrate directly and non-invasively in human volunteers that semantic representations in frontal and temporal areas are, to some degree, localized and possibly implemented as multiple maps. A completely distributed storage of semantic information is rendered unlikely.

Keywords: Functional magnetic resonance imaging (fMRI); Cortical activation; Psycholinguistics; Semantic map

1. Introduction

The study of higher cognitive functions has been greatly facilitated by the development of functional imaging techniques during the past decade. Whereas neuropsychological studies usually point to a single brain area that, when damaged, leads to the break-down of a specific function, functional methods make increasingly evident that vision, attention and language, to name three of the most intensively studied higher mental faculties, are based upon the integrated functioning of distributed cortical networks [7,16,42].

In particular, representations of high-level (supposedly semantic) information about the outside world appear to be located within large parts of the frontal and temporal lobes [10,14,22,25,26,40,53,59,61,62]. Damage to a small cortical area therefore does not usually result in deficits that are specific to certain domains. However, a number of neuropsychological studies have shown that brain damaged patients may exhibit selective impairments regarding specific semantic categories. These patients often suffered from rather extensive or diffuse lesions suggesting that multiple cortical sites must be impaired in order to produce such deficits.

Category-specific impairments are elicited during neuropsychological test sessions by means of picture naming or word comprehension tasks. Using the latter procedure, Goodglass et al. [19] found a high incidence of dissociations between semantic categories in a study of category-specific word comprehension deficits in 135 aphasic patients. The authors concluded that in aphasic patients category-specific dissociations may be the rule rather than the exception. The general frequency of category-specific deficits in neuropsychological patient populations is not yet determined, as the subsequently published papers consist mainly of case studies rather than large scale investigations (see Table 1). However, while these case studies do not allow quantitative conclusions, they provide clear-cut
Table 1
Summary of category-specific naming deficits in neuropsychological patient populations

<table>
<thead>
<tr>
<th>Category of the naming deficits</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Living things vs. inanimate objects</td>
<td>[63,65,1,39,51,48,52,30,9]</td>
</tr>
<tr>
<td>Animals</td>
<td>[20,23,4]</td>
</tr>
<tr>
<td>Indoor objects, furniture</td>
<td>[66]</td>
</tr>
<tr>
<td>Fruits and vegetables</td>
<td>[21,13]</td>
</tr>
<tr>
<td>Tools and kitchen utensils</td>
<td>[64]</td>
</tr>
<tr>
<td>Parts of the body</td>
<td>[12,47,49]</td>
</tr>
<tr>
<td>Artificial objects</td>
<td>[47,4]</td>
</tr>
</tbody>
</table>

Evidence for the existence of category-specific naming deficits.

From a neurobiological point of view, localized representations no doubt exist within (low-level) primary sensorimotor cortical areas. They are organized in a map-like manner, i.e., aspects of the topography of what is represented are preserved in brain topography [31,43,67]. Localized representations of high-level information have been inferred from intra-operative electrophysiological recordings [38]. From such recordings, it also became evident that large parts of the frontal and temporal lobes of both hemispheres are involved in the storage of high-level (possibly semantic) information (see Ref. [36] for a recent review). This is in line with neuro-imaging studies using PET (see above; for reviews, see Refs. [11,17,41,45]), suggesting that semantic processes are carried out not only in Broca’s and Wernicke’s area, but also in extended parts of the frontal and temporal cortex [61].

Within a neurocomputational framework, the spontaneous formation of semantic maps upon structured language input can be modeled by self-organizing feature maps, a type of artificial neural network which implements some principles of cortical organization (high connectivity, Hebbian learning and lateral inhibition; cf. Ref. [27]). In particular, Ritter and Kohonen [44] were able to demonstrate that self-organizing feature maps can produce semantic maps if either words and vectorized features of words, or vectorized short sentences, respectively, are provided as input. After training, similar word-meanings had become represented by adjacent nodes in the network, whereas dissimilar word-meanings were stored in distant nodes. Furthermore, semantic maps have been inferred from the results of word-association experiments, word-associations norms and lexical decision latencies in semantic priming paradigms [33,54,56].

In sum, neuropsychological, neurocomputational and psycholinguistic data suggest the existence of semantic maps, i.e., of localized representations of semantic information in the brain. If such semantic information is stored locally in the form of maps, then the differential activation of cortical regions caused by stimuli taken from different semantic domains should be detectable with the methodology of functional magnetic resonance imaging (fMRI). This latest brain imaging method has been successfully used to demonstrate cortical activation in language related tasks [2,29,46,50,55]. Like the PET studies mentioned above, these studies also provided non-invasive evidence for a rather widespread representation of language-related processes in left frontal and also in right frontal and temporal cortical areas. They also indicated considerable variance of language processing-related cortical areas between subjects.

It can be assumed that semantic maps show a great deal of interindividual variation, since their formation depends upon the experience of the individual. Hence, fMRI should be better suited to capture this variance, as it is not based upon group averages. In fact, evidence for category-specific activation was found in a pilot study carried out within a purely research fMRI environment [58]. Moreover, two recent PET studies found clear evidence for category-specific cortical activation in subjects naming animals or tools [8,28].

In the present study, we set out to test whether category-specific cortical activation can be detected with a conventional MR scanner, used in conjunction with appropriate stimulation procedures.

2. Subjects and methods

2.1. General setup

The study was carried out using a conventional MR system (see below) and additional hardware and software that allowed psychological experimentation within the scanner. The presentation of stimuli was controlled by an Apple Macintosh microcomputer, located outside the scanning room, running special purpose software (MacLab 2.0; cf. Ref. [6]) customized for each experiment. Stimuli were generated with standard image processing software (Adobe Photoshop 2.5). A videoprojector (Sharp Vision XG 3800E) was used to project the stimuli into the scanning room on a translucent screen, which could be viewed by the subject from within the scanner using prism spectacles. Stimuli were set up vertically and horizontally flipped (the manipulation is equivalent to a 180° rotation) to compensate for back-projection and prism-use. This setup allowed for viewing of stimuli obtaining a visual angle of approximately 24° in the horizontal and 12° in the vertical direction from within the scanner.

2.2. Subjects

A total of 12 subjects (nine male, three female; mean age: 30.7 years, range: 20–38 years; 10 right-handed, two left-handed) were recruited from the Heidelberg area. They had no history of neurological or psychiatric disorder and gave informed consent to the MR examination prior to the investigation.
2.3. Experimental procedure

A covert naming task was set up, in which subjects had to name 120 color pictures of either furniture and small household items or animals, displayed at a rate of one picture per 3 s. The two categories were chosen because for each of them there exists a large number of different specimen and because clinical dissociations have been found for both of them (see above). This stimulation regimen was supposed to create activity in cortical areas specifically devoted to the representation of items from these two domains. The two conditions were presented in an interleaved fashion. Each condition lasted 6 min and occurred three times, in six subjects starting with animals and in the other six subjects starting with furniture. One subject was studied twice with 2 weeks between the two sessions.

2.4. Imaging protocol

A conventional gradient system-equipped 1.5-Tesla whole-body MR system (MAGNETOM 63, Siemens, Erlangen, Germany) was used for image generation. For imaging of cortical regions, we used a circular-polarized head-coil for radio-frequency transmission and detection. Head fixation was accomplished by bi-temporal cushions and by an additional head fixation device (bitebar). To localize the planes of interest, we first acquired 19 sagittal $T_s$-weighted spin-echo images using the following acquisition parameters: repetition time $T_R = 600$ ms, echo time $T_E = 15$ ms, matrix size $MA = 128 \times 256$, field-of-view $FOV = 300$ mm, slice thickness $TH = 5$ mm and number of excitations $N_{EX} = 1$. Based on these images, four adjacent planes ($TH = 5$ mm, slice distance $SD = 0.5$ mm, $FOV = 220$ mm) were placed such that the cortical areas under investigation could be expected to be maximally included in the imaged area (see Fig. 1). We reasoned that semantic information was most likely represented in those cortical areas that traditionally have been linked with the production and comprehension of language. Hence, the slices were placed manually such that in each subject Broca’s speech area as well as Wernicke’s speech areas were covered.

For each plane under investigation, $T_s$-weighted spin-echo images ($T_R = 500$ ms, $T_E = 15$ ms, $MA = 128 \times 256$, $N_{EX} = 2$) were acquired. Thereafter, strongly $T_2^*$-weighted

Fig. 1. Left sagittal view of slice placement. For the actual determination of slice placement during the MR session, additional sagittal images were used. Numbers indicate slices for identification in subsequent figures. The orientation of the slices was such that they covered Broca’s speech area (inferior frontal gyrus, pars opercularis, Brodmann’s areas 44 and 45) as well as Wernicke’s speech area (lower part of supramarginal gyrus, angular gyrus as well as upper part of superior temporal gyrus, Brodmann’s areas 39–41).
images were generated using an optimized gradient-echo FLASH sequence at high spatial resolution (\(T_R = 240\) ms, 
\(T_E = 40\) ms, flip angle \(\alpha = 40^\circ\), \(MA = 128 \times 128\), \(N_{EX} = 4\)).

After data acquisition, the matrix size was interpolated to \(256 \times 256\) picture elements by zero-filling in the phase-encoding and read-out direction. In order to maximize the signal-to-noise ratio of the FLASH images, the acquisition scheme was set up as follows (cf. Ref. [3]): (1) the flip angle of the excitation pulse was chosen similar to the Ernst angle for gray brain matter \((\alpha_E = \arccos[\exp(-T_R/T_I)] = 40.0^\circ\) for \(T_I = 900\) ms); (2) the data sample interval was increased to 72 \(\mu\)s which allowed bandwidth reduction of the receiver lowpass filter to 13.88 kHz (\(108.5\) Hz/pixel); and (3) the shape of the total integral of the free induction decay (FID) signal was optimized by careful magnet shimming in each subject \((\Delta B_0/B_0 \leq 0.2\) ppm).

Fig. 2. Example of activation maps generated in the experiment. Slices 2 and 3 from subject 1 (a) and from subject 6 (b) are shown. In both (a) and (b), images in the top row display selective activation caused by naming animals, whereas the images at the bottom show the activity caused by naming furniture. Squares and circles indicate regions for which time courses of activation are presented in Fig. 3. Signal increase is color coded in steps of 1%.
2.5. Data analysis

Off-line analysis of image data for each subject included the following steps, performed on a DEC 3000/400 AXP workstation (Digital Equipment Corporation, Maynard, MA, USA), in the order presented below:

1. Residual movement artifacts were reduced by translating and rotating images of a given series such that superposition produced maximal image congruency (two dimensional affine image transformation).

2. The significance of differences in signal enhancement due to two different stimulus conditions was tested by applying the non-parametric Wilcoxon rank test for different median values on a pixel-by-pixel basis. The significance level was set to 0.05 in the one-tailed test, as we specifically tested only for positive differences.

3. In order to remove signal contamination due to stochastic noise in isolated pixels, data were further filtered using the following continuity criterion: In a 3 × 3 grid around an examined pixel there had to be at least five other significant pixels. It has been shown that such a cluster criterion provides considerable protection against type 1 errors [15].

4. The positive relative signal difference in significant
pixels was quantified on a scale from 1% to 5%. The hereby generated activation images display the amount of signal increase, which was color coded and overlaid onto the anatomical $T_1$-weighted spin-echo images.

3. Results

Images were analyzed by comparing the two activation conditions with each other, which resulted in images displaying rather little activation. In nine of the 12 subjects, relatively small regions in the middle and inferior frontal gyrus, as well as the superior temporal gyrus and inferior parts of the parietal lobe were identified as showing significant selective activation by either the animal naming or the furniture naming condition or both (see Fig. 2). In most cases, activation was bilateral although in some subjects we found more left lateralized activation. The two left-handed subjects showed bilateral activation.

In selectively activated cortical areas, we delineated regions-of-interest and plotted the time course of brain activity in these regions (see Fig. 3). To enhance the signal-to-noise ratio, mean values of the three data points per stimulation (taken from the three images per slice per stimulation period of 6 min) were computed.

As can be seen from Fig. 2a and from the summarizing Fig. 4, the areas activated by the two different naming conditions could often be recognized in more than one slice, which adds considerable validity to the data since the slices are processed completely independently of each other.

One subject was examined twice with two weeks between sessions in order to test for the stability of our findings over time. As can be seen from Fig. 5, several sites that had become activated during the first session also became active during the second session.

4. Discussion

Functional magnetic resonance imaging using a conventional 1.5-Tesla MR system was performed in normal volunteers to investigate cortical activation in a covert picture naming task. Subjects were scanned while they covertly named pictures of animals or furniture. Small regions of category-specific activation were found in frontal and temporo-parietal cortical areas located in horizontally oriented slices covering both Broca’s and Wernicke’s area. Since the tasks were identical except for the differences regarding categories, the results suggest that naming-induced recall of these categories involves specific small cortical regions within areas known to be involved in language processing. Moreover, the replication data obtained from one subject, while not perfect, demonstrate substantial overlap and rule out, at least for this single case, that our results are due to chance variations. Since we used a bitebar in conjunction with software motion artefact reduction strategies, our results are highly unlikely to be caused entirely by motion.

The plausibility of category-specific activation has been harshly criticized on the basis of the a priori conviction that localized semantic storage (and hence, activation) “makes effectively no sense in the context of 100 years of neuroscience” [5]. This view, however, is challenged by the results of several recent studies, as well as by the changing view of brain functioning. Firstly, as we have pointed out elsewhere [57], the results of three different studies from three different groups [8,28,58] on the cortical activation during naming tools show remarkable overlap (if not identity) of the activated cortical areas. Moreover, the large extension of semantic storage has been demonstrated in a PET study involving language processing in different modalities [61].
The existence of such map-like semantic domains is suggested by several lines of evidence, clinical, electrophysiological and computational. Though Jackson reminds us that "to locate the damage which destroys speech and localize speech are two different things" (1878; quoted from Ref. [44], p. 244), patients with domain-specific deficits due to cortical damage have been reported. Moreover, electrophysiological recordings from patients with temporal lobe epilepsy undergoing surgery have provided ample evidence in favor of highly localized cortical representations of lexical items [34,35]. In addition, the cortical architecture suggests that it functions similarly to computational self-organizing feature maps, which have been found to spontaneously generate maps of semantic input [44,60].

Taken together with the facts just mentioned, the results of the present study provide evidence of a category-specific
map-like organization of semantic representations in the middle and inferior frontal and in the superior and middle temporal cortex. With its high in-plane resolution of about 1 to 2 mm, fMRI can be expected to yield detailed pictures of semantic and other cortical maps, whose size has been estimated to be in the range of several millimeters. It should be noted, however, that the present experiment apparently pushes the methodology available to us (and to many clinicians in similar settings) to its limits. Moreover, higher cognitive tasks can hardly be expected to produce...
signals as clean as simple sensorimotor tasks. A chair may have reminded a subject of his or her chair at home on which the cat is usually sitting and a fish may have provoked the notion of an aquarium (i.e., an in-house furniture-like item). Finally, the general setup of an MRI scanner and the conditions of scanning provide a large number of distractors, which may not interfere with simple, reflex-like neural activity (as to be expected in the primary sensorimotor areas), but which almost certainly confounds active intentional thought processes such as naming.

These limitations call for the most conservative interpretation of our results. This is why we report our findings in a purely descriptive way. We neither want to imply that there exist 'centers' that store the information concerning different categories nor do we suggest similarities of our findings across subjects. Hence, we refrain from using any standard coordinate system to present our data. We merely claim that regarding semantic memory there is some form of localization. Given that every human being has a different life history and will therefore have experienced different spatio-temporal contingencies (which supposedly are the basis of cortical map formation; cf. Ref. [32]), there is no reason to believe that semantic maps should look similar in different individuals. As can be seen from Fig. 4, there appears to be no consistent pattern of categorical representations across individuals, a finding that is in line with early results from neurosurgical investigations [37].

The recent PET studies by Martin et al. [28] and by Damasio et al. [8] made stronger claims with respect to the interindividual stability of the topography of activation due to the retrieval of words for different category items. These statements appear to contradict the more cautious view just expressed. However, the stimulus material of animals and tools is particularly suited to generate activation in visual areas (when naming animals) or of motion-related areas (when naming tools) [28]. Hence, these areas were picked up by the PET technology used in both studies, relying on group averages. The studies therefore appear to be indicative of general processing strategies for specific types of information. They were not designed to reveal high-level representations in individual subjects. Moreover, the above mentioned studies found activation in lower temporal and the occipital areas which were not covered in our study and are less likely to be involved in the representation of high-level semantic information.

The fact that frontal and temporal cortical regions activated by stimuli from different semantic domains were located comparatively closely together in some of the cases in our study suggests that this pattern is due to semantic map-like representations and not due to processing strategies. Finally, the data support the view that multiple maps may exist at different cortical sites (e.g., frontal and temporal, or left and right frontal), possibly coding different high-level aspects of the categories. In the remainder of this discussion, we will address a number of systematic and methodological issues brought about by our experiment.

Not all subjects showed activation due to both categories and some subjects did not show any task-specific activation of cortical sites (cf. Fig. 4). For a number of reasons one may have to expect such a result. The generally small signal generated by cognitive tasks as well as artefacts due to head movements clearly diminish the power to detect activity-dependent changes. However, the findings are unlikely to result from motion artefacts, since we not only used a special head fixation device, but also inspected the images for motion and used a motion correction algorithm. Moreover, the patterns of activity observed do not resemble the typical rims that are caused by motion.

Since we did not use a control condition but subtracted the two activation conditions from each other, we cannot rule out category-specific deactivation as a possible cause for our results. While we are unaware of any published paper reporting such a finding, Le Bihan (Le Bihan, personal communication) has repeatedly observed category-specific frontal deactivation while subjects were performing a verbal fluency task. We have already started to address this issue using activation caused by naming items from three categories as control condition for the comparison of activation caused by naming items from one category [58]. Even if category-specific deactivation did occur, however, it would not change the general claim made in this paper, i.e., that semantic information is to some degree locally represented in the cortex.

It, furthermore, has to be kept in mind that the cortical areas involved in lexical information processing have been found to be highly variable across subjects [34,36]. As we were only able to generate images from four slices of 5-mm thickness in a reasonable amount of time (cf. Fig. 1), we simply may have missed active areas by aligning the slice planes according to standard knowledge rather than (yet unavailable) individual data. In future experiments on category-specific cortical activation, it is conceivable that first some areas are mapped out grossly and then the experiment might 'zoom in' to more specific tasks as well as more specified anatomical areas.

Finally, since it is well established that these maps are not static but rather subject to experience-driven reorganization, caused by changes of synaptic efficacy that follow Hebbian rules [18,24,32], we should expect high-level representations to be dynamic and adjustable to the experience of the subject. FMRI should be able to pick up such experience-driven changes in individual subjects.

Acknowledgements

This work was supported by a grant from the Deutsche Forschungsgemeinschaft (DFG Sp 364/1-3) and by an established investigator's award from the National Al-
liance for Research in Schizophrenia and Depression (NARSAD) to the first author.

References


