A Metabolic Imaging Study of Lexical and Phonological Naming Errors in Alzheimer Disease

Valeria Isella, PhD1,2, Cristina Rosazza, PhD3, Maria Gazzotti, PsychBA4, Jessica Sala, PsychBA4, Sabrina Morzenti, MedPhysBA2,5, Cinzia Crivellaro, MD2,6, Ildebrando Marco Appollonio, MD1,2, Carlo Ferrarese, PhD1,2, and Claudio Luzzatti, MD2,4

Abstract
Patients with Alzheimer disease (AD) produce a variety of errors on confrontation naming that indicate multiple loci of impairment along the naming process in this disease. We correlated brain hypometabolism, measured with 18fluoro-deoxyglucose positron emission tomography, with semantic and formal errors, as well as nonwords deriving from phonological errors produced in a picture-naming test by 63 patients with AD. Findings suggest that neurodegeneration leads to: (1) phonemic errors, by interfering with phonological short-term memory, or with control over retrieval of phonological or prearticulatory representations, within the left supramarginal gyrus; (2) semantic errors, by disrupting general semantic or visual-semantic representations at the level of the left posterior middle and inferior occipitotemporal cortex, respectively; (3) formal errors, by damaging the lexical–phonological output interface in the left mid–anterior segment of middle and superior temporal gyri. This topography of semantic–lexical–phonological steps of naming is in substantial agreement with dual-stream neurocognitive models of word generation.

Keywords
naming impairment, Alzheimer disease, FDG-PET, hypometabolism, phonemic errors, semantic errors, formal errors, lexicon, phonology, phonological short-term memory

Introduction
Models of word production posit a process composed by multiple representational/processing levels and sublevels.1-6 Essential steps following activation of the concept from the semantic system are retrieval of the corresponding lexical entry and phonological word form and activation and implementation of the associated articulatory program. The lexical and phonological stages of this process have been further fractionated into a lexical–semantic, a lexical–phonological, and a postlexical–phonological level, whose content is putatively related to, respectively, meaning, abstract lexical–phonological structure and phonological articulatory features of the word to be generated.7-9 Three types of word production errors are known to arise from dysfunction of stages between conceptual activation and articulation: semantic errors, formal errors, and nonwords deriving from phonological errors. Semantic errors (eg, dog for cat) are real words with a (purely) conceptual relationship with the target word, entailing a link with the lexicon and awareness of identity of the stimulus. Along the multistep process of word generation, they may therefore be mapped at the lexical–semantic level, but impairment of conceptual representations, or of control over their retrieval, is also

1 Neurology Department, S. Gerardo Hospital, University of Milano–Bicocca, Monza, Italy
2 Milan Center for Neuroscience (NeuroMI), Milan, Italy
3 Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy
4 Department of Psychology, University of Milano–Bicocca, Monza, Italy
5 Medical Physics, S. Gerardo Hospital, Monza, Italy
6 Nuclear Medicine, S. Gerardo Hospital, Monza, University of Milano–Bicocca, Italy

Corresponding Author:
Valeria Isella, PhD, School of Medicine, University of Milano–Bicocca, Via Cadore 48, 20900, Monza (MB), Italy.
Email: valeria.isella@unimib.it
known to cause semantic errors.\textsuperscript{5,7,10} Formal errors (\textit{mat} for \textit{cat}) are also real words, whose (purely) phonological resemblance with the target word denotes awareness of its phonological form. These errors can therefore be associated with the lexical–phonological processing\textsuperscript{2,9,11-15} as well as with a post-lexical–phonological level.\textsuperscript{2,11,12} Also phonemic errors (\textit{cag} for \textit{cat}) are phonologically similar to the target word, implying some access to the phonological word form but are not represented within the lexicon. They are thus best linked to a post-lexical–phonological level of word generation.

The neuroanatomical substrate of these 3 categories of errors and underlying cognitive processes are not completely defined. Three left hemisphere regions contend for locus of damage associated with semantic errors: posterior inferior–middle\textsuperscript{5,8,16,17} temporal cortex, posterior middle temporal gyrus,\textsuperscript{18-21} and mid\textsuperscript{3,22,23} or mid–anterior\textsuperscript{7,24-26} portion of the same gyrus (other areas correlated with semantic errors have been attributed a role in general semantic knowledge left angular gyrus and anterior ventral temporal cortex or in control of semantic retrieval left inferior parietal–frontal connections rather than in the lexical–semantic interplay).\textsuperscript{5,7,10} Knowledge about the neural correlates of formal errors is relatively scarce, being limited to results of 2 recent studies that have applied a lesion symptom mapping approach to heterogeneous computational parameters of word production impairment.\textsuperscript{7,27} Overall, these findings confirm the dual, lexical, and phonological, nature of formal errors and accordingly suggest a dual lesion pattern: Lexical-based formal errors would be associated with damage to the mid–anterior segments of the left middle and superior temporal gyri, and phonological-based errors with damage along a left superior temporal–inferior frontal path. Phonemic errors have extremely complex anatomical correlates, involving a large array of areas within the left hemisphere: mid and posterior superior temporal gyrus and sulcus,\textsuperscript{3,8,18,23,27,28} the so called Sylvian–parietal–temporal (Spt) area,\textsuperscript{5,6,8,27,29,30} supramarginal and post- and precentral gyri,\textsuperscript{7,20,26,27,31-33} as well as inferior frontal cortex and insula\textsuperscript{3,7,8,26,32,33} Within the framework of the dual stream model of speech,\textsuperscript{5} semantic errors are allocated to the ventral stream, which mediates conceptual–lexical interactions, phonemic errors to the dorsal stream, which acts as a lexical–phonological–articulatory interface, and formal errors to both streams.

Patients with Alzheimer disease (AD) often have word finding difficulties in spontaneous speech, tend to score poorly on formal tests of confrontation naming since early dementia stages, and deteriorate with disease progression.\textsuperscript{34,35} Qualitative scrutiny of picture naming performance in these patients reveals a great variety of incorrect responses including omissions (no answer or “don’t know” responses), circumlocations (\textit{the fruit associated with Adam and Eve for apple}), superordinates (\textit{fruit}), visual errors (\textit{circle}), and also semantic phonemic and formal errors.\textsuperscript{36-47} Although impairment of semantic memory or of access to semantic knowledge is considered the main cause of naming deficits in this form of dementia,\textsuperscript{48-52} such different types of incorrect responses suggest dysfunction at other levels of word production. In fact, naming performance of patients with AD has been shown to vary with the visual complexity of the pictorial stimuli;\textsuperscript{53-55} or to be influenced by phonological cues or phonological priming.\textsuperscript{43,47,55,56} In AD populations, correlation between performance on picture naming and distribution of atrophy on magnetic resonance imaging (MRI) or of hypometabolism on \textsuperscript{18}fluorodeoxyglucose positron emission tomography (FDG-PET) has invariably shown the involvement of a locus classically associated with semantic memory, that is, the left anterior ventral temporal cortex,\textsuperscript{57-65} but has also highlighted the contribution of other nodes of the left hemisphere naming network that intervene in other steps of the naming process: the dorsolateral\textsuperscript{58,63} or mesial\textsuperscript{59,61} temporal surface, the occipito-temporal junction,\textsuperscript{57,62,64} the inferior parietal lobule,\textsuperscript{58,61} as well as the posterior frontal cortex.\textsuperscript{57-59,61,65}

All of these studies, however, have considered only total number of correct answers as index of naming performance, whereas in the current study we focused on lexical and phonological error subtypes in order to obtain a more fine-grained topography of postsemantic and prearticulatory levels of the naming process. We explored the specific metabolic correlates of semantic, phonemic, and formal errors produced by patients with AD in a picture-naming task, with the final aim to confirm and possibly better define neural maps of lexical–phonological deficits in word generation. We hypothesized that semantic and formal errors would be associated with hypometabolism in the posterior and anterior regions of the left lateral temporal cortex, respectively, due to their semantic–lexical and lexical nature and that phonemic errors could be associated with dysfunction of the more posterior segment of the left dorsal pathway, since temporo–parietal regions are typical loci of degeneration in AD, whereas frontal or fronto–parietal areas tend to be involved only in a very advanced disease stage.

**Material and Methods**

**Participants**

Patients were recruited from the memory clinic of S. Gerardo Hospital, Monza. Criteria for inclusion were a diagnosis of probable AD according to standardized criteria by the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer’s Disease and Related Disorders Association\textsuperscript{66} (NINCDS-ADRDA), a Mini Mental State Examination\textsuperscript{37} (MMSE) score \textsuperscript{18} of 30, a minimum of 5 years of education, and Italian as mother tongue. Exclusion criteria were severe uncompensated eye diseases, large and/or multiple focal vascular lesions on brain MRI, and history of neuropsychiatric disorders, brain injury, mental insufficiency, or substance abuse.

A total of 63 patients with AD, 29 men and 34 women, were included in the study. Their individual sociodemographic and clinical features are reported in Appendix 1. Their average characteristics indicated a mild-to-moderate disease stage (Table 1). \textsuperscript{18} Fluorodeoxyglucose positron emission tomography scans showed significant hypometabolism in the temporal and posterior parietal regions, with left hemisphere predominance
Table 1. Study Cohort’s Sociodemographic and Clinical Characteristics.

| Characteristic          | Mean (Standard Deviation) | Minimum | Maximum |
|-------------------------|---------------------------|---------|---------|
| Age                     | 71.6 (8.0)                | 50      | 85      |
| Education (years)       | 8.6 (4.1)                 | 5       | 19      |
| Disease duration (months)| 26.3 (11.0)               | 12      | 48      |
| MMSE score              | 23.3 (3.4)                | 18      | 28      |

Abbreviation: MMSE, Mini Mental State Examination.

(Figure 1). Positron emission tomography with tracer for amyloid deposits was also available for 13 (20.6%) patients and was positive for all of them. All participants were unpaid volunteers and signed a written informed consent. The study was approved by our institution ethics committee and carried out in accordance with the ethical standards of the Helsinki Declaration.

Picture Naming and Errors Categorization

Confrontation naming was assessed as part of a neuropsychological battery tapping the main cognitive domains (attention, short- and long-term verbal memory, visuospatial and executive abilities, verbal fluency and language comprehension, mood and behavior), using a standardized test composed by 80 stimuli of the Snodgrass and Vanderwart pictorial set for each of the following 8 categories: animals, fruits, vegetables, body parts, furniture, tools, vehicles, and musical instruments (see Appendix 2 for the list of individual items and their psycholinguistic variables). Items were presented in randomized, fixed order (and randomized across categories). Patients were asked to name aloud the item shown in the drawing displayed at the center of an A4 sheet, with no time limits. All responses were recorded by the examiner, but only the first utterance was taken into account for computing the final accuracy score (repairs were therefore scored as errors). Maximum number of correct responses is 80 and cut off for normality is an age- and education-adjusted score ≥ 68.67

Phonemic, semantic, and formal errors were classified by consensus between 2 raters (M.G. and J.S.) following definitions reported in Table 2. Phonemic errors were neologisms or pseudowords derived from changes in the phonology of the target word. Semantic errors were real words related to the target word by a category-coordinate or associate relationship, but with no phonological or purely visual relationship (like in misrecognitions, eg, box for drum, ball for orange). Formal errors were real words with phonological, but not semantic, resemblance to the target. For the sake of specificity, responses meeting the definition of semantic or formal errors were excluded from the analysis if they were double errors (eg, a response phonologically related to a semantic relative of the target, like ephelant for giraffe), or if participants perseverated a response from a previous trial. If multiple incorrect responses were provided for a same item, they were all counted as errors and included in the analysis, in an attempt to maximize the number of errors within each category.

Other categories of errors produced during picture naming, such as omissions, circumlocutions, superordinates, and visual errors, were recorded but not analyzed as they were not of interest for the current study.

Acquisition, Processing, and Analysis of FDG-PET Imaging

Fluoro-deoxy-glucose positron emission tomography was performed within 3 months from completion of the naming test in the Department of Nuclear Medicine of S. Gerardo Hospital, on a General Electric Discovery LS PET/CT scanner. First, computed tomography was performed for attenuation correction, then PET scans were acquired for 15 minutes, with a thickness of 3.27 mm and a matrix of 128 × 128 pixels, and finally reconstructed following an ordered subset expectation maximization algorithm. Images were subsequently processed with Statistical Parametric Mapping (SPM) 8 (Wellcome Department of Imaging Neuroscience, London, United Kingdom; https://www.fil.ion.ucl.ac.uk/spm, running on MATLAB R2015a (MathWorks Inc, Sherborn, Massachusetts): They were reoriented along the anterior–posterior commissure, spatially normalized to the Montreal Neurological Institute reference space using an FDG-PET dementia-specific template provided on SPM,69 and smoothed with an isotropic 3D Gaussian kernel of 16 mm FWHM.

Two types of analysis were conducted with SPM on FDG-PET images. First, distribution of hypometabolism in patients with AD was assessed, for descriptive purposes, by comparing their images with images acquired on the same PET scanner in a group of 30 neurologically healthy controls. Controls were disease-free oncologic patients undergoing PET for disease staging (14 female, mean age 66.5 years, mean education 9.1 years, mean MMSE score 28.9). The comparison was carried out with the “2-sample t test” function in SPM, including age and sex as covariates. Second, the areas of hypometabolism associated with raw number of correct naming responses as well as phonemic, semantic, and formal errors were assessed within the cohort of 70 patients. This correlation between metabolism and naming was carried out with the “regression analysis” function in SPM, including age, sex, and MMSE as covariates. For both analyses (groups comparison and correlations), significance was set at P < .05 family wise error (FWE)-corrected and only clusters with a minimum size of 100 voxels were taken into account. Anatomical labeling of loci of hypometabolism was carried out with Talairach atlas and Automatic Labeling atlas using SPM8-integrated toolbox WFU_PickAtlas.

Results

Naming Performance

Mean score on the picture-naming test indicated only mild naming impairment (Table 3), but there was great interindividual variability, as evident from Appendix 1, which shows the
individual-naming scores. In particular, only one-quarter and one-third of the entire patients’ sample produced at least one phonemic or one formal error, respectively, and proportion of each of the 3 types of errors out of all the naming errors made by individual patients ranged from 2% to 20% for formal errors, to 25% for phonemic errors, and to 33% for semantic errors. The most numerous errors were semantic errors, followed by phonemic errors, while formal errors were the least common category (Table 3).

### Discussion

In a sample of 63 patients with AD, correlation between FDG-PET brain metabolism and performance on a picture naming task identified various loci of metabolic abnormalities within the left hemisphere that are associated with naming impairment. Global performance, that is, number of accurate responses, was related to dysfunction of the ventral temporal cortex, in agreement with prior evidence that supports a crucial role of the left fusiform gyrus in semantic–lexical retrieval.60,62,64 The 3 subtypes of naming errors considered in the study involved a specific metabolic correlate: posterior middle and posterior inferior temporal gyri for semantic errors, supramarginal gyrus, adjacent superior temporal cortex for phonemic errors, and mid–anterior segment of the middle temporal gyrus for formal errors. With the exception of semantic errors, the other 2 error categories were produced only by a minority of cases within the patients’ cohort and that the proportion of error subtypes (of all the naming errors) was highly variable across
participants may also have affected the reliability and generalizability of our correlations. Nevertheless, SPM yielded clear and sizable clusters at strict significance thresholds for all 3 types of errors.

The 2 left temporal clusters emerged in association with semantic errors have been found also in previous studies. The posterior portion of the middle temporal gyrus, in particular, has been found to be lesioned in a focal fluent language disorder characterized by production of numerous semantic errors, that is, transcortical sensory aphasia. This area lies on the ventral bank of the superior temporal sulcus and has been described as a highly patients with region operating multimodal interactions for word comprehension and production. Based on its functional properties, this region has in fact been assimilated to the “semantic hub” located in the left anterior ventral temporal cortex. Semantic errors deriving from its dysfunction might thus be due to impaired integration of information that is necessary for

Table 3. Patients’ Average Performance on the Picture Naming Test.

|                      | Mean   | Standard Deviation | Minimum  | Maximum  | Sum   |
|----------------------|--------|--------------------|----------|----------|-------|
| Total correct        | 62.0 (77.5%) | 13.8 (17.2%)    | 19 (23.8%) | 80 (100%) | 3905  |
| Semantic errors      | 1.0 (6.3%)  | 1.2 (8.3%)       | 0        | 5 (33.3%) | 63    |
| Formal errors        | 0.2 (1.5%)  | 0.4 (3.7%)       | 0        | 2 (20.0%) | 15    |
| Phonemic errors      | 0.4 (3.1%)  | 0.7 (5.7%)       | 0        | 4 (25.0%) | 27    |

*Percentages shown in brackets were calculated out of total number of stimuli (80) for total correct, and out of total number of errors produced by the entire cohort, for errors. Please note that total number of errors may not correspond to the difference between maximum test score and number of correct responses since multiple errors produced by a patient for a same item were all counted and included in the analyses.

Figure 2. Cluster of hypometabolism correlated with a lower number of correct responses on the picture naming test ($P < .05$ FWE-corrected, minimum cluster size = 100 voxels).

Table 4. Spatial Coordinates of Clusters Correlated With Total Number of Correct Responses on the Picture Naming Test and With Naming Error Subtypes.

| Cluster             | Size  | MNI Coordinates | Hemisphere | Region (Brodmann Area) |
|---------------------|-------|-----------------|------------|------------------------|
| Total correct       | 477   | –38 –16 –36      | Left       | Fusiform gyrus         |
| Phonemic errors     | 1466  | –54 –28 20       | Left       | Supramarginal gyrus (40)|
| Semantic errors     | 537   | –68 –30 4        | Left       | Middle temporal gyrus (22)|
| Formal errors       | 349   | –54 –64 –18      | Left       | Inferior temporal gyrus (37)|

Abbreviation: MNI, Montreal Neurological Institute.
activating the correct conceptual representation. This mechanism is more similar to the conceptual breakdown underlying semantic errors in patients with semantic dementia than to impairment of lexical retrieval. In effect, the lexical (semantic) level of the word generation process has been localized, by Indefrey and Levelt and by Dell, more anteriorly along the middle temporal gyrus. A view that has received support from studies demonstrating that mid–anterior temporal damage generates semantic errors above and beyond impairment of comprehension or of general semantic knowledge (probably linked to more basal lesions). The second cluster of hypometabolism that correlated significantly with semantic errors encompasses the left posterior inferior temporal cortex. In disagreement with Indefrey and Dell assumptions, Hickok and Poeppel mapped to this region and the adjacent middle temporal gyrus the lexical–semantic node of naming, receiving support from evidence that damage to this region is associated with pure anomia and with the same semantic errors + preserved comprehension behavioral pattern reported for more anterior lesions. Better understanding of the exact locus of interaction between semantics and lexical entries will help establish whether semantic errors associated with damage to the posterior inferior temporal gyrus derive from dysfunction at the interface between conceptual knowledge and lexical retrieval. An alternative account is suggested by studies that have highlighted a special property of this region: its vocation for visual semantics. Two recent functional MRI studies analyzed activations during picture and written or auditory word semantic tasks and clearly showed larger activation of the posterior inferotemporal cortex for the visual than the verbal condition. Some semantic errors, especially coordinate paraphasias (eg, orange for lemon, bus for truck), emerge for items that are visually similar to the target. The occipital–inferior temporal cluster may thus reflect the semantic plus visual character of a subset of errors produced by our patients, configuring this region as a visual semantic locus. The same account has been proposed for anomia in confrontation naming following damage to this region. In their commentary to a study correlating surgical lesions of the left inferotemporal region with anomia, Hope and Price claimed

Figure 3. Clusters of hypometabolism correlated with a higher number of phonemic errors (in red), semantic errors (in blue) and formal errors (in green; P < .05 FWE-corrected, minimum cluster size = 100 voxels).
that “rather than identifying the posterior ITG [inferior temporal gyrus] and posterior ILF [inferior longitudinal fasciculus] with lexical retrieval itself, we are proposing a more perceptual semantic account.”

Of all areas that were previously reported as lesional substrate of phonological errors, the left supramarginal gyrus, and more marginally, area Spt and the posterior superior temporal cortex emerged as specific correlates of phonemic errors in our patients with AD. Damage to the left temporoparietal junction is typical of conduction aphasia and more pertinent to the current study, typical of the language variant of AD, logopenic progressive aphasia, which is characterized by repetition deficits and phonological errors. A sensory-motor account of conduction aphasia purports that damage to Spt causes phonological paraphasias by interfering with the translation of phonological codes (syllable units activated in the posterior superior temporal cortex, according to Hickok) into an articulatory program. Another theory indicates the supramarginal gyrus as the critical lesion site and impairment of the short-term memory phonological store located in this area as the cause of errors. Moreover, great relevance has recently been attributed to other processes that are suggested to take place in the supramarginal gyrus: sensorimotor feedback over phonological retrieval and activation of prearticulatory representations (phoneme units, according to Hickok) to be transferred to the articulatory programming apparatus. Based on our findings, the cause of phonemic errors in AD is the impairment of one or more of these post-lexical–phonological operations within the supramarginal gyrus, rather than a sensory-motor interface deficit at the level of Spt since the hypometabolic cluster reached such area but was predominantly centered around the inferior parietal cortex.

Our results about formal errors are probably the most novel finding of the current study, for 2 reasons. First, prior data about the neural substrate of this type of lexical–phonological errors are extremely scarce. Second, the neural substrate of the node of the naming network whose dysfunction may be considered the primary source of this type of errors, that is, the lexical–phonological node has undergone revision in recent years and is no more associated with the posterior superior temporal gyrus and sulcus (see, for instance, Gow overview of evidence against the role of the posterior superior temporal cortex as the anatomical site of the phonological output lexical representations). In a computational implementation and extension of Hickok’s and Poeppel’s model, these areas have been ascribed post-lexical–phonological functions, namely representing phonology in syllable units. This view has received some support from results of 2 vascular lesion parameter mapping studies of Dell’s computational model. One of these studies, performed by Tochadse and collaborators, has gone 1 step further, identifying a possible “new” locus for the phonological lexical level. One of the computational factors they analyzed comprises formal and phonological errors and shows a correlation with a relatively vast area of vascular damage to the left fronto–temporo–parietal cortex. Within this area, the authors tentatively mapped a phonological lexical component to the anterior middle–superior temporal cortex, and a post-lexical–phonological component to the superior temporal, fronto–parietal, and fronto–insular cortex. Crucially, the peak coordinates of the anatomical correlate of formal errors emerged from the present study correspond to Tochadse mid–anterior cluster. More precisely, in their study, this cluster was not only associated with the phonological–formal factor but was also part of a large area correlated with a semantic computational factor (in accord with speech models that consider the lateral surface of the left anterior middle and superior temporal gyri as part of the language ventral pathway with a role in semantics and in lexical–semantic interface).

The lexicon represents the functional link between formal and semantic errors. The overlap of lesional correlates of these 2 error categories in the more anterior segments of the left middle and superior temporal gyri suggests that this area might be the substrate of lexical representations. Our results align with this hypothesis demonstrating a one-to-one mapping between neurodegeneration of this region and formal errors, in patients with AD.

In conclusion, our findings outline a neuroanatomical map of errors produced by patients with AD in confrontation naming that associates semantic errors with neurodegeneration in 2 areas of the left posterior temporal cortex supposed to subserve visual and more general semantic representations, formal errors with hypometabolism in the left anterior middle temporal gyrus, which might then represent the locus of phonological lexical processes, and phonemic errors with degeneration in the left supramarginal gyrus underpinning phonological short-term memory or pre-articulatory representations or words.
Appendix 1. The table shows individual socio-demographic and clinical features of study participants, and performance on the picture naming test. Percentages were calculated out of total number of stimuli (80) for total correct, and out of total number of errors produced by the entire cohort for error subtypes. Please note that total number of errors may not correspond to the difference between maximum test score and number of correct responses, since multiple errors produced by a patient for a same item were all counted and included in the analyses.

| Patient | Sex   | Age (Years) | Education (Years) | Symptoms Duration (Months) | MMSE | Total Correct n. % | Semantic Errors n. % | Formal Errors n. % | Phonemic Errors n. % |
|---------|-------|-------------|-------------------|---------------------------|------|---------------------|----------------------|---------------------|----------------------|
| CASE 1  | female| 73          | 5                 | 42                        | 21   | 54                  | 67.5                 | 0                   | 0                    |
| CASE 2  | female| 78          | 13                | 42                        | 18   | 49                  | 61.3                 | 5                   | 11.4                 |
| CASE 3  | male  | 84          | 5                 | 18                        | 25   | 52                  | 65.0                 | 3                   | 10.0                 |
| CASE 4  | female| 71          | 8                 | 48                        | 19   | 55                  | 68.8                 | 2                   | 10.5                 |
| CASE 5  | female| 77          | 11                | 12                        | 28   | 71                  | 88.8                 | 1                   | 11.1                 |
| CASE 6  | male  | 77          | 5                 | 36                        | 19   | 68                  | 85.0                 | 0                   | 0                    |
| CASE 7  | female| 80          | 5                 | 36                        | 23   | 63                  | 78.8                 | 2                   | 15.4                 |
| CASE 8  | female| 74          | 8                 | 12                        | 26   | 55                  | 68.8                 | 3                   | 9.4                  |
| CASE 9  | female| 78          | 5                 | 36                        | 19   | 65                  | 81.3                 | 0                   | 1                    |
| CASE 10 | male  | 75          | 8                 | 24                        | 26   | 33                  | 41.3                 | 0                   | 0                    |
| CASE 11 | female| 70          | 5                 | 12                        | 28   | 62                  | 77.5                 | 0                   | 0                    |
| CASE 12 | female| 83          | 5                 | 36                        | 22   | 65                  | 81.3                 | 0                   | 1                    |
| CASE 13 | female| 76          | 5                 | 18                        | 28   | 59                  | 73.8                 | 2                   | 12.5                 |
| CASE 14 | female| 63          | 5                 | 36                        | 18   | 73                  | 91.3                 | 0                   | 1                    |
| CASE 15 | male  | 57          | 8                 | 30                        | 27   | 72                  | 90.0                 | 0                   | 1                    |
| CASE 16 | female| 61          | 8                 | 24                        | 21   | 73                  | 91.3                 | 0                   | 0                    |
| CASE 17 | male  | 75          | 8                 | 24                        | 19   | 53                  | 66.3                 | 2                   | 8.7                  |
| CASE 18 | female| 57          | 11                | 24                        | 28   | 80                  | 100                  | 0                   | 0                    |
| CASE 19 | female| 72          | 5                 | 24                        | 23   | 71                  | 88.8                 | 2                   | 20.0                 |
| CASE 20 | male  | 69          | 10                | 24                        | 28   | 68                  | 85.0                 | 1                   | 7.1                  |
| CASE 21 | male  | 72          | 13                | 30                        | 20   | 62                  | 77.5                 | 3                   | 18.8                 |
| CASE 22 | male  | 53          | 13                | 30                        | 22   | 73                  | 91.3                 | 1                   | 8.3                  |
| CASE 23 | male  | 78          | 5                 | 36                        | 23   | 65                  | 81.3                 | 0                   | 0                    |
| CASE 24 | female| 81          | 12                | 18                        | 24   | 75                  | 93.8                 | 0                   | 0                    |
| CASE 25 | female| 70          | 6                 | 24                        | 24   | 70                  | 87.5                 | 0                   | 0                    |
| CASE 26 | female| 75          | 8                 | 18                        | 28   | 43                  | 53.8                 | 4                   | 11.1                 |
| CASE 27 | female| 84          | 5                 | 12                        | 24   | 75                  | 93.8                 | 0                   | 0                    |
| CASE 28 | male  | 50          | 13                | 42                        | 21   | 73                  | 91.3                 | 0                   | 0                    |
| CASE 29 | female| 67          | 5                 | 12                        | 26   | 73                  | 91.3                 | 1                   | 33.3                 |
| CASE 30 | female| 70          | 5                 | 24                        | 18   | 45                  | 56.3                 | 3                   | 11.5                 |
| CASE 31 | male  | 74          | 13                | 18                        | 24   | 61                  | 76.3                 | 1                   | 5.6                  |
| CASE 32 | female| 72          | 8                 | 36                        | 23   | 68                  | 85.0                 | 2                   | 18.2                 |
| CASE 33 | male  | 75          | 13                | 24                        | 20   | 65                  | 81.3                 | 0                   | 1                    |
| CASE 34 | male  | 73          | 8                 | 12                        | 21   | 33                  | 41.3                 | 1                   | 2.6                  |
| CASE 35 | female| 57          | 13                | 48                        | 18   | 61                  | 76.3                 | 1                   | 5.6                  |
| CASE 36 | female| 70          | 18                | 24                        | 22   | 69                  | 86.3                 | 0                   | 0                    |
| CASE 37 | male  | 64          | 10                | 36                        | 21   | 20                  | 25.0                 | 1                   | 1.6                  |
| CASE 38 | male  | 82          | 5                 | 12                        | 25   | 59                  | 73.8                 | 1                   | 5.0                  |
| CASE 39 | male  | 85          | 15                | 48                        | 19   | 80                  | 100                  | 0                   | 0                    |
| CASE 40 | male  | 62          | 5                 | 24                        | 26   | 46                  | 57.5                 | 1                   | 5.0                  |
| CASE 41 | female| 77          | 5                 | 18                        | 25   | 53                  | 66.3                 | 0                   | 0                    |
| CASE 42 | female| 77          | 5                 | 12                        | 27   | 62                  | 77.5                 | 2                   | 10.0                 |
| CASE 43 | male  | 79          | 5                 | 12                        | 28   | 71                  | 88.8                 | 0                   | 0                    |
| CASE 44 | male  | 73          | 13                | 24                        | 25   | 19                  | 23.8                 | 0                   | 0                    |
| CASE 45 | male  | 66          | 8                 | 12                        | 24   | 79                  | 98.8                 | 1                   | 20.0                 |
| CASE 46 | male  | 55          | 19                | 42                        | 18   | 69                  | 86.3                 | 4                   | 26.7                 |
| CASE 47 | male  | 76          | 5                 | 24                        | 25   | 72                  | 90.0                 | 0                   | 0                    |
| CASE 48 | male  | 74          | 8                 | 18                        | 28   | 58                  | 72.5                 | 1                   | 4.8                  |
| CASE 49 | female| 69          | 9                 | 36                        | 18   | 52                  | 65.0                 | 4                   | 11.8                 |

(continued)
### Appendix 1. (continued)

| Patient | Sex | Age | Education (Years) | Symptoms Duration (Months) | MMSE | Total Correct | Semantic Errors | Formal Errors | Phonemic Errors |
|---------|-----|-----|-------------------|----------------------------|------|---------------|----------------|--------------|----------------|
| CASE 50 | male | 67  | 9                 | 18                         | 27   | 78            | 97.5           | 0            | 0              | 0              |
| CASE 51 | male | 66  | 8                 | 24                         | 28   | 77            | 96.3           | 1            | 33.3          | 0              | 0              |
| CASE 52 | male | 72  | 13                | 12                         | 27   | 77            | 96.3           | 0            | 0              | 0              |
| CASE 53 | male | 78  | 16                | 48                         | 22   | 73            | 91.3           | 1            | 16.7          | 1              | 16.7           |
| CASE 54 | female | 68  | 11                | 36                         | 27   | 71            | 88.8           | 2            | 13.3          | 0              | 0              |
| CASE 55 | female | 64  | 5                 | 36                         | 22   | 69            | 86.3           | 0            | 0              | 0              |
| CASE 56 | male | 57  | 18                | 24                         | 27   | 77            | 96.3           | 0            | 0              | 0              |
| CASE 57 | male | 81  | 5                 | 36                         | 21   | 64            | 80.0           | 1            | 6.3           | 0              | 0              |
| CASE 58 | male | 74  | 8                 | 30                         | 21   | 70            | 87.5           | 0            | 0              | 0              |
| CASE 59 | female | 72  | 5                 | 12                         | 28   | 48            | 60.0           | 1            | 2.9           | 0              | 0              |
| CASE 60 | male | 75  | 18                | 24                         | 22   | 45            | 56.3           | 0            | 0              | 0              |
| CASE 61 | female | 73  | 5                 | 12                         | 27   | 68            | 85.0           | 0            | 0              | 0              |
| CASE 62 | female | 80  | 5                 | 36                         | 21   | 42            | 52.5           | 1            | 2.3           | 0              | 0              |
| CASE 63 | female | 77  | 5                 | 24                         | 23   | 54            | 67.5           | 1            | 5.0           | 0              | 0              |

### Appendix 2. List of the 80 items Included in the Picture Naming Test, With Psycholinguistic Variables (Modified From Laiacoma et al, 1993).

| Item             | Lexical Frequency | Prototypicality | Familiarity | Name Agreement |
|------------------|-------------------|-----------------|-------------|----------------|
| **TOOLS:**       |                   |                 |             |                |
| Pinza (pliers)   | 0                 | 58              | 3.38        | 47             |
| Cacciavite (screwdriver) | 0       | 214             | 3.42        | 58             |
| Sega (saw)       | 0                 | 394             | 2.92        | 60             |
| Vite (screw)     | 0                 | 43              | 3.20        | 58             |
| Chiave inglese (spanner) | 0    | 61              | 2.72        | 53             |
| Scalpello (chisel) | 0              | 103             | 2.46        | 38             |
| Scure (axe)      | 0                 | 14              | 2.28        | 47             |
| Forbice (scissors) | 0             | 4               | 3.98        | 60             |
| Martello (hammer) | 9                | 431             | 3.48        | 59             |
| Chiodo (nail)    | 12                | 248             | 3.28        | 52             |
| **VEGETABLES:**  |                   |                 |             |                |
| Sedano (celery)  | 0                 | 96              | 3.40        | 56             |
| Pannocchia (cob) | 0                 | 247             | 3.50        | 39             |
| Cipolla (onion)  | 0                 | 47              | 3.32        | 53             |
| Peperone (pepper) | 0              | 13              | 2.92        | 57             |
| Carciofo (artichoke) | 0         | 5               | 2.29        | 57             |
| Asparago (asparagus) | 0             | 138             | 2.68        | 56             |
| Fungo (mushroom) | 4                 | 2               | 2.88        | 60             |
| Carota (carrot)  | 5                 | 316             | 3.55        | 59             |
| Insalata (lettuce) | 8                | 19              | 3.42        | 21             |
| Pomodoro (tomato) | 15               | 215             | 3.78        | 52             |
| **ANIMALS:**     |                   |                 |             |                |
| Giraffa (giraffe) | 0                | 82              | 1.80        | 59             |
| Cammello (camel) | 0                 | 28              | 2.08        | 50             |
| Struzzo (oyster) | 0                 | 17              | 1.52        | 39             |
| Rana (frog)      | 0                 | 3               | 2.48        | 60             |
| Cigno (swan)     | 0                 | 14              | 1.97        | 34             |
| Bruco (caterpillar) | 0            | 30              | 1.72        | 39             |
| Mucca (cow)      | 5                 | 284             | 2.42        | 58             |
| Gallo (rooster)  | 10                | 7               | 2.22        | 59             |
| Farfalla (butterfly) | 10              | 48              | 2.92        | 60             |
### Appendix 2. (continued)

| Item                  | Lexical Frequency | Prototypicality | Familiarity | Name Agreement |
|-----------------------|-------------------|-----------------|-------------|----------------|
| **Topo (mouse)**      | 11                | 33              | 2.45        | 59             |
| **MUSICAL INSTRUMENTS:** |                   |                 |             |                |
| Tamburo (drum)        | 0                 | 322             | 2.60        | 59             |
| Arpa (harp)           | 0                 | 105             | 1.88        | 54             |
| Corno (horn)          | 0                 | 63              | 2.00        | 33             |
| Fisarmonica (accordeon)| 0                | 37              | 2.15        | 58             |
| Violino (violin)      | 0                 | 271             | 2.68        | 56             |
| Chitarra (guitar)     | 0                 | 231             | 3.58        | 57             |
| Flauto (flute)        | 0                 | 246             | 2.45        | 42             |
| Tromba (trumpet)      | 6                 | 279             | 2.60        | 57             |
| Pianoforte (piano)    | 17                | 329             | 3.42        | 60             |
| Campana (bell)        | 19                | IO              | 2.20        | 60             |
| **FRUITS:**           |                   |                 |             |                |
| Banana (banana)       | 0                 | 283             | 3.65        | 60             |
| Anguria (watermelon)  | 0                 | 47              | 3.05        | 54             |
| Ananas (pineapple)    | 0                 | 98              | 2.95        | 55             |
| Ciliegia (cherry)     | 3                 | 183             | 3.38        | 56             |
| Pera (pear)           | 5                 | 326             | 3.55        | 59             |
| Fragola (strawberry)  | 6                 | 58              | 3.20        | 59             |
| Limone (lemon)        | 16                | 134             | 3.25        | 57             |
| Mela (apple)          | 32                | 429             | 3.98        | 59             |
| Uva (grapes)          | 33                | 247             | 3.65        | 60             |
| Arancia (orange)      | 39                | 390             | 3.34        | 29             |
| **MEANS OF TRANSPORT:** |                 |                 |             |                |
| Autobus (bus)         | 0                 | 300             | 4.50        | 44             |
| Elicottero (helicopter)| 0                | 18              | 2.55        | 59             |
| Slitta (sled)         | 0                 | 1               | 2.80        | 50             |
| Barca a vela (sailing boat) | 0            | 1               | 2.92        | 60             |
| Camion (truck)        | 19                | 223             | 4.02        | 43             |
| Aeroplano (airplane)  | 20                | 280             | 3.78        | 59             |
| Bicicletta (bycicle)  | 24                | 193             | 3.78        | 60             |
| Motocicletta (motorcycle) | 24          | 174             | 3.25        | 60             |
| Automobile (car)      | 59                | 407             | 4.70        | 50             |
| Treno (train)         | 81                | 257             | 4.15        | 54             |
| **FURNITURE:**        |                   |                 |             |                |
| Sgabello (stool)      | 0                 | 72              | 3.08        | 56             |
| Sedia a dondolo       | 0                 | 5               | 3.25        | 60             |
| Scrivania (desk)      | 6                 | 230             | 4.32        | 56             |
| Cassettone (dresser)  | 7                 | 143             | 4.52        | 38             |
| Lampada (lamp)        | 14                | 227             | 4.20        | 51             |
| Divano (couch)        | 21                | 168             | 4.40        | 58             |
| Sedia (chair)         | 22                | 440             | 4.58        | 60             |
| Vaso (vase)           | 29                | 3               | 2.78        | 58             |
| Tavolo (table)        | 51                | 408             | 4.35        | 59             |
| Letto (bed)           | 176               | 328             | 4.72        | 60             |
| **BODY PARTS:**       |                   |                 |             |                |
| Labbra (lips)         | 29                | 25              | 4.50        | 42             |
| Orecchio (ear)        | 40                | 260             | 4.50        | 58             |
| Naso (nose)           | 41                | 281             | 4.52        | 55             |
| Dito (finger)         | 45                | 279             | 4.78        | 59             |
| Capelli (hair)        | 78                | 125             | 4.59        | 25             |
| Gamba (leg)           | 84                | 402             | 4.65        | 58             |
| Braccio (arm)         | 112               | 398             | 4.75        | 59             |
| Piede (foot)          | 174               | 295             | 4.78        | 60             |
| Occhio (eye)          | 291               | 303             | 4.88        | 60             |
| Mano (hand)           | 375               | 228             | 4.82        | 60             |

*Items were presented in randomized, fixed order, and randomized across categories.*
Acknowledgments
The authors would like to thank Dr Cristina Mapelli for her help in patients’ assessment.

Declaration of Conflicting Interests
The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding
The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iDs
Valeria Isella https://orcid.org/0000-0003-1850-1236
Claudio Luzzatti https://orcid.org/0000-0001-6334-6293

References

1. Schwartz MF, Dell GS, Martin N, Gahl S, Sobel P. A case-series test of the interactive two-step model of lexical access: evidence from picture naming. J Mem Lang. 2006;54(2):228-264. doi:10.1016/j.jml.2005.10.001.
2. Dell GS, Martin N, Schwartz MF. A case-series test of the interactive two-step model of lexical access: predicting word repetition from picture naming. J Mem Lang. 2007;56(4):490-520. doi:10.1016/j.jml.2006.05.007.
3. Indefrey P. The spatial and temporal signatures of word production components: A critical update. Front Psychol. 2011;2(2):7. doi:10.3389/fpsyg.2011.00255.
4. Indefrey P, Levelt WJM. The spatial and temporal signatures of word production components. Cognition. 2004;92(1-2):101-144. doi:10.1016/j.cognition.2002.06.001.
5. Hickok G, Poeppel D. The cortical organization of speech processing. Nat Rev Neurosci. 2007;8(5):393-402. doi:10.1038/nrn2113.
6. Hickok G. The architecture of speech production and the role of the phoneme in speech processing. Lang Cogn Neurosci. 2014;29(1):2-20. doi:10.1080/02643291.2013.834370
7. Dell GS, Schwartz MF, Nozari N, Faseyitan O, Branch Coslett H. Voxel-based lesion-parameter mapping: identifying the neural correlates of a computational model of word production. Cognition. 2013;128(3):380-396. doi:10.1016/j.cognition.2013.05.007.
8. Hickok G. Computational neuroanatomy of speech production. Nat Rev Neurosci. 2012;13(2):135-145. doi:10.1038/nrn3158.
9. Rapp B, Goldrick M. Speaking words: contributions of cognitive neuropsychological research. Cogn Neuropsychol. 2006;23(1):39-73. doi:10.1080/02643290542000049.
10. Jefferies E, Lambon Ralph MA. Semantic impairment in stroke aphasia versus semantic dementia: a case-series comparison. Brain. 2006;129(8):2132-2147. doi:10.1093/brain/awl153.
11. Wilshire CE, Saffran EM. Contrasting effects of phonological priming in aphasic word production. Cognition. 2005;95(1):31-71. doi:10.1016/j.cognition.2004.02.004.
12. Blanken G. Formal paraphasias: a single case study. Brain Lang. 1990;38(4):534-554. doi:10.1016/0093-934X(90)90136-5.
13. Gagnon DA, Schwartz MF, Martin N, Dell GS, Saffran EM. The origins of formal paraphasias in aphasics’ picture naming. Brain Lang. 1997;59(3):450-472. doi:10.1006/brln.1997.1792.
14. Schwartz MF. Theoretical analysis of word production deficits in adult aphasia. Philos Trans R Soc B Biol Sci. 2014;369(1634):9. doi:10.1098/rstb.2012.0390.
15. Blanken G. Lexicalisation in speech production: evidence from form-related word substitutions in aphasia. Cogn Neuropsychol. 1998;15(4):321-360. doi:10.1080/026432998381122.
16. DeLeon J, Gottesman RF, Kleinman JT, et al. Neural regions essential for distinct cognitive processes underlying picture naming. Brain. 2007;130(5):1408-1422. doi:10.1093/brain/awm011.
17. Cloutman L, Gottesman R, Chaudhry P, et al. Where (in the brain) do semantic errors come from? Cortex. 2009;45(5):641-649. doi:10.1016/j.cortex.2008.05.013.
18. Corina DP, Loudermilk BC, Detwiler L, Martin RF, Brinkley JF, Ojemann G. Analysis of naming errors during cortical stimulation mapping: implications for models of language representation. Brain Lang. 2010;115(2):101-112. doi:10.1016/j.bandl.2010.04.001.
19. Duffau H, Gatignol P, Mandonnet E, Peruzzi P, Tzourio-Mazoyer N, Capelle L. New insights into the anatomo-functional connectivity of the semantic system: a study using cortico-subcortical electrostimulations. Brain. 2005;128(4):797-810. doi:10.1093/brain/awh423.
20. Gow DW. The cortical organization of lexical knowledge: a dual lexicon model of spoken language processing. Brain Lang. 2012;121(3):273-288. doi:10.1016/j.bandl.2012.03.005.
21. Vigneau M, Beaucousin V, Houdé O, et al. Meta-analyzing left hemisphere language areas: phonology, semantics, and sentence processing. Neuroimage. 2006;30(4):1414-1432. doi:10.1016/j.neuroimage.2005.11.002.
22. Hamberger MJ, Miozzo M, Schevon CA, et al. Functional differences among stimulation-identified cortical naming sites in the temporal region. Epilepsy Behav. 2016;60:124-129. doi:10.1016/j.yebeh.2016.04.021.
23. Miozzo M, Williams AC, McKhann GM, Hamberger MJ. Topographical gradients of semantics and phonology revealed by temporal lobe stimulation. Hum Brain Mapp. 2017;38(2):688-703. doi:10.1002/hbm.23409.
24. Walker GM, Schwartz MF, Kimberg DY, et al. Support for anterior temporal involvement in semantic error production in aphasia: new evidence from VLSM. Brain Lang. 2011;117(3):110-122. doi:10.1016/j.bandl.2010.09.008.
25. Schwartz MF, Kimberg DY, Walker GM, et al. Anterior temporal involvement in semantic word retrieval: voxel-based lesion-symptom mapping evidence from aphasia. Brain. 2009;132(12):3411-3427. doi:10.1093/brain/awp284.
26. Schwartz MF, Faseyitan O, Kim J, Coslett HB. The dorsal stream contribution to phonological retrieval in object naming. Brain. 2012;135(12):3799-3814. doi:10.1093/brain/aw300.
27. Tochade M, Halai AD, Lambon Ralph MA, Abel S. Unification of behavioural, computational and neural accounts of word production errors in post-stroke aphasia. NeuroImage Clin. 2018;5:1. doi:10.1016/j.nic.2018.03.031.
28. Graves WW, Grabowski TJ, Mehta S, Gupta P. The left posterior superior temporal gyrus participates specifically in accessing lexical phonology. *J Cogn Neurosci.* 2008;20(9):1698-1710. doi:10.1162/jocn.2008.20113.

29. Wise RJS, Scott SK, Blank SC, Mummery CJ, Murphy K, Warburton EA. Separate neural subsystems within “Wernicke’s area.” *Brain.* 2001;124(Pt 1):83-95. doi:10.1093/brain/124.1.83.

30. Buchsbaum BR, Baldo J, Okada K, et al. Conduction aphasia, sensory-motor integration, and phonological short-term memory—an aggregate analysis of lesion and fMRI data. *Brain Lang.* 2011;119(3):119-128. doi:10.1016/j.bandl.2010.12.001.

31. Halai AD, Woollams AM, Lambon Ralph MA. Triangulation of language-cognitive impairments, naming errors and their neural bases post-stroke. *NeuroImage Clin.* 2018;17(C):465-473. doi:10.1016/j.nicl.2017.10.037.

32. Mirman D, Chen Q, Zhang Y, et al. Neural organization of spoken language revealed by lesion-symptom mapping. *Nat Commun.* 2015;6(1):6762. doi:10.1038/ncomms7762.

33. Vigneau M, Beaucousin V, Hervey A, et al. Meta-analyzing left hemisphere language areas: phonology, semantics, and sentence processing. *Neuromage.* 2006;30(4):1414-1432. doi:10.1016/j.neuroimage.2005.11.002.

34. Salmon DP. Neuropsychological features of mild cognitive impairment and preclinical Alzheimer’s disease. In: Pardon MC, BM, ed. Behavioral Neurobiology of Aging. Current Topics in Behavioral Neurosciences. Berlin, Heidelberg: Springer; 2011.

35. Verma M, Howard RJ. Semantic memory and language dysfunction in early Alzheimer’s disease: a review. *Int J Geriart Psychiatry.* 2012;27(12):1209-1217. doi:10.1002/gps.3766.

36. Bayles KA, Tomoda CK. Confrontation naming impairment in dementia. *Brain Lang.* 1983;19(1):98-114. doi:10.1016/0093-934X(83)90057-3.

37. Corbett F, Jeffries E, Burns A, Ralph MAL. Unpacking the semantic impairment in Alzheimer’s disease: qualitative changes with disease severity. *Behav Neurol.* 2012;25(1):23-34. doi:10.3233/BEN-2012-0346.

38. Lin CY, Chen TB, Lin KN, et al. Confrontation naming errors in Alzheimer’s disease. *Dement Geriat Cogn Disord.* 2014;37(2):86-94. doi:10.1159/000354359.

39. Salehi M, Reisi M, Ghasiison L. Lexical retrieval or semantic knowledge? Which one causes naming errors in patients with mild and moderate Alzheimer’s disease? *Dement Geriat Cogn Dis Extra.* 2017;7(3):419-429. doi:10.1159/000484137.

40. Cueto F, Rodriguez-Ferreiro J, Sage K, Ellis AW. A fresh look at the predictors of naming accuracy and errors in Alzheimer’s disease. *J Neuropsychol.* 2012;6(2):242-256. doi:10.1111/j.1748-6653.2011.02025.x.

41. Martin A, Fedio P. Word production and comprehension in Alzheimer’s disease: the breakdown of semantic knowledge. *Brain Lang.* 1983;19(1):124-141. doi:10.1016/0093-934X(83)90059-7.

42. Cormier P, Margison JA, Fisk JD. Contribution of perceptual and lexical-semantic errors to the naming impairments in Alzheimer’s disease. *Percept Mot Skills.* 1991;73(3031-5125):175-183. doi:10.2466/pms.1991.73.1.175.

43. Funnell E, Hodges JR. Progressive loss of access to spoken word forms in a case of Alzheimer’s disease. *Proc R Soc B Biol Sci.* 1991;243(1307):173-179. doi:10.1098/rspb.1991.0028.

44. LaBarge E, Balota DA, Storandt M, Smith DS. An analysis of confrontation naming errors in senile dementia of the Alzheimer type. *Neuropsychology.* 1992;6(1):77-95. doi:10.1037/0894-4105.6.1.77.

45. Barbarotto R, Capitani E, Jori T, Laiacoma M, Molinari S. Picture naming and progression of Alzheimer’s disease: an analysis of error types. *Neuropsychologia.* 1998;36(5):397-405. doi:10.1016/S0028-3932(97)00124-3.

46. Lukatela K, Malloy P, Jenkins M, Cohen R. The naming deficit in early Alzheimer’s and vascular dementia. *Neuropsychology.* 1998;12(4):565-572. doi:10.1037/0894-4105.12.4.565.

47. Balhazr MLF, Cendes F, Damasceno BP. Semantic error patterns on the Boston naming test in normal aging, amnestic mild cognitive impairment, and mild Alzheimer’s disease: is there semantic disruption? *Neuropsychology.* 2008;22(6):703-709. doi:10.1037/a0012919.

48. Chertkow H, Bub D. Semantic memory loss in dementia of Alzheimer’s type: what do various measures measure? *Brain.* 1990;113(2):397-417. doi:10.1093/brain/113.2.397.

49. Garrard P, Lambon Ralph MA, Patterson K, Pratt KH, Hodges JR. Semantic feature knowledge and picture naming in dementia of Alzheimer’s type: a new approach. *Brain Lang.* 2005;93(1):79-94. doi:10.1016/j.bandl.2004.08.003.

50. Hodges JR, Salmon DP, Butters N. Semantic memory impairment in Alzheimer’s disease: failure of access or degraded knowledge? *Neuropsychologia.* 1992;30(4):301-314. doi:10.1016/0028-3932(92)90104-T.

51. Hodges JR, Patterson K, Graham N, Dawson K. Naming and knowing in dementia of Alzheimer’s type. *Brain Lang.* 1996;54(2):302-325. doi:10.1006/brln.1996.0077.

52. Huff FF, Corkin S, Growdon JH. Semantic impairment and anomia in Alzheimer’s disease. *Brain Lang.* 1986;28(2):235-249. doi:10.1016/0093-934X(86)90103-3.

53. Goldstein FC, Green J, Presley R, Green RC. Dysnomia in Alzheimer’s disease: an evaluation of neurobehavioral subtypes. *Brain Lang.* 1992;43(2):308-322. doi:10.1016/0093-934X(92)90132-X.

54. Shuttleworth EC, Huber SJ. The naming disorder of dementia of Alzheimer type. *Brain Lang.* 1988;34(2):222-234. doi:10.1016/0093-934X(88)90134-4.

55. Tippett LJ, Farah MJ. A Computational model of naming in Alzheimer’s disease: unitary or multiple impairments? *Neuropsychology.* 1994;8(1):3-13. doi:10.1037/0894-4105.8.1.3.

56. Faust ME, Balota DA, Multhaup KS. Phonological blocking during picture naming in dementia of the Alzheimer type. *Neuropsychology.* 2004;18(3):526-536. doi:10.1037/0894-4105.18.3.526.

57. Apostolova LG, Lu P, Rogers S, et al. 3D mapping of language networks in clinical and pre-clinical Alzheimer’s disease. *Brain Lang.* 2008;104(1):33-41. doi:10.1016/j.bandl.2007.03.008.

58. Ahn HJ, Seo SW, Chin J, et al. The cortical neuroanatomy of neuropsychological deficits in mild cognitive impairment and Alzheimer’s disease: A surface-based morphometric analysis.
59. Frings L, Kloppel S, Teipel S, et al. Left anterior temporal lobe sustains naming in Alzheimer’s dementia and mild cognitive impairment. *Curr Alzheimer Res*. 2011;8(8):893-901. doi:10.2174/156720511798192673.

60. Grossman M, McMillan C, Moore P, et al. What’s in a name: voxel-based morphometric analyses of MRI and naming difficulty in Alzheimer’s disease, frontotemporal dementia and corticobasal degeneration. *Brain*. 2004;127(3):628-649. doi:10.1093/brain/awh075.

61. Domoto-Reilly K, Sapolsky D, Brickhouse M, Dickerson BC. Naming impairment in Alzheimer’s disease is associated with left anterior temporal lobe atrophy. *Neuroimage*. 2012;63(1):348-355. doi:10.1016/j.neuroimage.2012.06.018.

62. Hirono N, Mori E, Ishii K, et al. Neuronal substrates for semantic memory: a positron emission tomography study in Alzheimer’s disease. *Dement Geriatr Cogn Disord*. 2001;12(1):15-21. doi:10.1159/000051231.

63. Zahn R, Juengling F, Bubrowski P, et al. Hemispheric asymmetries of hypometabolism associated with semantic memory impairment in Alzheimer’s disease: a study using positron emission tomography with fluorodeoxyglucose-F18. *Psychiatry Res - Neuroimaging*. 2004;132(2):159-172. doi:10.1016/j.psr.2004.07.006.

64. Teipel SJ, Willoch F, Ishii K, et al. Resting state glucose utilization and the CERAD cognitive battery in patients with Alzheimer’s disease. *Neurobiol Aging*. 2006;27(5):681-690. doi:10.1016/j.neurobiolaging.2005.03.015.

65. Melrose RJ, Campa OM, Harwood DG, Osato S, Mandelkern MA, Sultzer DL. The neural correlates of naming and fluency deficits in Alzheimer’s disease: an FDG-PET study. *Int J Geriatr Psychiatry*. 2009;24(8):885-893. doi:10.1002/gps.2229.

66. McKhann GM, Knopman DS, Chertkow H, et al. The diagnosis of dementia due to Alzheimer’s disease: recommendations from the national institute on aging-Alzheimer’s association workgroups on diagnostic guidelines for Alzheimer’s disease. *Alzheimer’s Dement*. 2011;7(3):263-269. doi:10.1016/j.jalz.2011.03.005.

67. Laiacoma M, Barbarotto R, Trivelli C, Capitani E. Dissociazioni semantiche intercategoriali descrizione di una batteria standardizzata e dati normativi. *Archi di Psicolog Neurol e Psychiatr*. 1993;54(2):209-248.

68. Snodgrass JG, Vanderwart M. A standardized set of 260 pictures: norms for name agreement, image agreement, familiarity, and visual complexity. *J Exp Psychol Hum Learn Mem*. 1980;6(2):174-215. doi:10.1037/0278-7393.6.2.174.

69. Della Rosa PA, Cerami C, Gallivanone F, et al. A standardized [18F]-FDG-PET template for spatial normalization in statistical parametric mapping of dementia. *Neuroinformatcs*. 2014;12(4):575-593. doi:10.1007/s10210-014-9235-4.

70. Boatman D. Transcortical sensory aphasia: revisited and revised. *Brain*. 2002;123(8):1634-1642. doi:10.1093/brain/123.8.1634.

71. Liebenthal E, Desai RH, Humphries C, Sabri M, Desai A. The functional organization of the left STS: a large scale meta-analysis of PET and fMRI studies of healthy adults. *Front Neurosoc*. 2014;8(289):1-10.

72. Wilson SM, Bautista A, McCarron A. Convergence of spoken and written language processing in the superior temporal sulcus. *Neuroimage*. 2017;171:67-74. doi:10.1016/j.neuroimage.2017.12.068.

73. Binder JR. Current controversies on Wernicke’s area and its role in language. *Curr Neurol Neurosci Rep*. 2017;17(8):58. doi:10.1007/s11910-017-0764-8.

74. Turken AU, Dronkers NF. The neural architecture of the language comprehension network: converging evidence from lesion and connectivity analyses. *Front Syst Neurosci*. 2011;5:1. doi:10.3389/fsyste.2011.00001.

75. Dronkers NF, Wilkins DP, Van Valin RD, Redfern BB, Jaeger JJ. Lesion analysis of the brain areas involved in language comprehension. *Cognition*. 2004;92(1-2):145-177. doi:10.1016/j.cognition.2003.11.002.

76. Visser M, Jefferies E, Embleton KV, Ralph MAL. Both the middle temporal gyrus and the ventral anterior temporal area are crucial for multimodal semantic processing: distortion-corrected fMRI evidence for a double gradient of information convergence in the temporal lobes. *J Cogn Neurosci*. 2012;24(8):1766-1778. doi:10.1162/jocn_a_00244.

77. Wei T, Liang X, He Y, et al. Predicting conceptual processing capacity from spontaneous neuronal activity of the left middle temporal gyrus. *J Neurosci*. 2012;32(2):481-489. doi:10.1523/jneurosci.1953-11.2012.

78. Lambon-Ralph MA, Jefferies E, Patterson K, Rogers TT. The neural and computational bases of semantic cognition. *Nat Rev Neurosci*. 2016;18(1):42-55. doi:10.1038/nrn.2016.150.

79. Herbet G, Mortiz-Gasser S, Boisue M, Duvaux S, Cocheureau J, Duffau H. Converging evidence for a cortico-subcortical network mediating lexical retrieval. *Brain*. 2016;139(11):3007-3021. doi:10.1093/brain/aww220.

80. Weems SA, Reggia JA. Simulating single word processing in the classic aphasia syndromes based on the Wernicke-Lichtheim-Geschwind theory. *Brain Lang*. 2006;98(3):291-309. doi:10.1016/j.bandl.2006.06.001.

81. Jackson RL, Bajada CJ, Rice GE, Lambon Ralph MA, Cloutman LL. An emergent functional parcellation of the temporal cortex. *Neuroimage*. 2017;170:385-399. doi:10.1016/j.neuroimage.2017.04.024.

82. Hope TMH, Price CJ. Why the left posterior inferior temporal lobe is needed for word finding. *Brain*. 2016;139(11):2823-2826. doi:10.1093/brain/aww240.

83. Grossman M, Irwin DJ. Primary Progressive aphasia and stroke aphasia. *Contin Lifelong Learn Neurol*. 2018;24(3, BEHAVIORAL NEUROLOGY AND PSYCHIATRY):745-767. doi:10.1212/CON.0000000000000618.

84. Baldo JV, Dronkers NF. The role of inferior parietal and inferior frontal cortex in working memory. *Neuropsychology*. 2006;20(5):529-538. doi:10.1037/0894-4105.20.5.529.

85. Baldo JV, Katseff S, Dronkers NF. Brain regions underlying repetition and auditory-verbal short-term memory deficits in aphasia: evidence from voxel-based lesion symptom mapping.
86. Paulesu E, Frith CD, Frackowiak RSJ. The neural correlates of the verbal component of working memory. *Nature*. 1993;362(6418):342-345. doi:10.1038/362342a0.

87. Price CJ. A review and synthesis of the first 20 years of PET and fMRI studies of heard speech, spoken language and reading. *Neuroimage*. 2012;62(2):816-847. doi:10.1016/j.neuroimage.2012.04.062.

88. Papagno C, Comi A, Riva M, et al. Mapping the brain network of the phonological loop. *Hum Brain Mapp*. 2017;38(6):3011-3024. doi:10.1002/hbm.23569.

89. Goldstein L, Pouplier M, Chen L, Saltzman E, Byrd D. Dynamic action units slip in speech production errors. *Cognition*. 2007;103(3):386-412. doi:10.1016/j.cognition.2006.05.010.

90. Butler RA, Ralph MAL, Woollams AM. Capturing multidimensionality in stroke aphasia: mapping principal behavioural components to neural structures. *Brain*. 2014;137(12):3248-3266. doi:10.1093/brain/awu286.

91. Price CJ, Humphreys GW. Contrasting effects of letter-spacing in alexia: further evidence that different strategies generate word length effects in reading. *Q J Exp Psychol Sect A*. 1995;48(3):573-597. doi:10.1080/14640749508401406.