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Where (in the brain) do semantic errors come from?

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Abstract

Background: Semantic errors result from the disruption of access either to semantics or to lexical representations. One way to determine the origins of these errors is to evaluate comprehension of words that elicit semantic errors in naming. We hypothesized that in acute stroke there are different brain regions where dysfunction results in semantic errors in both naming and comprehension versus those with semantic errors in oral naming alone.

Methods: A consecutive series of 196 patients with acute left hemispheric stroke who met inclusion criteria were evaluated with oral naming and spoken word/picture verification tasks and magnetic resonance imaging within 48 hours of stroke onset. We evaluated the relationship between tissue dysfunction in 10 pre-specified Brodmann's areas (BA) and the production of coordinate semantic errors resulting from (1) semantic deficits or (2) lexical access deficits.

Results: Semantic errors arising from semantic deficits were most associated with tissue dysfunction/infarct of left BA 22. Semantic errors resulting from lexical access deficits were associated with hypoperfusion/infarct of left BA 37.

Conclusion: Our study shows that semantic errors arising from damage to distinct cognitive processes reflect dysfunction of different brain regions.

Keywords

aphasia; perfusion-weighted magnetic resonance imaging; semantics; acute ischemic stroke

Semantic errors, such as naming a horse as “cow”, are often taken to be evidence of an impaired semantic system. For example, this sort of error in picture naming (called, “coordinate semantic error”) is very common among patients with semantic dementia, who have trouble on a variety of semantic memory tasks with various input and output modalities, such as word/picture matching, synonym matching, and word or picture association tasks (Snowden, Goulding et al., 1989; Hodges, Patterson et al., 1992; Jefferies and Lambon Ralph, 2006). Although some patients with semantic deficits fail to produce any response or produce only unintelligible jargon or neologisms, many make semantic coordinate errors in naming. Semantic coordinate

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errors are also common among individuals with impaired access to semantic representations or underspecified semantic representations due to stroke, although such patients sometimes also make associative semantic errors, such as horse named as “barn” (Coltheart, 1980; Nickels, 1995; Hillis, Rapp et al., 1990; Jefferies and Lambon Ralph, 2006). Occasionally, semantic errors in picture naming arise as a result of impaired access to semantics specifically from vision, as indicated by relatively spared naming from tactile input or definition (Humphreys, Riddoch et al., 1988; Hillis and Caramazza, 1995a; Marsh and Hillis, 2005).

However, these “coordinate” semantic errors can also occur as a result of dysfunction in accessing phonological representations of words. For example, Caramazza and Hillis (1990) described two patients who made frequent semantic errors in oral reading and oral naming of pictures, but made no semantic errors in comprehension of words or in written naming of the same items that elicited semantic errors in oral naming. For example, when asked to name a clam, patient RGB said “octopus” but wrote *clam*. These patients provide strong evidence that semantic errors can come from impaired access to lexical representations for output, without damage to the semantic system. Semantic errors in these cases have been explained by the hypothesis that individual features of a compositional semantic representation activate all lexical representations to which they correspond. Normally, only the target lexical representation will be activated by all of the semantic features, and will therefore be “selected” for output. However, when the target lexical representation is unavailable due to a brain lesion, another lexical representation that is partially activated by the semantic features might be selected for output instead (see Hillis and Caramazza (1995b) for discussion; see also Morton & Patterson, 1980 for an account of “post-semantic” semantic errors in reading). These patients generally are aware that the semantic errors are not quite right, but are often unable to correct them.

One way to evaluate whether semantic errors result from disrupted access to semantics, versus disrupted access to lexical representations, is to evaluate comprehension of words that elicit semantic errors in naming. Patients with impaired semantic representations or multi-modality access to semantics make semantic errors in comprehension tasks, as well as naming tasks from a variety of input modalities. Patients whose disruption occurs in modality-specific access to semantics from vision make errors in all tasks that require linking a visual stimulus with meaning, including word/picture matching tasks and picture association tasks that require distinctions between semantically related items (Hillis & Caramazza, 1995a). In contrast, patients whose semantic errors result from impaired access to lexical representation of words (for output) perform normally on word/picture verification and picture association tasks.

If semantic errors can reflect damage to distinct cognitive processes underlying naming, it is plausible that they can result from distinct loci of damage in the brain. Goodglass and Wingfield (1997) reported that patients with errors in naming but not comprehension had lesions in left angular gyrus or left inferior temporal cortex, while patients with errors in naming and comprehension of the same words had lesions involving superior temporal gyrus. However, their patients had large lesions and were studied long after potential reorganization and made several types of errors. Therefore, they were unable to show statistically significant associations between deficits and lesion sites, because some patients with lesions in the “critical” areas had recovered from naming and/or comprehension. In this paper, we test the hypothesis that semantic errors in naming can reflect disruption of distinct cognitive processes associated with damage to different areas of the brain. We identified areas of the brain where acute tissue dysfunction (infarct and/or hypoperfusion) resulted in (1) semantic errors in naming and comprehension (indicating impaired semantics or access to semantics) versus (2) semantic errors in oral naming but not comprehension (indicating impaired access to lexical representations from intact semantic representations). To evaluate the specificity of these results, we also examined the areas of acute tissue dysfunction associated with a mixture of

semantic and phonological errors or purely phonological errors in naming (with and without comprehension deficits).

Methods

Participants

A consecutive series of 236 right-handed patients with acute, left hemisphere ischemic stroke, who provided informed consent or whose next of kin provided informed consent (in patients with comprehension deficits) and met the following inclusion criteria, were initially enrolled. Inclusion criteria included: premorbid proficiency in English, no known hearing loss or uncorrected visual impairment; no history of dementia, previous symptomatic stroke, or other neurological disease; and no hemorrhage on initial scans. Additionally, we attempted to complete all testing within 24 hours of stroke onset; however, we included some patients who were tested between 24 and 48 hours of stroke onset (usually because they were admitted close to or after 24 hours after initial symptoms). After enrollment, 31 patients were excluded either because they were not able to complete tests of naming and word comprehension and have an interpretable MR examination within 48 hours of stroke onset, or because they were mute, produced a single perseverative response, or made no response in naming (such that their performance could not be adequately interpreted). An additional 9 were excluded because they were found to have bilateral, brainstem, or no strokes on MRI. Among the final 196 included patients, the mean age was 59.8 ± 16.2 standard deviation (SD) years; the mean education level was 12.3 ± 3.4 years; and 55% were female, which is representative of all acute stroke patients admitted to our service.

A group of 50 hospitalized controls with no evidence of infarct or hypoperfusion on MRI (patients admitted with transient ischemic attack or coronary artery disease, who were asymptomatic at the time of testing and MR examination) also were administered the language tests described below. These participants were selected as controls to obtain normative data from individuals in the same age group and with similar health status (except stroke) and from the same catchment area as the stroke patients, and who took the tests under similar conditions in the hospital. Their mean age was 64.7 ± 10.7 SD years.

Language tests

Within 48 hours of stroke onset, participants were presented pictures of objects for oral naming, and an additional set of pictured objects for spoken word/picture verification. Some patients named 30 pictured objects, but the majority named only a smaller set of 17. The stimulus sets were matched for word length, frequency, and semantic categories. For word/picture verification, each of 17 items was presented three times: once with a semantically related foil; once with a phonologically related foil; and once with the target, in counterbalanced order across three presentations of the same set of items. The same item was presented only once every 17 items (not consecutively). The patient was required to accept the target word and reject both foils to receive credit for the item. This word/picture verification test has been shown to be more sensitive to word comprehension deficits than more traditional forced choice word/picture matching tests (Breese and Hillis, 2004). The mean error rate for the 50 normal controls on this word/picture matching test was $0.12\% \pm 0.86$ SD (range 0-6% error). For oral naming, the patient was presented with a line drawing from Snodgrass and Vanderwart (1980) for untimed naming. If the participant produced the superordinate name (e.g., horse named as "animal"), they were asked to be more specific. The final response was scored. The mean error rate for the same age-matched normal control subjects on this oral picture naming test was $0.84\% \pm 2.1$ SD (range 0-6%). Semantic errors among patients included: (1) semantic coordinate errors (e.g. dog named as "cat"); (2) associative semantic errors (e.g. dog named as "bark"), or (3) circumlocutions (dog named as "the thing that barks"). Phonological errors

consisted of 3 error subtypes: (1) phonemic- nonwords related to target by initial or final phoneme(s); (2) neologisms- nonwords phonologically unrelated to target; and (3) formal - real words related to target by initial or final phoneme(s). Since the focus of this paper is on semantic errors, these error types were not analyzed separately in this study.

Imaging

Within 24 hours of language testing, patients underwent MR examination, including diffusion weighted imaging (DWI) with computation of apparent diffusion coefficient (ADC) maps, which reveal infarct or dense ischemia within minutes to hours of stroke onset, perfusion-weighted imaging (PWI, which reveals areas of hypoperfusion that correspond to dysfunction), Fluid Attenuated Inversion Recovery (FLAIR, which is sensitive to old infarcts), and T2*-weighted gradient-echo (which is sensitive to hemorrhage). Hypoperfusion was defined as > 4 sec delay in time to peak (TTP) arrival of contrast to the voxels within each region of interest, relative to the homologous region in the right hemisphere. The following Brodmann's areas (BA) were examined for hypoperfusion: 6, 44, 45, 19, 21, 22, 37, 38, 39, and 40, because chronic lesions involving these regions have been reported to be associated with impaired naming and/or comprehension. Technicians blinded to the language test results identified the presence or absence of tissue dysfunction (dense ischemia or infarct defined as bright on DWI and dark on ADC maps and/or hypoperfusion on PWI, as defined above) in each BA, with a point-to-point percent agreement of > 96%. In addition, areas of tissue dysfunction defined in the same way were outlined on the MNI atlas by a blinded technician and analyzed using MRICro <http://www.sph.sc.edu/comd/rorden/mricro.html>) for the voxel-based analysis.

Statistical Analysis

We first categorized patients into groups: (1) patients who made purely semantic errors in naming but no semantic errors in word comprehension; (2) patients who made semantic and phonological errors in naming, but no semantic errors in word comprehension; (3) patients who made purely semantic errors in naming and also made semantic errors in comprehension; (4) patients who made semantic and phonological errors in naming as well as semantic errors in comprehension; (5) patients who made purely phonological errors in naming (with or without comprehension deficits); (6) patients with normal performance on naming and comprehension; or (7) unclassifiable. Patients in the first 4 groups made semantic errors on >10% of their naming responses; patients in groups 1 and 3 made only semantic errors (coordinate or associate semantic errors), circumlocutions (e.g., dog-> "the thing that barks"), and/or omissions; the focus of this paper is on these patients. To be classified as producing semantic errors in naming, the patient had to make semantic coordinate errors (e.g. horse named as "cow") on at least 10% of items; to be classified as making semantic errors in naming and comprehension, they had to make coordinate semantic errors on >10% of the items in comprehension, and at least one item on naming (and >10% of their intelligible responses had to be semantic errors). No normal control subject made semantic errors on >10% of items on either test. Patients who made semantic errors on >10% of items in word *comprehension* but had no intelligible naming responses (e.g. only neologisms) were scored as "unclassifiable", since many of these patients might have had semantic deficits as the cause of their naming errors, but potential semantic errors were unrecognizable. Patients in groups 2, 4, and 5 made phonological errors (defined above) on > 10% of items.

Then, for Group 3 (who made semantic errors due to semantic deficits, as indicated by semantic errors on > 10% of items in word comprehension and only semantic errors in naming), we identified Brodmann areas where tissue dysfunction (the independent variables) contributed to the rate of semantic errors in word comprehension (the dependent variable) using simultaneous linear regression. For patients in Group 1 (who made no semantic errors in comprehension), we identified Brodmann areas where the presence of tissue dysfunction (the

independent variables) contributed to the rate of semantic errors in naming (the dependent variable) using simultaneous linear regression. There were too few patients in other groups to use regression analyses to identify areas where tissue dysfunction is associated with these patterns of errors. We computed chi-squared tests to evaluate the association between tissue dysfunction in each BA and membership in each group. Patients in Groups 2, 4, 5, who all made phonological errors, were combined to identify areas associated with production of phonological errors in naming. An alpha level of 0.05 after Bonferroni correction for multiple comparisons was used to identify significant associations. Finally, for purposes of visualization, we used MRICro and the Brain Image Database (BRAID; Herskovits, 2000) to carry out a whole-brain analysis of the voxels most associated (by Fisher exact tests) with (1) Group 3 performance (production of semantic errors both in naming and in word comprehension, with >10% of total responses being semantic errors), and (2) Group 1 performance (production of purely semantic errors in naming, with this type of error consisting of >10% of total responses, together with spared word comprehension), and Group 1 + 3 performance (purely semantic errors in naming with or without semantic errors in comprehension) compared to no semantic errors.

Results

Semantic errors resulting from semantic deficits (Group 3)

A total of 56 patients (29% of the participants) made purely semantic errors in oral naming with concomitant semantic errors in word/picture verification, indicating impaired semantic memory or impaired access to lexical-semantics. The rate of semantic errors in word/picture verification (a measure of the severity of the semantic deficit) in this group was only independently predicted by hypoperfusion and/or infarct of BA 22 (Table 1).

Purely semantic errors resulting from lexical access deficits (Group 1)

A subset of 20 patients (10% of participants) made semantic errors but not phonological errors in oral naming responses to at least 10% of pictures and made no errors in word/picture verification, indicating that their semantic errors were likely due to impaired access to lexical representations for output. The rate of semantic errors in naming in this group was only independently predicted by hypoperfusion and/or infarct of BA 37 (Table 2).

Mixed Error Types were far less common in acute stroke than previously reported for chronic stroke

Only two patients made both semantic and phonological errors in naming with no comprehension deficits, and nine patients made both types of errors in naming as well as semantic errors in comprehension. These patients all had relatively large areas of hypoperfusion/infarct in the frontotemporal cortex, involving BA 6, 37, and/or 22, and a few with hypoperfusion/infarct also in 21, 38, and/or 19, but with no areas significantly associated with these error patterns.

Phonological Errors

To determine if the significant associations between the presence of particular naming errors and certain areas of tissue dysfunction predominantly reflected the likelihood of ischemia in those areas rather than the error type, we examined the association between production of phonological errors (>10% of total responses) in naming and tissue dysfunction in each area. The production of phonological errors in naming was associated with hypoperfusion and/or infarct in left BA 6 only ($\chi^2_1 = 9.2$; $p = 0.02$ after correction for multiple comparisons). Phonological errors were not associated with any of the areas associated with production of semantic errors in naming, by chi square tests.

Voxel-based analysis

Finally, Figure 2a shows the voxels of the MNI atlas where tissue dysfunction (hypoperfusion and/or dense ischemia or infarct, as defined above) was associated with the production of semantic errors in oral naming and in word comprehension (Group 3) compared to semantic errors in naming only (Group 1). This figure provides further evidence that the areas of tissue dysfunction associated with this pattern of errors are predominantly in left superior temporal cortex and associated deep white matter, with some additional associated voxels in left supramarginal gyrus. Figure 2b shows the voxels of the MNI atlas where tissue dysfunction (hypoperfusion and/or dense ischemia or infarct, as defined above) was associated with the production of at least 10% semantic errors (and no phonological errors) in oral naming without errors in word comprehension (Group 1) compared to no semantic errors in either task (Groups 5 and 6 combined). This figure provides further evidence that the areas of tissue dysfunction associated with this pattern of errors are predominantly in left fusiform cortex (part of BA 37), although it also shows that voxels in BA 19 (posterior occipital cortex) were also associated with production of semantic errors in naming due to lexical deficits. Finally, Figure 2c shows the voxels most associated with production of purely semantic errors in naming (with or without semantic errors in comprehension; Groups 1 and 3) compared to no semantic errors in either task (Groups 5 and 6). The most strongly associated voxels were in left BA 37, but there were also associated voxels in left BA 22 (superior temporal cortex), BA 39 (angular gyrus), 40 (supramarginal gyrus), 18 and 19 (occipital cortex), and 44 (posterior inferior frontal gyrus), and insula. The association between dysfunction in the insula and production of semantic errors arising from either deficit (lexical or semantic) may be due to larger infarcts in patients who made semantic errors (with or without word comprehension errors), compared to those who made no semantic errors, since the insula is the most commonly infarcted area in all large middle cerebral artery strokes (see Hillis, Work et al., 2004 for discussion).

Discussion

Our results provide evidence that semantic errors can result not only from disruption of different cognitive mechanisms, but can also result from damage or dysfunction of different brain regions. Hypoperfusion and/or infarct of BA 22 (superior temporal cortex, sometimes referred to as “Wernicke’s area”) predicted semantic errors in both naming and comprehension in acute stroke, indicating that this region is critical for linking words to their meanings. The production of a semantic error (e.g. dog-> “cat”; horse-> “deer”) must, however, reflect the operation of the spared brain tissue. One explanation that fits with a number of observations in the literature is that BA 22 is not a location for the suppository of semantic features, but an area critical for linking a modality-independent lexical representation to a distributed set of semantic features that collectively comprise the meaning of the word (presumably represented in spared areas of cortex outside of BA 22). If the “links” are spared to some defining features but not others, the individual will have an impoverished set of defining features associated with the word, but the features will still be part of the general concept or semantic memory (which also includes personal information like <my horse is a Tennessee Walker> and general information, like <cowboys ride horses> that do not define horses). For example, referring to a schematic representation of the cognitive processes required for naming in Figure 3, a patient with damage of this sort might have access to an abundance of personal and general knowledge about horses (and so, might be able to saddle and ride one), but will not “know” what subset of this knowledge or semantic features make a horse a horse. A subset of this knowledge will also be accessed by a picture of a deer, a cow, etc. Without the links that identify which of the features are critical to being called a “horse”, the person might accept any semantically related item as the referent of the word, as seen in semantic errors in word/picture verification. Likewise, in naming, any lexical representation that is consistent with an inappropriately selected subset of this knowledge or semantic feature might be activated for naming, resulting in the production

of semantic errors in naming also. A role of left BA 22 in access to semantic representations for naming and comprehension is also supported by functional neuroimaging studies that show activation in this area in both tasks (e.g. Fridriksson and Morrow, 2005).

We also found that the majority of people with infarct or hypoperfusion in left BA 21 (inferior temporal cortex), and 50% with ischemia in left BA 38, made semantic errors in naming and word comprehension. These areas have been identified as critical for semantic memory in a number of investigations (see also Sharp, Scott and Wise, 2004). Atrophy of bilateral or left anterior-inferior temporal cortex, including BA 21 is associated with severe impairments of semantic memory, as observed in semantic dementia and herpes encephalitis (Gorno-Tempini, Dronkers et al., 2004; Jeffries and Lambon Ralph, 2006; Hodges, Patterson et al., 1992). These basal temporal regions may be essential for semantic memory (semantic representations, or at least a subset of the features), while left BA 22 (posterior superior temporal cortex; Wernicke's area) may be critical for linking lexical representations to the set of features that comprise lexical-semantic representations or defining features. Stroke more often causes infarct in BA 22 than in BA 21, due to more collateral blood flow to inferior temporal cortex (Caviness, Makris et al., 2002). The difference in the vulnerability of BA 22 versus BA 21 to damage due to stroke versus SD may account for qualitative differences in the patterns of errors across tasks in patients with comprehension deficits due to the two etiologies (Jeffries and Lambin-Ralph, 2006). Previous studies have explained these distinct patterns of semantic errors across tasks as resulting from an executive disorder after stroke but a semantic memory disorder in SD (Jeffries and Lambon-Ralph, 2006) or by impaired "access" versus "storage", although the latter distinction is often quite difficult to make (see Rapp & Caramazza, 1989 for discussion). In reference to Figure 3, we propose that patients with tissue dysfunction in left BA 21 or 38 may have had impoverished semantic representations because of disruption of some of the semantic features themselves. A patient with such a deficit would accept semantically related words as the target in word/picture verification tasks, and would make semantic errors in naming, because a variety of lexical representations would be consistent with the subset of spared semantic features (e.g. "horse", "deer", and "cow" are all compatible with the subset of semantic features <hooves>, <herbivore>, <quadruped>). However, unlike a patient with ischemia in BA 22, the patient might have insufficient spared knowledge to constrain appropriate behavior in response to horses. So, the patient might try to milk a horse for milk to drink, or attempt to ride a deer (not likely successfully!). In our study, at least some stroke patients had imaging abnormalities indicating neural dysfunction in left BA 21, although no patients had dysfunction of bilateral BA 21. No patient showed the sort of object agnosia that is often described in SD, at least from clinical observation. The patients behaved normally in their environment, using objects appropriately.

Tissue dysfunction in left BA 37 (posterior middle and inferior temporal/fusiform gyrus) predicted production of only semantic errors in naming with spared word comprehension, indicating that this area is critical for accessing lexical representations for output (see also (Rayner, Foundas et al., 1997; Foundas, Daniels et al., 1998; Hillis, Tuffiash et al., 2002; Hillis, Kleinman et al., 2006). Functional imaging studies have shown activation in part of left BA 37 in a variety of lexical tasks, indicating that a portion of this region may be intimately involved in modality-independent lexical processing, such as Braille in the blind, sign language in the deaf, and naming (Buchel, Price and Friston, 2003; Price and Devlin, 2003 & 2004; Cohen, Jobert, Le Bihan, and Dehaene, 2004). In reference to Figure 3, we believe that BA 37 (or part of it) is critical for linking the subset of semantic features that define the word (what makes a horse a horse) to modality-specific orthographic and phonological word forms for production tasks such as naming, even though all of these representations themselves depend on other areas of the cortex. This linking mechanism is schematically shown as the "modality-independent lexical representation." It is the access mechanism that is impaired in most cases of pure anomia – when one can neither write nor say the name, but it is on "the tip of the

tongue.” Tissue dysfunction in this area has been previously associated with anomia and has not been associated with spoken word comprehension deficits in this or in previous studies (Raymer, Foundas et al., 1997; Foundas, Daniels et al., 1998; Deleon, Gottesman et al., 2007).

Numerous functional studies have indicated a role of prefrontal regions in semantic tasks (Gitelman, Nobre et al., 2005). Most of these studies have indicated that prefrontal regions are more important for controlled response selection, either in semantic tasks (Thompson-Schill, D'Esposito et al., 1997; Demb, Desmond et al., 1995; Wagner, Pare-Blagoev et al., 2001) or more generally (Thompson-Schill, Kurtz et al., 1998; Thompson-Schill and Gabrielli, 1999; Thompson-Schill, Aguirre et al., 1999), rather than for accessing meanings of individual words (Bookheimer, 2002; see also Price, Mummery et al., 1999). We did not find any association between neural dysfunction in left prefrontal regions and the rate or presence of semantic errors in comprehension, consistent with the hypothesis that this area is not essential for spoken word comprehension. However, in the voxel-based analysis, there were voxels in BA 44 and 46 that were associated with the production of at least 10% semantic errors in naming without semantic errors in comprehension, suggestive of a role of these areas in lexical output. Tissue dysfunction in left BA 6 was associated with production of phonological errors in naming.

The presence, but not rate, of semantic errors in naming with or without semantic errors in comprehension, was also associated with areas within left angular gyrus and supramarginal gyrus (see Figures 2c). These areas have long been considered critical for naming (e.g. Goodglass & Wingfield, 1997). These areas have also been associated with activation during functional imaging tasks that involve semantic processing, indicating that it is at least engaged in some aspect of semantic processing. The role of this area in naming demands further study.

In summary, two distinct patterns of performance across tasks, both observed with production of semantic errors in naming, were associated with different areas of compromised neural tissue. Production of semantic errors resulting from impaired semantics or access to semantics, as reflected by semantic errors in word/picture verification and naming, was associated with hypoperfusion and/or infarct in left BA 22 and 19 (superior temporal cortex and adjacent occipital cortex), and somewhat less frequently with left BA 39 (angular gyrus) and 40 (supramarginal gyrus), 21 and/or 38 (inferior and anterior temporal cortex). Further investigation is needed to determine if neural dysfunction in these areas interferes with separate components of semantic processing, but this seems likely from studies of dementia versus stroke-related aphasia. Hypoperfusion/infarct in left BA 37 (posterior middle/inferior temporal and fusiform cortex) was associated with semantic errors in naming but not in comprehension, providing further evidence that this area may be essential for accessing modality-independent lexical representations from intact semantic representations. Both correct and error responses themselves must reflect function of spared tissue. In contrast, hypoperfusion/infarct only in left BA 6 was associated with production of phonological errors in naming. Future studies will evaluate the role of various prefrontal regions in naming, and areas where tissue dysfunction results in various types of phonological errors. Functional neuroimaging studies of recovering aphasic patients show different areas of activation in spared cortex associated with production of semantic versus phonological errors in naming (Fridriksson, Baker, Moser, submitted).

In this study we identified areas of tissue dysfunction that are statistically associated with particular patterns of errors after stroke. However, some individuals have lesions in these areas but do not show the associated pattern of errors. The reason for this inconsistency could be due to weaknesses in the methods for identifying the deficits of interest or weaknesses in the methods for identifying regions of interest in the brain (e.g. because of the individual variability in cytoarchitectural fields). An alternative or additional explanation is that there is some individual variability in structure-function relationships in the brain. These accounts are

probably not distinguishable, and are both likely to be true to some extent. There are undoubtedly weaknesses in the methods, and there is probably also some variation across individuals in how language is organized in the brain.

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Figure 1.

Top panel. DWI (left) and PWI (right) scans of a patient who made semantic errors in naming and comprehension, with infarct and hypoperfusion of left BA 21 and 22. Lower panel. DWI and PWI scans of a patient who made semantic errors in naming but not comprehension, with hypoperfusion of left BA 37. Blue areas on PWI are hypoperfused.

Figure 2.

Negative logarithm statistical maps of Fisher exact test p-value for given voxel presented in radiological convention (left on right). Panel A. Voxels of the MNI atlas where tissue dysfunction (hypoperfusion and/or dense ischemia or infarct, as defined above) was associated with the production of at least 10% errors in word comprehension and oral naming. Panel B. Voxels where tissue dysfunction was associated with the production of purely semantic errors in oral naming without semantic errors in word comprehension. Panel C. Voxels where tissue dysfunction was associated with the production of purely semantic errors in oral naming with or without semantic errors in word comprehension. Range of $-\log(p)$ values is presented on color bar below the images.ext for details of comparison groups).

Figure 3.
 Schematic representation of the cognitive processes underlying naming

Table 1

Simultaneous Linear Regression for Rate of Semantic Errors in Comprehension in Group 3

Brodman's Area	Standardized Coefficients (Beta)	T	Significance
6	-0.02	-0.24	Ns
44	0.14	1.20	Ns
45	-0.04	-0.42	Ns
19	0.19	1.90	Ns
37	-0.04	-0.42	Ns
21	0.03	0.30	Ns
22	0.26	2.61	.010
38	-0.03	-0.47	Ns
39	0.16	1.65	Ns
40	-0.09	-0.96	Ns

Furthermore, there was a significant association between (1) production of purely semantic errors in oral picture naming plus semantic errors in word/picture verification on > 10% of items on both tasks and (2) hypoperfusion and/or infarct of BA 22 ($\chi^2_1 = 17$; $p < 0.0001$); BA 19 ($\chi^2_1 = 10.8$; $p = 0.01$), and BA 39 ($\chi^2_1 = 7.9$; $p = 0.04$) after correction for multiple comparisons. See Figure 1 (upper panel) for an illustrative case. After correction, there was not a significant association between this pattern of semantic errors in naming and word comprehension for BA 21 (inferior temporal cortex) or 38 (temporal pole). However, this lack of statistically significant association may reflect the relatively small number of patients with hypoperfusion/infarct in these areas, because 14/26 (54%) patients with tissue dysfunction in left BA 21 and 4/8 (50%) with tissue dysfunction in left BA 38 showed this pattern. The only other areas where $\geq 50\%$ of patients with imaging abnormalities in that area showed this pattern of errors were left BA 19 and 22. Although BA 19 was not significantly associated with semantic errors in naming and comprehension in the linear regression, the lack of significance might be due to insufficient power.

Table 2

Simultaneous Linear Regression for Rate of Semantic Errors in Naming in Group 1

Brodman's Area	Standardized Coefficients (Beta)	T	Significance
6	-0.10	-0.73	Ns
44	0.06	0.39	Ns
45	-0.25	-1.68	Ns
19	0.10	0.64	Ns
37	0.30	2.11	0.037
21	-0.18	-1.48	Ns
22	0.04	0.32	Ns
38	0.02	0.23	Ns
39	-0.11	-0.79	Ns
40	0.19	1.43	Ns

Furthermore, left BA 37 was the only area where $\geq 50\%$ of the patients with purely semantic errors in naming and spared word comprehension had hypoperfusion and/or infarct. See Figure 1 (lower panel) for an illustrative case. The other patients in this group had tissue dysfunction in a variety of sites, including BA 44, 39, or 40 (one or two in each).