The naming impairments in Alzheimer’s disease (AD) have been attributed to a variety of cognitive processing deficits, including impairments in semantic memory, visual perception, and lexical access. To further understand the underlying biological basis of the naming failures in AD, the present investigation examined the relationship of various classes of naming errors to regional brain measures of cerebral glucose metabolism as measured with 18 F-Fluoro-2-deoxyglucose (FDG) and positron emission tomography (PET). Errors committed on a visual naming test were categorized according to a cognitive processing schema and then examined in relationship to metabolism within specific brain regions. The results revealed an association of
semantic errors with glucose metabolism in the frontal and temporal regions. Language access errors, such as circumlocutions, and word blocking nonresponses were associated with decreased metabolism in areas within the left hemisphere. Visuoperceptive errors were related to right inferior parietal metabolic function. The findings suggest that specific brain areas mediate the perceptual, semantic, and lexical processing demands of visual naming and that visual naming problems in dementia are related to dysfunction in specific neural circuits. © 1999 National Academy of Neuropsychology. Published by Elsevier Science Ltd

INTRODUCTION

Impaired naming is frequently observed in patients with Alzheimer’s disease (AD). A prevailing notion is that confrontation naming errors are attributable to a breakdown in the structure of semantic memory (Bayles & Tomoeda, 1983; Huff, Corkin, & Growdon, 1986; Martin & Fedio, 1983; Schwartz, Marin, & Saffran, 1979; Smith, Murdoch, & Chenery 1989). Other investigations ascribe naming deficits to a failure in perceptual processing, word-finding, semantic processing, or their combination (Barker & Lawson, 1968; Frank, McDade, & Scott, 1996; Goldstein, Green, Presley, & Green, 1992; Kirshner, Webb, & Kelly, 1984; Rochford, 1971). Evidence for a primary role of semantic processing and access in the naming deficit of AD is summarized by Tippett and Farah (1994). Their model supports a theory that injury to any of several cognitive processing units may lead to naming difficulties, but that a central deficit in accessing semantic information may be more critical for the naming impairment of AD dementia. Another study, using a taxonomy for the various types of errors committed in naming visual objects, found that AD patients made predominantly semantic errors but that visual errors were also common, particularly as the disease progresses (Hodges, Salmon, & Butters, 1991). Given the tremendous heterogeneity in the AD process (see Cummings & Benson, 1992 for review), it is conceivable that there are many different sources of naming failures in AD, due to the number of neural systems compromised by the disease.

Several lines of evidence suggest that many neural areas with differing cognitive functions are involved in naming performance. First, in cases of circumscribed neuronal changes (as occurs with Pick’s disease) impaired naming has been typically observed following damage of the left temporal and frontal lobes, particularly the anterior portion of the temporal pole (Graff-Radford et al., 1990). Deficits also arise following focal insult to the right hemisphere, although the profile of impairment is quite different from that of left hemisphere injury and includes frequent perceptual errors (Riddoch & Humphreys, 1987). Functional imaging studies done in normal controls under conditions of behavioral activation suggest that neural circuits in the inferior prefrontal cortex and in the middle and anterior section of the superior temporal gyrus are important in the naming of visual objects (Bookheimer, Zeffiro, Blaxton, Gaillard, & Theodore, 1995). Areas in the supplemental motor area of the frontal lobe are important in word retrieval and in the motor planning aspects of speech (Wise et al., 1991) and areas encompassing the angular gyrus in the parietal-occipital junction are suggested to play roles in the visual recognition and identification of objects (Kosslyn, Alpert, & Thompson, 1995). Whether disturbances in these brain areas contribute to the naming failures of AD is not yet known. However, each of these brain regions implicated in naming is also affected by AD neuropathology (Arnold, Hyman, Flory, Damasio, & Van Hoesen, 1991; Pearson, Esiri, Hiorns, Wilcock, & Powell, 1985).

The purpose of the present investigation was to further explore the neural bases of naming errors in AD. To accomplish this aim, we examined the relationship of various
Naming and PET 349

classes of naming errors in AD to regional brain measures of cerebral glucose metabolism as measured with 18 F-Fluoro-2-deoxyglucose (FDG) and positron emission tomography (PET), a method we and others have used to highlight the neural circuits involved in specific cognitive processing deficits (Rapoport, 1991; Welsh, Hoffman, Earl & Hansen, 1994). If various cognitive functions are responsible for the naming deficits of AD, we predicted that specific regional differences in brain metabolism would emerge corresponding to selective cognitive processing errors, such as impairments in semantic knowledge, visual processing, or lexical access.

METHODS

Subjects

The 54 elderly subjects included this study were drawn from the first 100 patients enrolled in our neuropsychological-PET imaging protocol between September 1988 and January 1990. All subjects were patients seeking evaluation of a memory complaint in the Memory Disorders Clinic at the Joseph and Kathleen Bryan Alzheimer’s Disease Research Center (Bryan ADRC). Only patients with diagnoses of AD or other primary degenerative dementias were included. All diagnoses were made by neurologists blind to the PET imaging study results. The diagnoses of probable, possible and definite AD were assigned in accordance with the published criteria (McKhann et al., 1984). In this sample, 15 individuals were diagnosed probable AD, 20 had the more conservative diagnosis of possible AD, 4 individuals came to autopsy over the course of study and were diagnosed definite AD, and 15 individuals were diagnosed “dementia,” to indicate a progressive degenerative condition where the etiology was unclear but there were some atypical features that precluded a confident diagnosis of AD. All subjects had completed the neuropsychological battery from the Consortium to Establish a Registry for Alzheimer’s Disease (CERAD; Morris, Mohs, Rogers, Fillenbaum, & Heyman, 1988). A knowledgeable informant, usually a family member, completed a measure of functional abilities, the Dementia Severity Rating Scale (DSRS; Clark & Ewbank, 1996), an informant version of the more familiar Clinical Dementia Rating scale (CDR; Hughes et al., 1982). The DSRS consists of 11 items that assess memory, orientation, judgment, social interactions, home activities, and personal care. The version used in this study is scaled from 11 to 62. Scores of 32 or less imply a CDR of 0.5 (questionable dementia) to 1.0 (mild dementia). Scores of 33 or greater imply a CDR of 2.0 (moderate dementia) or higher. The patients enrolled in the PET imaging study were followed longitudinally with repeat neuropsychological evaluation as part of their routine clinical management and care.

Naming Assessment

Visual naming was assessed using the abbreviated Boston Naming Test from the CERAD neuropsychological battery (Morris et al., 1988). This test consists of 15 line drawings of common objects and is derived from the 60-item series of the Boston Naming Test. The items are presented in a standard order, stratified by their relative frequency of occurrence in the English language (five items each of high, moderate, and low frequency). Neither semantic nor phonemic cues were given; however, nonspecific prompts were used if the initial response was too general (e.g., “Is there another name for that?” if the patient called the canoe item “boat”). Since patients were followed lon-
...gitudinally, the naming protocol used in these analyses was taken from the testing session occurring closest to the date of the PET scan.

Demographic and psychometric data for the four diagnostic groups are shown in Table 1. A one-way analysis of variance (ANOVA) of the mean education levels indicated a significant group difference, \( F(3, 50) = 3.00, p < .05 \). Post-hoc analyses using Tukey’s test revealed no differences among the groups, however the less conservative Duncan’s test indicated that the possible AD group had significantly fewer years of education than the definite AD group. There were no differences among the four groups with respect to their age at evaluation, general level of mental status using Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975) scores, overall naming performance, or dementia severity (DSRS). Consequently, the groups were combined to create a more heterogeneous sample and to increase statistical power.

**Naming Error Classification Procedures**

Errors were classified using the system devised by Hodges et al. (1991), which is briefly summarized here. Each error was assigned to 1 of 10 categories. Visual errors were coded when the named item was similar in appearance to the target but from a different semantic category (e.g., “building” for harmonica) or when an individual feature of the target was named (e.g., “netting” for hammock). There were three types of semantic errors: superordinate errors, within-category errors, and associative errors. Superordinate errors were those in which the response was an overgeneralization of the target (e.g., “animal” for camel). Within-category errors were coded when the patient named an item from the same semantic category, but the error was not visually similar to the target (e.g., “Halloween” for mask). Associative errors occurred when the name volunteered might also describe the target’s function or named a specific example within the stimulus class (e.g., “Vesuvius” for volcano). An error that was both from the same semantic category as the target and was visually similar was classified as an ambiguous error (e.g., “geyser” for volcano).

Lexical accessing errors included circumlocutions, phonemic distortions, and nonresponses. Circumlocutions errors were coded for responses that were phrases (not the required name) describing the target (e.g., “clamps to pick up ice cubes” for tongs). Phonemic errors were naming errors that shared at least one syllable with the target (e.g., “hamrick” for hammock). Nonresponses were coded in instances where the patient responded “I don’t know” or failed to provide a verbal response. Two final classes of er-

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Means (M) and Standard Errors (SE) of Demographic Characteristics of the Sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group</td>
<td>Age</td>
</tr>
<tr>
<td>----------</td>
<td>-----</td>
</tr>
<tr>
<td>Probable AD</td>
<td>64.73</td>
</tr>
<tr>
<td>Possible AD</td>
<td>68.65</td>
</tr>
<tr>
<td>Definite AD</td>
<td>66.50</td>
</tr>
<tr>
<td>Dementia</td>
<td>65.60</td>
</tr>
</tbody>
</table>

\(^a\)Mini-Mental State Examination (Folstein, Folstein, & McHugh, 1975).  
\(^b\)Dementia Severity Rating Scale (Clark & Ewbank, 1996). Scores of \( \leq \)32 correspond to very mild or mild dementia, with higher scores reflecting a higher degree of functional impairment. Scores of \( > \)33 correspond to a dementia severity rating of moderate or higher.
errors were coded for errors that were not visually or semantically related to the target: perseverations and unrelated errors. *Perseverations* were coded if an item name was the repetition of a previous response. *Unrelated* errors were coded if the response bore no clear relationship to the target.

Only the first uncued response was classified unless a series of responses were volunteered, ending in the correct response (e.g., “It’s a net . . . no it’s not . . . it’s a hammock”). In these cases no error was recorded. As described above, when the patient’s response was an overgeneralization, a neutral prompt was given to permit subject clarification. Therefore, in the present study, overgeneralizations followed by a second response were disregarded, and the second response was scored. The errors committed on the test were coded independently by two raters. Classification discrepancies between the raters were resolved by discussion prior to the PET analyses. All subsequent statistical analyses were performed on the consensus ratings.

**Positron Emission Tomography**

The PET studies of glucose metabolism were performed with all subjects in the resting state following a 4-hour fasting period prior to the study. The procedures used were identical to those previously reported (Welsh et al., 1994) and were in accordance with the policies of the Duke Institutional Review Board for the Protection of Human Subjects. Images were obtained with subjects in the supine position with eyes open and ears unoccluded in a dimly lit room with low-level ambient noise. Intravenous lines were placed 30 minutes before the injection of 10 millicuries of the labeled 18F Fluoro-2-deoxyglucose (FDG) tracer. During the 30-minute uptake period, the subjects remained awake and quiet with verbal interactions avoided.

Fluorine-18 was produced in the Duke University Medical Center cyclotron and FDG was synthesized in a CTI-Berkley automated system (Barrio et al., 1981). Scans were obtained with a CTI-ECAT III (911-2A, Knoxville, TN) scanner with resolution of 8.6 mm. Studies were corrected for attenuation by the calculated or geometric method (Huang, Hoffman, Phelps, & Kuhl, 1979). A total of 12 to 15 image planes were obtained for each individual parallel to the canthomeatal line covering the entire intracranial contents with 8mm center-to-center spacing. Reconstruction of images was done with a Hann (0.5cm-1) filter and calculated attenuation correction.

The transaxial images were independently interpreted by two neuroimaging experts (JMH, VL) and were rated using a semiquantitative rating system previously described (Hoffman et al., 1996). On the basis of visual inspection, FDG uptake was graded in the various brain areas using a 3-point scale: markedly reduced FDG uptake (0), reduced FDG uptake (1), and normal FDG uptake (2). Figure 1 provides examples of each of these assignments at three different planes of section (frontal, temporal, and parietal lobes). Ratings were made without awareness of subject identity, diagnosis, and neuropsychological findings. Disagreements in PET ratings between the two raters were resolved by consensus.

The brain areas rated included the frontal, temporal, parietal, and occipital lobes, with separate ratings for the left and the right hemispheres. The temporal lobe was subdivided into mesial and lateral areas and the lateral temporal cortex was further subdivided into anterior and posterior regions. Because of differing involvement of superior and inferior visual pathways in visual recognition, inferior and superior parietal metabolism were rated separately and individual ratings were made for the primary occipital area and both the inferior and superior visual association cortices.
RESULTS

The number of errors and rates of occurrence for each type are presented in Table 2. The error frequencies were calculated in two different ways: first, by summing the number of each error type and then dividing this number by the total number of errors of commission in our sample and multiplying by 100. The second approach summed the errors within a type and divided this number by the total number of errors (both omissions and commissions). Visual errors and nonresponses were the predominant error types in this sample, accounting for 21 and 25% of the naming errors, respectively. Errors that could be subsumed under a general semantic category (within-category, superordinate, and associative errors) comprised 16% of the total errors committed. Circumlocutions were less frequent (12%). Unrelated and phonemic errors were even less common (8 and 4%, respectively) and perseverations were rare (<1%).

The relationship between the various error types and regional blood flow was explored with correlational analyses. In general, we expected that the language-based er-

FIGURE 1. Qualitative ratings for frontal, temporal, and parietal regions. Examples of the qualitative rating scheme are presented for each of the brain regions examined in this study. Examples of frontal, temporal, and parietal lobe metabolism are depicted in rows 1, 2, and 3, respectively. The far left panels illustrate normal metabolism (rating = 2) for each brain region; the middle panels illustrate the rating of mild hypometabolism (rating = 1) for the same brain regions, and grossly hypometabolic activity (rating = 0) is illustrated for the corresponding areas in the far right panels. Reprinted from Archives of Clinical Neuropsychology. © 1994, with permission from Elsevier Science Ltd. Welsh, K. A., Hoffman, J. M., Earl, N. L., & Hansen, M. W. Neural correlates in dementia: Regional brain metabolism (FDG-PET) and the CERAD neuropsychological battery, 9, p. 400.
errors would be related to a different set of regions than the visual errors and that the left hemisphere would be implicated to a greater extent, particularly for the linguistic and semantic errors. However, the analyses were not hypothesis driven, but exploratory and descriptive in nature. Correction for multiple comparisons was not made, and the alpha level for statistical significance was set at $p < .05$ for each correlation. It is, therefore, important to acknowledge the possibility that some of these correlations may have reached significance by chance. For this reason, any individual correlation must be interpreted cautiously, however, the focus in this study is not on any individual relationship, but rather in exploring the overall pattern of relationships.

Pearson correlations between the number of errors in the various categories and regional FDG uptake for the left and right cerebral hemispheres are shown in Tables 3 and 4, respectively. Correlations for ambiguous and unrelated errors were judged to be of minor theoretical interest and, therefore, are not included in these tables. Correlations for the perseveration category were not analyzed because only one participant had these errors. Correlations for the primary visual cortex are also omitted from the table because metabolism in this region was normal in greater than 80% of our patient sample.

**TABLE 2**
Distribution of Error Types

<table>
<thead>
<tr>
<th>Error Type</th>
<th>Number</th>
<th>Error Rate for Commissions</th>
<th>Overall Error Rate Omissions plus Commissions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonresponse</td>
<td>51</td>
<td>na</td>
<td>25%</td>
</tr>
<tr>
<td>Visual</td>
<td>42</td>
<td>27%</td>
<td>21%</td>
</tr>
<tr>
<td>Ambiguous</td>
<td>28</td>
<td>18%</td>
<td>14%</td>
</tr>
<tr>
<td>Within category</td>
<td>14</td>
<td>9%</td>
<td>7%</td>
</tr>
<tr>
<td>Superordinate</td>
<td>8</td>
<td>5%</td>
<td>4%</td>
</tr>
<tr>
<td>Associative</td>
<td>10</td>
<td>7%</td>
<td>5%</td>
</tr>
<tr>
<td>Circumlocutory</td>
<td>25</td>
<td>16%</td>
<td>12%</td>
</tr>
<tr>
<td>Phonemic</td>
<td>8</td>
<td>5%</td>
<td>4%</td>
</tr>
<tr>
<td>Perseveration</td>
<td>1</td>
<td>1%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Unrelated</td>
<td>17</td>
<td>11%</td>
<td>8%</td>
</tr>
</tbody>
</table>

*Note.* Error rates for commissions are the number of errors of each type expressed as a proportion of the total number of errors excluding nonresponses. na = not applicable.

**TABLE 3**
Pearson Correlations Between Naming Errors and Left Hemisphere Hypometabolism

<table>
<thead>
<tr>
<th>Error Type</th>
<th>Brain Area</th>
<th>Nonresponse</th>
<th>Visual</th>
<th>Within Category</th>
<th>Superordinate</th>
<th>Associative</th>
<th>Circumlocutory</th>
<th>Phonemic</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Frontal</td>
<td>−.29*</td>
<td>.12</td>
<td>.09</td>
<td>−.39*</td>
<td>−.29*</td>
<td>−.12</td>
<td>−.04</td>
</tr>
<tr>
<td></td>
<td>Mesial temporal</td>
<td>−.31*</td>
<td>−.14</td>
<td>.12</td>
<td>−.01</td>
<td>−.10</td>
<td>−.23</td>
<td>−.11</td>
</tr>
<tr>
<td></td>
<td>Anterior lateral</td>
<td>−.32*</td>
<td>−.07</td>
<td>.14</td>
<td>−.11</td>
<td>−.29*</td>
<td>−.26</td>
<td>.03</td>
</tr>
<tr>
<td></td>
<td>Posterior lateral</td>
<td>−.35*</td>
<td>−.08</td>
<td>.22</td>
<td>−.13</td>
<td>−.32*</td>
<td>−.29*</td>
<td>.01</td>
</tr>
<tr>
<td></td>
<td>Temporal</td>
<td>−.39*</td>
<td>−.13</td>
<td>.30*</td>
<td>−.07</td>
<td>−.15</td>
<td>−.24</td>
<td>.06</td>
</tr>
<tr>
<td></td>
<td>Inferior parietal</td>
<td>−.38*</td>
<td>−.14</td>
<td>.27</td>
<td>−.10</td>
<td>−.23</td>
<td>−.22</td>
<td>.11</td>
</tr>
<tr>
<td></td>
<td>Superior parietal</td>
<td>−.44*</td>
<td>−.19</td>
<td>.07</td>
<td>−.01</td>
<td>−.34*</td>
<td>−.12</td>
<td>.32*</td>
</tr>
<tr>
<td></td>
<td>Inferior visual</td>
<td>−.44*</td>
<td>−.19</td>
<td>.20</td>
<td>−.02</td>
<td>−.22</td>
<td>−.30*</td>
<td>.13</td>
</tr>
<tr>
<td></td>
<td>Association cortex</td>
<td>−.44*</td>
<td>−.19</td>
<td>.20</td>
<td>−.02</td>
<td>−.22</td>
<td>−.30*</td>
<td>.13</td>
</tr>
</tbody>
</table>

*p < .05.
Most of the correlations between regional glucose utilization and the number of errors were negative, as expected, indicating that reduced metabolic activity is generally associated with an increase in naming errors. Visual errors were significantly correlated with right inferior parietal metabolism. The relationship of brain metabolism and errors in semantic processing varied according to error type. Superordinate errors correlated with frontal lobe activity bilaterally. Associative errors were related to metabolism in the left frontal lobe and with both the left anterior and left posterior lateral temporal regions. In addition, associative errors correlated with activity in the left inferior visual association areas. Circumlocutions, a type of word accessing error, were related to metabolic activity in the left posterior lateral temporal and left superior visual association areas. Nonresponse errors, another type of accessing error, were also significantly related to reduced metabolic activity in many left hemisphere regions, in this instance the left frontal lobe, left mesial temporal lobe, left anterior and posterior lateral temporal areas, and the left inferior and superior parietal lobes. Nonresponses were also correlated with metabolism in the inferior and superior visual association areas in both the left and right brain hemispheres. By contrast, no significant negative correlations were found for phonemic errors, the third type of lexical error considered in these analyses.

In contrast to the 19 negative correlations that were significant at the .05 level, there were 2 significant positive correlations. Given the exploratory nature of this study, the positive correlations that emerged must be considered as spurious. However, if future work also demonstrated positive correlations between visual areas and linguistic errors, this might be interpretable in terms of a serial model: specifically, a serial model might predict that damage to one area would preclude errors that reflect failure at a later stage of processing. To take an extreme example, if there were no output from the visual areas on which linguistic processes could operate, then linguistic errors, that is, errors that bear a phonemic or semantic relationship to the target, would not occur.

### DISCUSSION

The findings from this study suggest that there are at least three major error types that characterize the naming impairments of AD: visuoperceptive, semantic, and lexical...
accessing failures, each of which is related to at least partially dissociable patterns of regional brain hypometabolism. Visual errors were related strictly to a specific sector of the right parietal lobe. In contrast, errors of nonresponse, a form of either lexical or semantic accessing failure, were associated with each region in the left hemisphere; among the right hemisphere regions, only the two visual association areas emerged as significant. Semantic associative errors and circumlocutions were also significantly correlated only with left hemisphere regions: both associative errors and circumlocutions were related to left temporal regions; associative errors were also related to the left frontal lobe and the inferior visual association area. Not all forms of semantic or lexical accessing impairments were related to left temporal lobe dysfunction, however. Knowledge of objects at the most generic level, the superordinate level, was related to bilateral frontal lobe hypometabolism.

These results suggest that the cognitive processes needed to recognize and name objects likely require a wealth of both verbally and nonverbally coded information residing throughout very specific regions in the right and left hemispheres, which then converge, either in a parallel or serial processing manner, leading to the naming response. This interpretation of multiple converging operations finds support from a number of other brain-behavior investigations (see Damasio, Damasio, Tranel, & Brandt, 1991 for an overview). Semantic impairments associated with impaired naming performance have been related to relatively pronounced hypometabolic defects in the left lateral temporal lobe (Martin, 1987); whereas, severe deficits in lexical retrieval, as is seen in some cases of AD and Pick’s disease, have been associated with lesions confined to the left anterior temporal region of the temporal pole and the anterior portion of the inferior temporal region (Damasio et al., 1991; Graff-Radford et al., 1990; Semenza & Zettin, 1989). Damage to the right parietal lobe, on the other hand, has been shown to result in impaired object recognition under some conditions and incorrect name assignment for the viewed object as a result (Riddoch & Humphreys, 1987; Warrington & Taylor, 1973).

In sum, the findings from this study suggest that there are likely several different cognitive processes operating in visual naming in AD (visual analysis, semantic processing, and lexical access), each subserved by slightly different neural systems that converge to permit identification of visual objects and retrieval of their lexical descriptor. Using the information from this type of study, future studies with brain activation paradigms (i.e., measuring brain activity during the naming task) may provide insights into how specific neural circuits throughout the brain interact to mediate object naming. Finally, the broad consistency between the pattern of results observed in the current studies and general neuropsychological explanations of naming suggests that archival data from resting PET scans may provide a more accessible method for exploring the neural bases of cognitive functioning.

REFERENCES


