The Anatomy of Category-specific Object Naming in Neurodegenerative Diseases

S. M. Brambati1,2, D. Myers1, A. Wilson1, K. P. Rankin1, S. C. Allison1, H. J. Rosen1, B. L. Miller1, and M. L. Gorno-Tempini1

Abstract

Neuropsychological studies suggest that knowledge about living and nonliving objects is processed in separate brain regions. However, lesion and functional neuroimaging studies have implicated different areas. To address this issue, we used voxel-based morphometry to correlate accuracy in naming line drawings of living and nonliving objects with gray matter volumes in 152 patients with various neurodegenerative diseases. The results showed a significant positive correlation between gray matter volumes in bilateral temporal cortices and total naming accuracy regardless of category. Naming scores for living stimuli correlated with gray matter volume in the medial portion of the right anterior temporal pole, whereas naming accuracy for familiarity-matched nonliving items correlated with the volume of the left posterior middle temporal gyrus. A previous behavioral study showed that the living stimuli used here also had in common the characteristic that they were defined by shared sensory semantic features, whereas items in the nonliving group were defined by their action-related semantic features. We propose that the anatomical segregation of living and nonliving categories is the result of their defining semantic features and the distinct neural subsystems used to process them.

INTRODUCTION

Neuropsychological studies have shown that categorizing items is a basic operation of the semantic system. Warrington and McCarthy (1983, 1987) and Warrington and Shallice (1984) were the first to describe patients with selective semantic impairments for living but not nonliving items or vice-versa. Subsequently, many other patients with similar dissociations have been described (for a review, see Gainotti, 2000).

Various theoretical models have been proposed to explain the cognitive mechanism underlying category specificity: (1) The sensory and functional/motor theory states that categories are defined by the type of information necessary to recognize them. Living items require object-related information appreciable through perceptual channels (shape, color, sound, etc.), whereas tools and body parts are more recognizable from information concerning action, activity, or the motor scheme to use them (Martin, Ungerleider, & Haxby, 2000; Warrington & McCarthy, 1983, 1987; Warrington & Shallice, 1984); (2) The domain-specific theory suggests that evolutionary pressure has led to specific adaptations for recognizing and responding to animals and plants, but not to objects (Caramazza & Shelton, 1998); and (3) The correlated-structure principle theory proposes that conceptual organization reflects the statistical co-occurrence of the properties of objects rather than an explicit division into “living” and “nonliving” categories (Garrard, Lambon Ralph, Hodges, & Patterson, 2001; Tyler & Moss, 2001; Caramazza, Hillis, Rapp, & Romani, 1990).

The anatomical organization of category-specific semantic information is controversial. In well-documented single cases, mostly of infective or neurodegenerative etiology, patients with deficits for living items consistently showed lesions in the anterior portions of the temporal lobe (Gainotti, 2000). Large group studies have not been conducted because cerebrovascular accidents in the anterior temporal lobe are rare. Functional neuroimaging experiments in normal subjects have shown category-specific activations (Devlin et al., 2002; Cappa, Perani, Schnur, Tettamanti, & Fazio, 1998; Martin, Wiggs, Ungerleider, & Haxby, 1996; Mummery, Patterson, Hodges, & Wise, 1996; Perani et al., 1995). Although there are inconsistencies across studies, living items tend to activate predominantly posterior visual association cortices (Perani, Schnur, et al., 1999; Mummery, Patterson, Hodges, & Price, 1998; Martin et al., 1996; Perani et al., 1995). Thus, the evidence for a role of the anterior temporal lobe in the semantic processing of living objects is found in patient studies, but not in functional neuroimaging experiments. The occurrence of functional
magnetic resonance imaging (fMRI) susceptibility artifacts in the anterior temporal lobes is a possible reason for the lack of activations detected with the blood oxygen level-dependent technique. However, positron emission tomography (PET) experiments have also failed to show consistent anterior temporal activations for living item stimuli. Only a meta-analysis of seven individual PET studies (Devlin et al., 2002) found activations for living objects in the temporal poles bilaterally. This large multistudy dataset provided sufficient sensitivity to detect anterior temporal activations despite their inconsistency across subjects and lack of significance in each study taken alone.

Selective impairment for nonliving items has been described in patients with lesions in the left dorsolateral peri-sylvian regions (Gainotti, 2000). Consistently, functional neuroimaging studies found activations specific to nonliving stimuli in the left posterior middle and superior temporal gyri and the left inferior frontal cortex (Devlin et al., 2002; Gorno-Tempini, Cipolotti, & Price, 2000; Chao, Haxby, & Martin, 1999; Moore & Price, 1999a; Perani, Schnur, et al., 1999; Cappa et al., 1998; Mummery et al., 1998; Damasio, Grabowski, Tranel, Hichwa, & Damasio, 1996; Martin et al., 1996; Mummery et al., 1996).

In the present study, we investigated the anatomical organization of processing different categories of stimuli in a group of patients affected by neurodegenerative disease. We used voxel-based morphometry (VBM) on structural MRI images to correlate accuracy scores in a picture-naming task with gray matter volumes in each voxel. The semantic features that normal subjects used to define each of our stimuli have been studied extensively (Garrard et al., 2001). This allowed us to interpret our anatomical findings not only on the basis of category-dependence but also in relation to the type of semantic features typical of each category. Furthermore, we included patients with known damage to the anterior temporal lobe (such as semantic dementia [SD] and Alzheimer’s disease [AD]) and used a structural neuroimaging technique that is not affected by artifacts in this region. Thus, we were able to investigate the role of the anterior temporal lobe in processing different semantic categories.

METHODS
Subjects
MRI images were collected from a group of 152 subjects (age range 35–95, mean age 65.3) including 64 women and 88 men evaluated at the University of California San Francisco (UCSF) Memory and Aging Center.

Demographic and clinical variables are reported in Table 1. Subjects were grouped into three categories: those with primary progressive aphasia (PPA, n = 40; Mesulam, 1982), those with neurodegenerative disease who did not meet criteria for PPA (non-PPA, n = 77), and clinically normal subjects (NS, n = 55). The PPA group was composed of patients with progressive non-fluent aphasia (PNFA, n = 14), semantic dementia (SD, n = 20), and logopenic progressive aphasia (LPA, n = 6) (Gorno-Tempini, Dronkers, et al., 2004). For the purposes of statistical analysis of demographic and naming data, patients with PNFA and LPA were considered as a single group called “primary progressive aphasia without semantic dementia” (PPA w/o SD) and patients with SD were grouped in a single category called “semantic dementia” (SD).

### Table 1. Demographic Characteristics of the Subjects Included in this Study

<table>
<thead>
<tr>
<th></th>
<th>NS (n = 35)</th>
<th>AD (n = 19)</th>
<th>CBD/PSP/DLB (n = 12)</th>
<th>FTD (n = 27)</th>
<th>MCI (n = 10)</th>
<th>MNRC (n = 9)</th>
<th>PPA w/o SD (n = 20)</th>
<th>SD (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>65.2 (11.4)</td>
<td>68.1 (8.9)</td>
<td>68.3 (9.3)</td>
<td>59.9 (6.1)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>73.5 (9.0)</td>
<td>68.4 (16.0)</td>
<td>64.5 (9.3)</td>
<td>63.6 (6.7)</td>
</tr>
<tr>
<td>Male/Female</td>
<td>13/22</td>
<td>14/5</td>
<td>8/4</td>
<td>22/5</td>
<td>4/6</td>
<td>4/5</td>
<td>8/12</td>
<td>15/5</td>
</tr>
<tr>
<td>MMSE</td>
<td>29.6 (0.6)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>17.8 (7.0)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>24.6 (4.0)</td>
<td>25.5 (3.8)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>29.0 (1.4)</td>
<td>29.0 (1.1)&lt;sup&gt;e&lt;/sup&gt;</td>
<td>24.4 (5.0)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>22.4 (6.8)</td>
</tr>
<tr>
<td>CDR</td>
<td>0.0 (0.0)&lt;sup&gt;f&lt;/sup&gt;</td>
<td>1.0 (0.6)&lt;sup&gt;d,g&lt;/sup&gt;</td>
<td>0.6 (0.6)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>1.0 (0.5)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>0.5 (0.0)</td>
<td>0.4 (0.2)</td>
<td>0.6 (0.5)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>0.9 (0.7)&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Education</td>
<td>16.9 (2.8)</td>
<td>15.3 (3.4)</td>
<td>16.3 (2.8)</td>
<td>15.3 (2.8)</td>
<td>15.3 (2.0)</td>
<td>16.6 (3.0)</td>
<td>15.3 (2.0)</td>
<td>16.9 (2.9)</td>
</tr>
</tbody>
</table>

NS = clinically normal subjects; AD = Alzheimer’s disease; PSP/CBD/DLB = patient with dementia and predominant motor symptoms (progressive supranuclear palsy, corticobasal degeneration, dementia with Lewy bodies); FTD = frontotemporal dementia; MCI = mild cognitive impairment; MNRC = patients that did not meet any research criteria; PPA w/o SD = primary progressive aphasia without semantic dementia patients; SD = semantic dementia; MMSE = Mini-Mental State Examination; CDR = Clinical Dementia Rating.

<sup>a</sup>p < .05 vs. MCI.

<sup>b</sup>p < .05 vs. AD, CBD/PSP/DLB, PPA w/o SD, SD.

<sup>c</sup>p < .05 vs. each of the other groups.

<sup>d</sup>p < .05 vs. NS.

<sup>e</sup>p < .05 vs. SD.

<sup>f</sup>p < .05 vs. each of the other groups but MCI.

<sup>g</sup>p < .05 vs. MNRC.
out semantic dementia” (PPA w/o SD). The SD group was considered separately because these patients’ naming scores were expected to be lower than those of any other group (Gorno-Tempini, Dronkres, et al., 2004; Galton et al., 2001; Hodges, Bozeat, Lambon Ralph, Patterson, & Spatt, 2000; Lambon Ralph, Graham, Ellis, & Hodges, 1998). The non-PPA group included patients with AD (n = 19), mild cognitive impairment (MCI, n = 10), frontotemporal dementia (FTD, n = 27), dementias with predominant motor symptoms (PSP/CBD/DLB, n = 12), and patients that did not meet any published research criteria (MNRC, n = 9).

All participants underwent a neuropsychological screening battery as previously described (Gorno-Tempini, Dronkers, et al., 2004; Rosen et al., 2002). General intellectual function was assessed using the Mini-Mental State Examination (MMSE) (Folstein, Folstein, & McHugh, 1975), and functional status was tested using the Clinical Dementia Rating Scale (CDR) (Morris, 1993).

Statistical analyses were performed with SPSS 12.0 for Windows (release 12.0.0, SPSS, Chicago, IL). The study was approved by the UCSF committee on human research. All subjects provided written informed consent before participating.

**Naming Test**

All subjects were administered a picture-naming test consisting of a set of stimulus items from the black-and-white line drawing corpus by Snodgrass and Vanderwart (1980). The battery included 64 items selected to represent concepts belonging to living and nonliving categories (Bozeat, Lambon Ralph, Patterson, Garrard, & Hodges, 2000). The living stimuli included eight items belonging to each of the following categories: domestic land animals, foreign land animals, fruits, and birds. The nonliving stimuli included eight items belonging to each of the following categories: small household items, large household items, vehicles, and tools. Living and nonliving stimuli were matched for visual complexity (two-sample t test: t = 1.682, ns) (Snodgrass & Vanderwart, 1980), whereas the subcategories of fruit and domestic animals, vehicles and large household items, and tools and small household items were matched for familiarity (Snodgrass & Vanderwart, 1980).

Black-and-white line drawings were reproduced on white horizontally oriented sheets of paper and were presented one-at-a-time to the participants. Subjects were instructed to name each picture as unambiguously as possible using no more than one word. Participants were given as much time as they needed to respond.

We employed this particular set of stimuli because their semantic characteristics have been investigated in a previous study by Garrard et al. (2001). In their study, the authors asked a group of 20 normal volunteers to provide semantic properties associated with the stimuli, which were subsequently classified as sensory or functional. Therefore, a “feature database” of this set of items is available and it is particularly useful to investigate the relationship between concept semantic knowledge and type of feature knowledge (sensory and functional) associated with the stimuli.

**Statistical Analysis of Behavioral Data**

Statistical analyses were conducted to assess group differences in overall naming accuracy and in naming accuracy for each category (see Table 2).

To test for group differences in total naming accuracy, we used a univariate analysis of variance (General Linear Model), in which we entered the sum of scores across all subcategories as the dependent variable, and diagnostic group (NS, AD, CBD/PSP/DLB, MCI, FTD, MNRC, PPA w/o SD, or SD) as a fixed factor. Total naming score varied significantly across groups [F(7,144) = 58.44, p < .001]. Tukey’s method was used for post hoc pairwise comparisons. Post hoc analysis revealed significant lower naming performance in SD and AD patients when compared to all the other groups.

**Table 2.** Means and Standard Deviations of Naming Test Scores Grouped by Clinical Diagnosis

<table>
<thead>
<tr>
<th></th>
<th>NS (n = 35)</th>
<th>AD (n = 19)</th>
<th>CBD/PSP/DLB (n = 12)</th>
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</thead>
<tbody>
<tr>
<td>Total Naming</td>
<td>62.5 (1.8)</td>
<td>49.5 (13.2)</td>
<td>61.0 (4.2)</td>
<td>58.8 (7.4)</td>
<td>61.0 (2.7)</td>
<td>60.3 (3.9)</td>
<td>58.6 (4.1)</td>
<td>19.6 (16.0)</td>
</tr>
<tr>
<td>Mean nonliving</td>
<td>7.9 (0.2)</td>
<td>6.2 (1.6)</td>
<td>7.7 (0.4)</td>
<td>7.6 (0.7)</td>
<td>7.7 (0.3)</td>
<td>7.6 (0.5)</td>
<td>7.4 (0.6)</td>
<td>2.9 (2.2)</td>
</tr>
<tr>
<td>Mean all living</td>
<td>7.8 (0.3)</td>
<td>6.1 (1.9)</td>
<td>7.6 (0.7)</td>
<td>7.1 (1.2)</td>
<td>7.6 (0.4)</td>
<td>7.5 (0.5)</td>
<td>7.3 (0.6)</td>
<td>2.0 (1.8)</td>
</tr>
<tr>
<td>Mean living matched by familiarity</td>
<td>7.8 (0.3)</td>
<td>6.6 (1.6)</td>
<td>7.6 (0.8)</td>
<td>7.3 (1.1)</td>
<td>7.8 (0.3)</td>
<td>7.6 (0.5)</td>
<td>7.6 (0.5)</td>
<td>2.9 (2.5)</td>
</tr>
<tr>
<td>Mean living not matched by familiarity</td>
<td>7.7 (0.4)</td>
<td>5.7 (2.3)</td>
<td>7.5 (0.7)</td>
<td>6.8 (1.5)</td>
<td>7.3 (0.6)</td>
<td>7.4 (0.6)</td>
<td>6.9 (1.0)</td>
<td>1.0 (1.5)</td>
</tr>
</tbody>
</table>

*p < .05 vs. each of the other groups in pairwise comparisons.

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<td>7.6 (0.5)</td>
<td>7.6 (0.5)</td>
<td>2.9 (2.5)</td>
</tr>
<tr>
<td>Mean living not matched by familiarity</td>
<td>7.7 (0.4)</td>
<td>5.7 (2.3)</td>
<td>7.5 (0.7)</td>
<td>6.8 (1.5)</td>
<td>7.3 (0.6)</td>
<td>7.4 (0.6)</td>
<td>6.9 (1.0)</td>
<td>1.0 (1.5)</td>
</tr>
</tbody>
</table>

*p < .05 vs. each of the other groups in pairwise comparisons.

*pp < .05 vs. each of the other groups in pairwise comparisons, except FTD.
To look for category effects, we used a repeated measures design (General Linear Model) and entered the mean scores for naming living (fruits, birds, domestic and foreign animals) and nonliving (small household items, large household items, vehicles, and tools) subcategories as a two-level within-subjects factor, and diagnostic group as a between-subjects factor. Results showed a significant main effect of category \([F(1,144) = 21.09, p < .001]\), group \([F(7,144) = 58.44, p < .001]\), and category by group interaction \(F(7,144) = 4.6, p < .001\). Subjects named significantly fewer living than nonliving items. SD groups showed greater deficits for living compared with nonliving items. However, these results were confounded by familiarity differences.

To look for category effects that were not confounded by familiarity, we used a repeated measures design with mean score on familiarity-matched living and nonliving categories as the within-subjects factor, and diagnostic group as the between-subjects factor. Results showed a significant main effect of group \([F(7,144) = 45.8, p < .001]\), but no main effect of category \([F(1,144) = 0.1, p = .715]\) and a trend toward a category by group interaction \(F(7,144) = 1.9, p = .07\).

Taken together, behavioral data showed that when living and nonliving categories were matched by familiarity, no significant category effect was observed between and within diagnostic groups.

### Neuroimaging Data

MRI scans were obtained on a 1.5-T Magnetom VISION system (Siemens, Iselin, NJ). A volumetric magnetization prepared rapid gradient-echo MRI (MPRG, \(TR/TE/TI = 10/4/300\) msec) was used to obtain T1-weighted images of the entire brain, 15-degree flip angle, coronal orientation perpendicular to the double spin-echo sequence, 1.0 \times 1.0\ mm in-plane resolution, and 1.5 mm slab thickness.

### Voxel-based Morphometry Analysis

VBM analysis included two steps: spatial preprocessing (normalization, segmentation, Jacobian modulation, and smoothing) and statistical analysis. Both steps were implemented in the SPM2 software package (Wellcome Department of Imaging Neuroscience, London; www.fil.ion.ucl.ac.uk/spm) running on Matlab 6.5.1 (MathWorks, Natick, MA).

MRI images were preprocessed using an optimized method for the spatial normalization of gray matter (Good et al., 2001). Ad hoc template and a priori images were created by averaging 30 age-matched normal control scans that had been normalized and segmented in the Montreal Neurological Institute (MNI) stereotaxic space.

A two-step segmentation procedure was applied to each scan included in this analysis. First, T1-weighted images were segmented in native space. Each gray matter image was then normalized to the gray matter template. Parameters obtained from gray matter normalization were then applied to the original T1 images. Finally, the normalized images were segmented again into gray matter, white matter, and cerebrospinal fluid. Gray matter voxel values were multiplied by the Jacobian determinants derived from the spatial normalization step (Jacobian modulation) to preserve the initial volumes. Modulated gray matter images were then spatially smoothed with a 12-mm full-width half-maximum isotropic Gaussian kernel.

The VBM technique has been validated in neurodegenerative disease by comparing results in AD and SD with findings of classical region-of-interest manual tracing, the gold standard for in vivo quantitative assessment of gray matter atrophy (Good et al., 2002). However, VBM has limitations, such as possible misregistration between subjects, and is not capable of providing any information about the molecular mechanism underpinning gray matter volume loss in different diseases. In this study, patients with heterogeneous naming scores and with different patterns of gray matter atrophy were included to provide variability in the sample, and thus, increase the power of the correlation analysis.

A covariate-only statistical model was used to correlate naming scores and gray matter volumes. All subjects were entered as a single group regardless of clinical diagnosis (see Figure 1 for specific design matrices). Different types of neurodegenerative diseases are characterized by distinctive cognitive and neurological manifestations and are associated with specific patterns of gray matter atrophy, as revealed by previous VBM studies (Boxer et al., 2006, 2003; Boccardi et al., 2005; Gorno-Tempini, Dronkers, et al., 2004; Burton, et al., 2002; Chetelat et al., 2002; Good et al., 2002; Rosen et al., 2002; Baron et al., 2001; Chan et al., 2001; Galton et al., 2001; Mummery et al., 1999). We accounted for global level of atrophy by scaling each image by its total gray matter volume. Age and gender were entered as nuisance covariates. The significance of each effect of interest was determined using the theory of Gaussian fields. We accepted a statistical threshold of \(p < .05\) (SPM family-wise error [FWE], corrected for multiple comparisons).

Two different statistical models were implemented to assess the global effect of total naming score (General Naming Effect) and the unique effects of category scores (Category-specific Naming Effect).

#### General Naming Effect

To look for general naming effect, we used the sum of naming scores of all subcategories as a single covariate (see design matrix in Figure 1A). The general naming effect was tested using a \([1] t\)-contrast, assuming that decreasing naming abilities would be associated with decreased gray matter volumes.
In order to investigate effects that were unique to each category of stimuli and not confounded by familiarity, we entered naming scores for domestic animal, large and small household items, vehicle, fruit, and tool subcategories as covariates (see design matrices in Figure 1B and C). Foreign animals and birds were excluded from the analysis. The threshold for display is $p < .001$, uncorrected. Maps of significant correlation are superimposed on axial sections of the unsmoothed template image and on the 3-D rendering of the MNI standard brain. The coordinates of the sections correspond to the peak of each significant effect (see Table 3).

**Figure 1.** Brain areas that positively correlate with: (A) total naming score; (B) living scores; (C) nonliving scores. Design matrices and contrasts are displayed for each analysis. The threshold for display is $p < .001$, uncorrected. Maps of significant correlation are superimposed on axial sections of the unsmoothed template image and on the 3-D rendering of the MNI standard brain. The coordinates of the sections correspond to the peak of each significant effect (see Table 3).

**Category-specific Naming Effect**

In order to investigate effects that were unique to each category of stimuli and not confounded by familiarity,
this analysis because of familiarity differences (see the Behavioral Results section). The following contrasts were performed:

1. **Living.** The unique effect for living subcategories (i.e., domestic animals and fruits) was tested using a \([1 0 0 1 0 0]\) \(t\)-contrast. This contrast revealed brain regions in which higher naming scores for living items corresponded to greater regional gray matter volumes.

2. **Nonliving.** The unique effect for nonliving subcategories (i.e., tools, vehicles, and large and small household items) was tested using a \([0 1 1 1 0 1]\) \(t\)-contrast. This contrast revealed brain regions in which higher naming scores for nonliving items corresponded to greater regional gray matter volumes.

3. **Manipulability.** This contrast was performed to test the hypothesis that manipulable objects rely on unique neural systems because their recognition depends upon activation of motor schemes necessary to grasp and manipulate them (sensory/motor theory; Martin et al., 2000). The unique effect for manipulable subcategories (small household items, tools) were tested using a \([0 0 1 0 0 1]\) \(t\)-contrast. This contrast revealed brain regions in which higher naming score for manipulable items corresponded to greater regional gray matter volumes.

## RESULTS

### Neuroimaging Results

#### General Naming Effect

There was a significant positive correlation between accuracy in naming scores and gray matter volumes in the bilateral superior and inferior temporal gyri, anterior fusiform gyri and hippocampi, and in the left parahippocampal gyrus, middle temporal gyrus and temporal pole, \((p < .05, \text{FWE corrected for multiple comparisons})\) (Table 3 and Figure 1A).

<table>
<thead>
<tr>
<th>Table 3. Results of the VBM Correlation Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Brain Region (Brodmann’s Area)</strong></td>
</tr>
<tr>
<td>---------------------------------------------</td>
</tr>
<tr>
<td><strong>Global Naming Effect</strong></td>
</tr>
<tr>
<td>L Antero-mesial temporal pole: parahippocampus</td>
</tr>
<tr>
<td>L Superior temporal gyrus (BA 22)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>L Hippocampus</td>
</tr>
<tr>
<td>L Fusiform gyrus (BA 20)</td>
</tr>
<tr>
<td>L Inferior temporal gyrus (BA 20)</td>
</tr>
<tr>
<td>L Temporal pole</td>
</tr>
<tr>
<td>L Middle temporal gyrus (BA 20/21)</td>
</tr>
<tr>
<td>R Fusiform gyrus (BA 20)</td>
</tr>
<tr>
<td>R Superior temporal gyrus (BA 22)</td>
</tr>
<tr>
<td>R Hippocampus</td>
</tr>
<tr>
<td>R Inferior temporal gyrus (BA 20)</td>
</tr>
</tbody>
</table>

| **Category-specific Naming Effects**        |       |       |       |             |             |
| Living                                      |       |       |       |             |             |
| R Antero mesial temporal pole: parahippocampus | 17    | 1     | \(-28\) | 5.1         | 4.9         |

| Nonliving                                   |       |       |       |             |             |
| L Posterior middle temporal gyrus (BA 20/21/37) | \(-69\) | \(-35\) | \(-3\)  | 5.2         | 4.9         |
|                                             | \(-54\) | \(-28\) | \(-9\)  | 5.2         | 4.8         |
|                                             | \(-43\) | \(-58\) | 13     | 4.9         | 4.7         |

Threshold of significance is \(p < .05\) (FWE corrected for multiple comparisons).
Category-specific Naming Effects

Living. Accuracy in naming living subcategories (domestic animals and fruits) significantly correlated with gray matter volumes in the right antero-mesial temporal pole at the level of the parahippocampal gyrus ($p < .05$, FWE corrected for multiple comparisons) (Table 3 and Figure 1B). The relationship between gray matter volume and naming scores in domestic animal and fruit subcategories at the peak voxel is reported in Figure 2A.

The right anterior temporal lobe area that correlated with performance in naming living items was located in a region that is commonly atrophied in SD (Gorno-Tempini, Dronkers, et al., 2004; Good et al., 2002; Rosen et al., 2002; Chan et al., 2001; Galton et al., 2001; Mummery et al., 1999), raising the question of a diagnosis-related effect. However, because atrophy in SD is predominantly left-sided (Gorno-Tempini, Dronkers, et al., 2004; Good et al., 2002; Chan et al., 2001; Mummery et al., 1999), an SD group effect alone cannot explain the results. Furthermore, removal of SD patients from the analysis did not eliminate the positive correlation between accuracy in naming living objects and gray matter volume in the right medial-temporal pole; in fact, the correlation persisted, albeit at a predictably lower level of significance ($p < .004$, uncorrected).

Nonliving. Accuracy in naming nonliving subcategories (vehicles, tools, small and large household items) significantly correlated with gray matter volume in the posterior portion of the left middle temporal gyrus ($p < .05$, FWE corrected for multiple comparisons) (Table 3 and Figure 1C). The relationships between gray matter volume and naming scores in tool, vehicle, large and small subcategories at the peak voxel is reported in Figure 2B.

Figure 2. Relationships between gray matter volumes in arbitrary units ($y$-axis) and living (A) and nonliving (B) subcategory naming scores ($x$-axis) at the peak voxel for each category.
Manipulability. Accuracy in naming manipulable subcategories (small household items and tools) did not significantly correlate with gray matter volume in any regions at the pre-established threshold \( (p < .05, \text{FWE corrected for multiple comparisons}) \). Furthermore, the inclusion of the fruits as an additional manipulable subcategory did not significantly change the result.

To verify whether category-specific naming results could be influenced by disease severity, we reran the correlation analysis entering the MMSE score as a confounding variable. The correlation between gray matter volume and living accuracy in the medial-temporal pole was still significant at a threshold of \( p < .05, \text{FWE corrected} \). The left posterior middle temporal result for nonliving items was still present at a threshold of \( p < .2, \text{FWE corrected} \) \((p < .001, \text{uncorrected})\). These findings suggest that category-specific naming effects cannot be ascribed to disease severity.

DISCUSSION

We correlated accuracy in naming different categories of stimuli with voxelwise gray matter volumes in more than 100 patients with neurodegenerative diseases using VBM. We found that greater accuracy in naming living items corresponds to greater gray matter volume in the right anterior temporal lobe, whereas better performance in naming nonliving items positively correlates with the amount of gray matter in the left posterior middle temporal gyrus. No region specifically correlates with naming manipulable items. We discuss these category-related anatomical results in relation to semantic processing because neuropsychological studies have shown that categorical effects most often arise at the semantic rather than lexical level of processing (Capitani, Laiacona, Mahon, & Caramazza, 2003; Gainotti, 2000; but see also Damasio, Tranel, Grabowski, Adolphs, & Damasio, 2004).

This study indicates that the right anterior temporal lobe is involved in processing living items. This result is consistent with previous single case studies in patients with a deficit for living items who show bilateral anterior temporal damage (Gainotti, 2000). However, our findings point to a greater role of the right-sided anterior temporal region. The living stimuli used in this study were characterized by shared sensory semantic features (e.g., “eagle has wings,” “horse has a tail”), suggesting that the right anterior temporal lobe might be involved in processing this type of feature more than the category of living items per se. If this was the case, then the same region should be involved in processing other stimuli that are characterized by shared sensory features such as familiar faces, and patients with right anterior temporal lobe damage should show deficits in recognizing both living items and familiar faces. Although isolated right-sided anterior temporal lobe lesions are rare, patients with relatively focal right anterior temporal lobe damage have been shown to have difficulty in recognizing familiar people (Gorno-Tempini, Rankin, et al., 2004; Gainotti, Barbier, & Marra, 2003; Joubert et al., 2003; Spierer & Spinnler, 2003; Gentileschi, Spierer, & Spinnler, 2001; Kitchener & Hodges, 1999; Hanley, Young, & Pearson, 1989). When investigated, most of these patients also showed at least a trend toward a greater deficit in recognizing living than nonliving items (Gorno-Tempini, Rankin, et al., 2004; Joubert et al., 2003; Kitchener & Hodges, 1999; Hanley et al., 1989). Therefore, our data and single case lesion studies point to a role of the right anterior temporal lobe in processing not categorical knowledge per se, but stimuli that have in common the fact that they are characterized by shared sensory semantic features. This region could operate as a “convergence zone” (Damasio et al., 2004), which is necessary for the identification of items for which the integration of overlapping sensory semantic characteristics is necessary for recognition. However, functional neuroimaging studies have not consistently pointed to the anterior temporal lobes as crucial sites for recognizing living items. PET and fMRI studies have instead demonstrated significant activation of more posterior visual association regions (Perani, Schnur, et al., 1999; Mummery et al., 1998; Martin et al., 1996; Perani et al., 1995). Various factors could have determined this more posterior pattern of activations: greater visual complexity of living compared to nonliving objects, susceptibility of the fMRI technique to artifacts in the anterior temporal regions, and intersubject variability. Consistent with this view, Devlin et al. (2002) found living-related anterior temporal activations only when they compiled data from seven different PET studies (Phillips, Noppeney, Humphreys, & Price, 2002; Gorno-Tempini et al., 2000; Moore & Price, 1999a, 1999b; Mummery et al., 1998, 1999) because activations of the temporal poles were not strong or consistent enough to be identified in each individual study.

Our results show that the left posterior middle temporal gyrus is specifically involved in processing nonliving items. This finding is consistent with neuropsychological studies showing left hemispheric lesions in patients with selective deficits in processing nonliving items (Gainotti, 2000). It also supports functional neuroimaging studies showing activation in this area for nonliving objects (Devlin et al., 2002; Chao et al., 1999; Cappa et al., 1998; Mummery et al., 1996, 1998; Damasio et al., 1996; Martin et al., 1996). Garrard et al. (2001) showed that the nonliving items that we used in this study were characterized by “functional” action-related features describing an action, activity, or use of an item (for instance, “a suitcase can be carried,” “an airplane can fly”), suggesting that the left posterior middle temporal gyrus is
involved in processing action-related information more than nonliving objects as a category. Consistently, several functional neuroimaging studies found this area activated not only for nonliving items but also in semantic tasks involving actions and/or action verb stimuli, such as picture naming of actions (Damasio et al., 2001), passive listening to sentences describing actions (Tettamanti et al., 2005), and generation of action words (Martin, Haxby, Lalonde, Wiggs, & Ungerleider, 1995). In our study, manipulability did not seem to play a major role in determining anatomical segregation because small household items and tools did not show a differential effect. Furthermore, we did not find the premotor involvement for nonliving objects that were previously reported in neuroimaging studies (Vitali et al., 2005; Chao & Martin, 2000; Martin et al., 1996). To show this effect, tasks that tap into the execution phase of actions more directly might be necessary.

In conclusion, this neuroanatomical study of category specificity in patients with neurodegenerative diseases suggests that living and nonliving objects are processed by segregated neural systems, as predicted by major theoretical models concerning category specificity (Caramazza & Shelton, 1998; Warrington & Shallice, 1984). The study suggests that the neuroanatomical segregation of living and nonliving categories arises not from an explicit division of conceptual knowledge but from the semantic features of the categories themselves and the distinct semantic neural subsystems necessary to process them.

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