Neural regions essential for distinct cognitive processes underlying picture naming

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We hypothesized that distinct cognitive processes underlying oral and written picture naming depend on intact function of different, but overlapping, regions of the left hemisphere cortex, such that the distribution of tissue dysfunction in various areas can predict the component of the naming process that is disrupted. To test this hypothesis, we evaluated 116 individuals within 24 h of acute ischaemic stroke using a battery of oral and written naming and other lexical tests, and with magnetic resonance diffusion and perfusion imaging to identify the areas of tissue dysfunction. Discriminant function analysis, using the degree of hypoperfusion in various Brodmann's areas—BA 22 (including Wernicke's area), BA 44 (part of Broca's area), BA 45 (part of Broca's area), BA 21 (inferior temporal cortex), BA 37 (posterior, inferior temporal/fusiform gyrus), BA 38 (anterior temporal cortex) and BA 39 (angular gyrus)—as discriminant variables, classified patients on the basis of the primary component of the naming process that was impaired (defined as visual, semantics, modality-independent lexical access, phonological word form, orthographic word form and motor speech by the pattern of performance and types of errors across lexical tasks). Additionally, linear regression analysis demonstrated that the areas contributing the most information to the identification of patients with particular levels of impairment in the naming process were largely consistent with evidence for the roles of these regions from functional imaging. This study provides evidence that the level of impairment in the naming process reflects the distribution of tissue dysfunction in particular regions of the left anterior, inferior and posterior middle/superior temporal cortex, posterior inferior frontal and inferior parietal cortex. While occipital cortex is also critical for picture naming, it is likely that bilateral occipital damage is necessary to disrupt visual recognition. These findings provide new evidence that a network of brain regions supports naming, but separate components of this network are differentially required for distinct cognitive processes or representations underlying the complex task of naming pictures.

Keywords: aphasia; magnetic resonance perfusion weighted imaging; naming; anomia; language

Abbreviations: BA = Brodmann's area; DWI = diffusion-weighted imaging; PWI = perfusion-weighted imaging; TTP = time to peak

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Introduction

Impaired ability to name objects or actions is nearly ubiquitous among individuals with aphasia. However, aphasic individuals may have trouble naming pictures for different reasons. Naming a pictured object is a complex process. It involves a number of relatively distinct (but interacting) mental representations and cognitive processes. To illustrate, naming a picture of a particular horse as ‘horse’ demands at least the following processes: (1) recognition of the visual stimulus as an instance of a familiar concept; (2) access to the meaning of horse (or what makes a horse a horse); (3) access to the phonological word form (the learned pronunciation of the word) and (4) motor programming and planning of articulation (as well as implementation of the movement sequences) to say the word. Although these functions may not be completely segregated anatomically, they can be individually impaired by brain damage. Therefore, they are depicted as distinct levels of processing in a schematic
representation of the representations and processes underlying naming shown in Fig. 1. This 'model' can be criticized on a variety of grounds, as discussed below, but serves as a basis for distinguishing the various impairments in picture naming that are observed consequent to brain lesions.

The meaning, or 'semantic' component is complex, and probably includes (at least) an amodal representation of everything we know about an item, including general knowledge and personal knowledge about the item, as well as those features that make it what it is and distinguishes it from related items (what we will refer to, for simplicity, as 'the defining features' or 'lexical-semantics'). To link the complex semantic representation to a word form representation it is necessary to select the defining features from the entire semantic representation. That is, to name a picture of a horse, we need to select information about what makes a horse a horse and not a deer (e.g. mane, can be domesticated). We do not need to access information about how they are used in a particular region of the world, or about horses we have known. This linking mechanism might take the form of executive processes for selecting a lexical representation from semantics (Jeffries and Lambon-Ralph, 2006) or identification mechanisms (Miller and Johnson-Liard, 1976; Hillis et al., 1990). The defining features ('lexical-semantics') selected by an executive function or identification mechanism can be thought of as a subset of the distributed semantic representation. That is, what we mean by 'lexical-semantics' is restricted to the type of semantic information needed to name pictures or to determine whether or not a picture depicts an instance of the referent of a particular word.

The distinction between the entire semantic representation and lexical-semantics is best captured by distinct patterns of performance when each is disrupted. Disruption or degradation of the semantic representation, including amodal general and personal knowledge, is seen in patients with semantic dementia, who late in the disease use all but the most familiar items inappropriately (e.g. spread butter with a can opener). This behaviour is rarely observed in patients with aphasia caused by unilateral stroke, probably because disruption of the amodal general and personal knowledge requires left (and perhaps to a lesser degree, right) anterior inferior and lateral temporal damage as shown in patients with semantic dementia (Mummery et al., 2000; Gorno-Tempini et al., 2004). Stroke rarely causes damage to anterior, inferior temporal cortex (Hether et al., 1998; Caviness et al., 2002; Wise, 2003) or bilateral temporal cortex. Disruption of mechanisms for linking this semantic representation (including amodal general and personal knowledge) to a particular word form representation (for both word comprehension and naming), via lexical-semantics, is frequently observed after stroke, in patients with transcortical sensory aphasia, Wernicke’s aphasia or global aphasia. These patients typically have damage to superior temporal gyrus, inferior parietal cortex or prefrontal cortex (Goodglass and Wingfield, 1997; Hart and Gordon, 1990; Hillis et al., 2001). However; damage to these areas might result in reduced activation of more rostral temporal cortex (Wise, 2003).

Both patients with damage to lexical-semantics after stroke and patients with semantic dementia make semantic errors in naming and comprehension, but show distinctive patterns across tests and stimuli, as elegantly demonstrated by Jeffries and Lambin-Ralph (2006). In their study, patients with semantic dementia were sensitive to familiarity of the item, showed item consistency across tests and made mostly 'coordinate' semantic errors (e.g. deer for horse). Patients with post-stroke aphasia were not sensitive to familiarity, did not show item consistency, made associative semantic errors (e.g. hay for horse) as well as coordinate semantic errors and often named items correctly in response to phonemic cues. The authors interpreted the latter pattern as evidence that the amodal semantic core is intact, and accounted for the pattern of errors as a reflection of impaired executive processes. However, the pattern of performance might also be explained by underspecified lexical-semantic information that is consistent with a number of different word-form representations (e.g. <large, hooved, herbivore> would be consistent with 'horse', 'cow', 'donkey', 'deer' etc. and might lead to inconsistent responses to the same item across tests and trials of the same test (see Hillis et al., 1990 or Hillis and Caramazza, 1995a for further details of this account). The phonemic cue would provide additional information that would allow the patient to select the correct word. The fact that such patients can be ‘mis-cued’ to produce the wrong word with an incorrect phonemic cue (Howard and Orchard-Lisle, 1984; Hillis and Caramazza, 1995b; Howard and Gatehouse, 2006) is consistent with the view that a correct response to a phonemic cue does not imply that the meaning of the item is intact. Furthermore, since features of the semantic representation that are not part of lexical-semantics would be spared in stroke patients with impaired lexical-semantics, they might access some of these spared features in naming and produce associative semantic errors, as well as coordinate semantic errors, as reported by Jeffries and Lambon-Ralph (see also Hillis et al., 1990). Additionally, patients with impaired amodal general knowledge (SD) might try to saddle a deer, while a patient with impaired lexical-semantics would not. Thus, impairments of lexical-semantics versus impairments of the more inclusive semantic representation would explain the distinct patterns of performance in naming and behaviour after stroke versus semantic dementia. Many theories of the cognitive processes underlying naming also specify an intermediate level of representation between the semantic representation and the phonological word form—a modality-independent lemma. Although the original use of the term 'lemma' referred to a representation with semantic content (Kempen and Huijbers, 1983), more recent papers have assumed that the lemma has
no semantic content (Dell, 1986; Levelt, 1989, 1999; Levelt et al., 1991; Dell et al., 1997). Instead, the lemma mediates access to the phonological word form or orthographic word form (the learned spelling of the word) from semantics, and specifies the syntactic role of the word (e.g. grammatical word class and gender; Garrett, 1988; Roelofs, 1992; Badecker et al., 1995). Whether or not this level of representation is essential has been hotly debated (Roelofs, 1992; Caramazza and Miozzo, 1997, 1998; Roelofs et al., 1998). There is evidence that syntactic information is accessed independently from phonological information in naming (Caramazza and Miozzo, 1997; Vigliocco et al., 1999), but one does not require completed access to the other (inconsistent with the two-stage model of Levelt (1989); but consistent with models that assume cascaded or parallel activation of different representations, such as Dell, 1986). As the role of a syntactic level of representation remains controversial, we will not further explore the neural correlates of this level of processing. Nevertheless, we will assume that there is a level or site of processing that allows access to both the phonological and orthographic word forms, but is independent of semantics (both amodal general and personal knowledge and lexical-semantics). This assumption is based on (1) the tip-of-the-tongue state, in which neither the orthographic nor the phonological word form is accessible and (2) the observation that a common deficit after focal brain damage is the inability to retrieve either the phonological or the orthographic word form, in the face of intact knowledge of the meaning of the object and word (pure anomia). A much less common, but reported, pattern is the selective impairment in accessing either the phonological or orthographic word form, but not both, despite intact motor output in both modalities (Ellis et al., 1983; Caramazza and Hillis, 1990; Rapp et al., 1997; Hillis et al., 1999). The more common pattern of anomia, reflected in the association between impaired oral and written naming with intact word comprehension, could be explained by adjacent areas of the brain that are responsible for access to phonological and orthographic word forms, or could be explained by a common element needed for both. The latter can more easily account for a high concordance between oral and written naming with respect to the items affected. This level of processing, which we will call ‘modality independent lexical access’, might be best represented as the ‘hidden links’ in computational models of lexical access (e.g. Plaut and Shallice, 1993) or the ‘L-level’ (which avoids claims about whether this level is best represented as a ‘lexeme’ or a ‘lemma’ level) in computational models of Rapp and Goldrick (2000). The theoretical distinction between ‘modality-independent lexical access’ and ‘lexical-semantics’ is that modality-independent lexical access is required specifically for word production (not word comprehension), while ‘lexical-semantics’ is necessary for linking words to their meanings in both production and comprehension. Both components are assumed to be processing mechanisms or access procedures that are important for linking more distributed representations, as schematically represented in Fig. 1. In this figure, modality-independent lexical access is shown as a single node for a single item, but this level might be a distributed representation as well, as in parallel distributed processing (PDP) models such as those in Seidenberg and McClelland (1989), Plaut and Shallice (1993) and others. In addition,
arrows indicate that there might be not only feedforward activation between levels, but also feedback interaction, although the degree of feedback interaction is a matter of controversy (Rapp and Goldrick, 2000).

These various representations and processes underlying naming are revealed by patients with distinct patterns of performance across tasks. Patients who have trouble at the visual recognition level of the naming process may have trouble accessing a ‘structural description’ of horse, so that they cannot distinguish a drawing of a horse from an unreal but visually similar drawing (e.g. a drawing of horse with a dog’s head) or may not be able to match unusual views of horses to one another. This pattern of performance is sometimes known as ‘aperceptive visual agnosia’. Other patients may access a structural description (so they can accomplish the above tasks), but may not be able to name the horse due to impaired access to lexical-semantics (or to the entire semantic representation) of horse from the structural description. Such a deficit is often known as ‘optic aphasia’ (Lhermitte and Beauvois, 1973; Riddoch and Humphreys, 1987; Manning and Campbell, 1992, 1995c; Marsh and Hillis, 2005) (or ‘associative agnosia’ DeRenzi and Saetti, 1997; Chanoine et al., 1998). A patient with this deficit would be able to identify which horse is different from three identical drawings plus one distinct drawing of horses, but might not be able to sort photographs or drawings of horses versus deer (Hillis and Caramazza, 1995c). Nevertheless, as the semantic representation is intact (but inaccessible from vision) in these patients, they would be able to verbalize the difference between horses and deer and correctly name ‘horse’ in response to a verbal description (Hillis and Caramazza, 1995c). In contrast, patients with impairment of the semantic representation (including amodal knowledge and lexical-semantics, such as patients with SD) might perform poorly on any semantic tasks, including naming (of pictures or to definitions), sorting pictures of horses versus deer or pointing to pictures associated with horses. Still other patients would fail to correctly name a horse from a picture or from a description of a horse, because of a deficit at the level of lexical-semantics. Such a patient may have an unstable or underspecified lexical-semantic representation of horse. For example, patients with impaired lexical-semantics might access sufficient information to identify a horse as an animal, but may not access information about what makes a horse different from a deer. For example, as shown in Fig. 1, they might access many components of lexical-semantics, but if they failed to activate those that distinguish a horse from a deer (e.g. mane) or if they inadvertently activated spurious components (e.g. non-domesticated), such patients would make semantic paraphasias (e.g. calling a horse a ‘deer’) in oral and written naming and in word/picture matching. However, they would have no difficulty saying whether or not some horses can be ridden, pointing to pictures associated with horses, or other tasks that depend on amodal general or personal knowledge or the intact components of lexical-semantics.

Other patients accurately access complete lexical-semantics, and so they perform well in word/picture matching and other comprehension tasks, but cannot retrieve the phonological or orthographic word form. These patients may have disruption of the naming process at the level of modality-independent lexical access, or their problem may occur in directly accessing the phonological and orthographic word form representations from semantics. In this paper, we will refer to the pattern of equivalent impairments in oral naming and written naming, with spared comprehension, as disruption at the level of the modality-independent lexical access, recognizing that the pattern can be alternatively explained by two separate ‘downstream’ impairments. Patients with impaired modality-independent lexical access make semantic paraphasias in both speech and writing, but are aware that the paraphasias are errors. Other errors include circumlocutions (e.g. horse → ‘big animal, races, cowboys ride them’), associative semantic errors (horse → ‘hay’), or omissions. Similar errors are made by patients whose naming problem arises only in accessing the phonological word form. However, such patients may be able to spell the word, indicating that access to modality-independent access and access to the orthographic word form are spared. For example, such a patient might say ‘deer’ in response to a picture of a horse, but may simultaneously write horse correctly (e.g. Caramazza and Hillis, 1990; Rapp et al., 1997). Other patients show the opposite pattern; they might incorrectly write deer but correctly say ‘horse’ in response to the picture of the horse, indicating intact modality-independent lexical access and access to phonological word forms, but impaired access to orthographic word forms (Caramazza and Hillis, 1991; Hillis et al., 1999). Again, these patients are typically aware of their errors, because lexical-semantic representations are intact. In both cases, the errors cannot be due to a problem in motor planning or execution of speech or writing, because they perform the movements necessary for articulating or writing the word, but in producing the wrong words. In other patients, however, the naming impairment is primarily due to motor programming or planning of speech articulation (apraxia of speech). These patients make various off-target attempts to produce the words, make errors that increase with articulatory complexity (e.g. polysyllabic words, consonant blends), and have halting, effortful prosody. Still other patients may have impaired rate, range or strength of muscles involved in speech (dysarthria) or writing (hemiparesis), but these output problems are not generally considered naming deficits.

The various components of the naming process depicted in Fig. 1 may depend on different brain regions or may depend on a network of brain regions that underlie all of the components. Consistent with either hypothesis, functional imaging studies of naming show widespread
activation of left perisylvian and extrasylvian cortex during picture naming (Howard et al., 1992; Hirsch et al., 2001; Abrahams et al., 2003; Grabowski et al., 2003; Martin et al., 2005; Harrington et al., 2006; Price et al., 2005, 2006; Kemeny et al., 2006; Saccuman et al., 2006). Likewise, damage to many different brain regions can impair picture naming (Goodglass and Wingfield, 1997). It is plausible that lesions in different brain regions disrupt different components of the naming process, but all resulting in impaired naming. There is some evidence for this possibility. For example, impaired naming of both pictures and tactile stimuli in the presence of intact word comprehension (a pattern indicative of disruption at the level of modality-independent lexical access or phonological word form) is associated with tissue dysfunction (reduced blood flow and/or infarct) in left Brodmann’s area (BA) 37, part of the posterior middle/inferior temporal and fusiform gyri (Raymer et al., 1997; Foundas et al., 1998; Hills et al., 2002a; Hills et al., 2005). Furthermore, restored neural function (by restoring blood flow) in left BA 37 is associated with improvement in naming but not comprehension (Hillis et al., 2005; Sabsevitz et al., 2006). Converging evidence that this area is important for naming comes from functional imaging studies of normal subjects that show activation of left middle temporal gyrus (Howard et al., 1992) and fusiform gyrus (Grabowski et al., 2003; Kemeny et al., 2006; Price et al., 2006; Saccuman et al., 2006) during naming tasks. In contrast, impaired word comprehension, attributable to impairment at the level of lexical-semantics or linking word forms and lexical-semantics representations, is associated with tissue dysfunction in left BA 22, (Lesser et al., 1986; Hart and Gordon, 1990; Hills et al., 2001) and restored tissue function in this area results in recovery of both comprehension and naming, consistent with restored lexical-semantics (Hills et al., 2001; Hills et al., 2002; Hills and Heidler, 2002). Converging evidence from functional imaging studies shows activation in left BA 22, in addition to inferior frontal gyrus (BA 44/45) and inferior temporal (BA 21) during word comprehension tasks (Papathanassiou et al., 2000; Booth et al., 2002a; Fridriksson and Morrow, 2005). However, other studies only show more anterior or inferior temporal (BA 20/21/38), parietal (BA 7/40) or frontal activation tasks in semantic decisions about words, especially concrete words (e.g., Zahn et al., 2000; Sabsevitz et al., 2005). For example, Mummery et al. (1998) found activation in more anterior/medial temporal cortex during perceptual decisions about words (e.g. same colour?) and activation in temporo-parietal-occipital junction during associative or locative decisions about words. Some of the more widespread activation seen during these semantic tasks may reflect activation of the complex semantic representation (general and personal knowledge about the item, in addition to lexical-semantics). It is also plausible that the various cognitive processes underlying naming emerge from distinct patterns of connectivity across the same, or overlapping, brain regions specialized for particular inputs or outputs (Price et al., 2005; see also Mesulam, 1998, for a similar view). In this case, although all component processes might rely on the same regions, one component process might rely more heavily on the functioning of some regions (and connections between them) than on others.

Based on these preliminary data, we hypothesized that the relative location(s) of damage or dysfunction in acute stroke patients might discriminate between patients with damage to separate components of the naming process. As an initial test of this hypothesis, we identified the ‘earliest’ or primary component of the naming process that was impaired in each of 116 patients with acute stroke, based on the pattern of performance across lexical tasks and the types of errors made in naming. By ‘earliest’ we mean the first component in the cognitive architecture depicted in Fig. 1. It is often difficult to detect disruption in more distal components of the process, when there is a deficit in an earlier, or more proximal, component. That is, patients who make semantic errors (e.g. ‘dog’ for cat) in all naming and comprehension tasks have a disrupted semantic representation; they may or may not also have impairment in accessing phonological and orthographic word forms from the semantic representation. Diffusion-weighted imaging (DWI; which shows areas of acute infarct or dense ischaemia) and perfusion-weighted imaging (PWI, which shows areas of hypoperfused, dysfunctional tissue) of the patients were analysed to identify the entire area of tissue dysfunction in each patient. We used discriminant function analysis to identify distributions of dysfunction across areas that discriminated between groups of patients defined by their earliest disrupted component of the naming process.

Material and methods

Participants

We studied a consecutive series of right-handed individuals who were admitted to the Johns Hopkins Hospital or Johns Hopkins Bayview Medical Center within 24 h of onset of acute, left hemisphere ischaemic stroke, and had none of the following exclusion criteria: (i) contraindication for MRI or contrast; (ii) below an education level of tenth grade; (iii) dementia or other premorbid neurological condition; (iv) uncorrected hearing or visual loss; and (v) lack of proficiency in English prior to stroke; (vi) diminished level of consciousness; or (vii) unable to give consent or indicate a family member to give consent. Informed consent was attained from each patient or a designated family member, using procedures and forms approved by the Johns Hopkins Institutional Review Board. A total of 116 patients were enrolled in this study.

Test battery

Patients were administered a series of language tasks within 24 h of presentation, which included the following tests: (i) auditory and written word comprehension (n = 51 trials each); (ii) tactile naming (n = 17 objects); (iii) oral and written naming of pictured
objects \((n = 34)\); (iv) oral reading \((n = 34)\); (v) spelling to dictation \((n = 34)\); (vi) repetition \((n = 34)\); (vii) visual and auditory lexical decision \((n = 34)\); and (viii) spoken yes/no questions \((n = 10)\). For word comprehension, three trials of word/picture verification with each stimulus were presented. That is, the patient was shown a picture of an object three times: once with a semantic foil, once with a phonological foil and once with the target word. These three presentations of the pictures were presented in a random sequence, intermixed with other picture/word pairs. The patient had to accurately identify the correspondence between the picture and the target word and reject the correspondence between the picture with both the semantic and the phonological foil in order for the response to be scored as correct.

**Imaging**

Each patient had an MRI scan, including DWI trace images \((b_{\text{max}} = 1000 \text{ s/mm}^2)\), TR/TE of 10 000 ms/120 ms and PWI (TR/TE of 2000/60 ms) sequences on a GE Signa 1.5 tesla, echo planar imaging capable scanner, with 5 mm slices. Apparent diffusion coefficient (ADC) maps were generated from the \(b = 1000\) and \(b = 0\) images to confirm that DWI lesions were acute. PWI images were generated after injection of 20 cc GdDTPA (gadolinium) at 5 cc/s. PWI scans were post-processed to maps of time to peak (TTP) arrival of the gadolinium in each voxel. The DWI and TTP maps were co-registered to T2-epi images (generated with the same slices). For each image, a technician blinded to language testing selected the Damasio and Damasio (1989) BA template that most closely corresponded to the anatomical slice was selected, and manually drew the following BAs onto each slice 10, 11, 18, 19, 20, 21, 22, 37, 38, 39, 40, 44 and 45. The severity of hypoperfusion in each left hemisphere BA was defined as the mean number of seconds delay in TTP arrival of contrast in that BA, relative to the TTP delay in the homologous region of in the normal (right) hemisphere. Areas with a mean delay of \(>7\) s or DWI abnormality were assigned a value of 7.0 s delay, since this severity of hypoperfusion or infarct represents complete dysfunction (Neumann-Haefelin et al., 1999; Hillis, Wityk et al., 2001; Thijs et al., 2001; Sobsey et al., 2004). Infarct was defined as bright on DWI and dark on ADC maps. Although some areas that are bright on DWI and dark on ADC are potentially salvageable if blood flow is immediately restored, such areas are densely ischaemic and not functional.

**Data analyses**

Patients were classified into groups with disruption of different components of the naming process, as identified by the pattern of performance across tasks and the types of errors made. See Table 1 for the criteria for identifying disruption of each component of the naming process. These criteria are based on single case studies of patients who have been reported to have deficits at each level of the naming task, on the basis of detailed analysis of performance across a wide range of tasks (e.g. Butterworth et al., 1984; Howard and Orchard-Lisle, 1984; Kay and Ellis, 1987; Caramazza and Hillis, 1990; Hillis et al., 1990; Howard and Gatehouse, 2006). Although many authors have used more detailed criteria involving many more tests (e.g. Howard and Gatehouse, 2006), our criteria are shared by many studies and serve as a 'working definition' based on the schematic architecture of the naming process shown in Fig. 1. For example, impairment at the level of 'lexical-semantics' (the subset of semantic information required to be able to name an object and determine whether or not a picture depicts an instance of items referred to by that name) would be reflected in impairments in both spoken and written word comprehension (measured in our study with word/picture verification), as well as oral and written naming of both pictures and objects (see Hillis et al., 2000 for discussion). It is widely agreed that patients with semantic impairments make semantic errors in naming (Howard and Gatehouse, 2006; Jeffries and Lambon-Ralph, 2006), although patients with deficits at the level of visual perception (e.g. accessing semantics from a visual/structural description) or in accessing the phonological word form can also make such errors (Hillis and Caramazza, 1995a; Howard and Gatehouse, 2006). However, patients with visual/perceptual deficits will make such errors only in response to visual stimuli, and patients with impaired access to the phonological word form make semantic errors in oral but not written naming. In contrast, patients with impaired lexical-semantics make semantic errors in all of these tasks (Hillis et al., 1990). We did not attempt to distinguish between impairments in access versus representation, because such distinctions may require extensive testing (Shallice, 1987) or may be impossible (Caramazza et al., 1990).

A score of \(>10\%\) errors on a particular task was selected as the criterion for impairment for that lexical task, because (i) this cutoff was \(>2\) standard deviations below the mean for normal subjects on our original normative data from non-brain damaged subjects and (ii) no normal subject made more than \(10\%\) errors on any of these tasks. Regrettably, we did not have sufficient time in the acute stage of stroke to administer tasks that would distinguish between deficits in lexical-semantics or more broadly in semantics, including amodal general and personal knowledge (although the latter is uncommon after stroke).

Discriminant function analysis utilizing SPSS (SPSS for Windows, Rel. 12.0.1 2003; SPSS Inc.) was used to identify the areas of hypoperfusion and/or infarct on MRI scans that could discriminate between patients with disruption in different components of the naming process. In this analysis, the input consists of the independent (‘discriminant’) variables—the areas of tissue dysfunction (severity of hypoperfusion in each Brodmann area, defined by mean TTP) in each patient and the group membership defined by level of impairment (see Table 1) of that patient. Data are entered in a stepwise fashion (to identify the least number of areas that could distinguish between groups), and a series of discriminant functions (based on the status of each of the independent variables) are identified that each represent a pattern in the independent variables that distinguished a particular group from the other groups. Discriminant functions that could distinguish between groups with an alpha level of \(P < 0.05\) were considered significant.

**Subsequent analyses**

As we cannot rule out the possibility that patients with comparably impaired oral and written naming have deficits in access to both phonological and orthographic word forms (rather than impaired modality-independent lexical access), and as there were small numbers of patients in some of the groups, we carried out two additional analyses. First, we combined patients with deficits in modality-independent lexical access with patients with impaired access to phonological and orthographic word
forms into one group (into a single ‘lexical access’ impairment group), and retained the other groups. Second, we created two deficit groups, semantic (with >10% errors in naming and word/picture verification) and post-semantic (≥10% errors in naming, but <10% errors in word/picture verification) in addition to the ‘no deficit’ group. We carried out discriminant function analysis in the same way as described above with these classifications.

To demonstrate that the original classification can generalize to a new set, which would be essential from a clinical perspective, we carried out discriminant function analysis in the same way as described above with these classifications. Linear regression analyses were performed to determine the contribution of degree of hypoperfusion in each of the BAs identified in the primary discriminant function analysis to error rate on auditory word/picture verification and to error rate in oral naming.

Results

Using these criteria, one patient was classified as having impairment at a visual/perceptual (structural disruption) level; 46 patients were classified as having impairment at the level of the lexical-semantic system; 17 patients were classified as having impairment at the level of modality-independent lexical access; two patients were classified as having impairment at the level of the phonological word form; eight patients were classified as having impairment of the orthographic word form level, and two patients were classified as having impairment of motor speech. Another 40 patients were classified as having no naming deficits. Table 2 shows the range of scores for each task by patients in each group based on the ‘earliest’ level of processing that was found to be impaired.

Table 1 Criteria for impairment

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<tr>
<th>Level of impairment</th>
<th>Impairment criteria</th>
<th>Group size</th>
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<tbody>
<tr>
<td>Visual/perceptual</td>
<td>Tactile naming &gt; (20%) Picture naming</td>
<td>1</td>
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<tr>
<td>Lexical-semantics</td>
<td>&gt;10% error in:</td>
<td>46</td>
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<td></td>
<td>Spoken Word/Picture Verification AND</td>
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<td>Written Word/Picture Verification AND</td>
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<td>Oral Naming of Pictures AND</td>
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<td>Written Naming of Pictures AND</td>
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<td></td>
<td>Semantic errors in at least one of the above tasks</td>
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<tr>
<td>Modality-independent lexical access</td>
<td>&gt;10% error in:</td>
<td>17</td>
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<td></td>
<td>Oral Naming of Pictures AND</td>
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<td>Tactile Naming AND</td>
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<td>Written Naming AND</td>
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<td></td>
<td>&lt;10% error in:</td>
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<td></td>
<td>Spoken Word/Picture Verification</td>
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<td>Phonological word form</td>
<td>&gt;10% error in:</td>
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<td>Tactile Naming AND</td>
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<td>Oral Naming of Pictures AND</td>
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<td>&lt;10% errors in Written Naming of Pictures</td>
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<tr>
<td></td>
<td>Semantically and/or phonologically related errors</td>
<td></td>
</tr>
<tr>
<td></td>
<td>and/or circumlocutions in at least one of the above tasks</td>
<td></td>
</tr>
<tr>
<td>Orthographic word form</td>
<td>&gt;10% error in:</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>Written Naming of Pictures AND</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Spelling to Dictation of Irregular Words AND</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Semantically and/or visually related errors and/or omissions</td>
<td></td>
</tr>
<tr>
<td></td>
<td>or phonologically plausible errors (e.g. ‘phone’ spelled ‘foan’) in spelling</td>
<td></td>
</tr>
<tr>
<td>Motor speech</td>
<td>&gt;10% error in:</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Tactile Naming AND</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Oral Naming of Pictures AND</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Oral Reading AND</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Repetition AND</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Production of articulatory errors</td>
<td></td>
</tr>
</tbody>
</table>

Initial analysis

Multiple (five) discriminant functions were found that could classify cases into groups based on the level of disruption of the naming process (as defined by Table 2), using the status of each of seven BAs (of the 13 BAs entered; see imaging section). Each discriminant function has different coefficients, thus weighting each of these BAs differentially. Together, these five discriminant functions successfully distinguished the behaviourally-defined groups (Wilk’s; lambda = 0.255; $F^2 = 93.5$; df35, $P < 0.0001$).
The seven independent variables, mean severity of hypoperfusion within each BA, that were incorporated into the discriminant functions were: BA 22 (including Wernicke’s area), BA 44 (part of Broca’s area), BA 45 (part of Broca’s area), BA 21 (inferior temporal cortex), BA 37 (posterior, inferior temporal/fusiform gyrus), BA 38 (anterior temporal cortex) and BA 39 (angular gyrus). Table 3 displays the correlations between each independent variable and each discriminant function. The mean TTP in the other six analysed BAs (10, 11, 18, 19, 20 and 40) did not contribute to classifying the patients.

Function 1 (most highly correlated with the degree of hypoperfusion in BA 22 ($r = 0.899$) had the highest value in the group of patients with disruption of naming at the level of semantics. Function 2 was most correlated with the severity of hypoperfusion in BA 37 ($r = 0.995$) and had the highest value in cases with disruption at the level of modality-independent lexical access. Function 3, with highest correlations with degree of hypoperfusion in BA 44 ($r = 0.870$) and BA 45 ($r = 0.862$), had the highest value in cases with motor speech impairment.

Function 4 was most correlated with the degree of hypoperfusion in BA 39 ($r = 0.401$); this function had the highest value in the two patients with disruption at the level of phonological word form. Finally, the addition of Function 5, which correlated most highly with severity of hypoperfusion in BA 38 ($r = 0.786$), accounted for only an additional 0.1% of the variance; it had the highest absolute (negative) value in the one patient with disruption at the level of visual perception/structural description.

In summary, for patients with impaired lexical-semantics, Function 1 (correlated with dysfunction in left BA 22, which includes all or part of Wernicke’s area) was the highest discriminating function. Among patients with disruption at the level of modality-independent lexical access, Function 2 (correlated with degree of tissue dysfunction in left BA 37, posterior middle temporal/fusiform gyrus) was highest. For patients with impairment at the level of the phonological word form, Functions 2 and 4 (correlated with degree of tissue dysfunction in left BA 39, angular gyrus) had the highest values. Among patients with disruption at the level of the orthographic word form,

### Table 2
Range of error rates on each test for each group (defined by initial deficit, as defined in Table 1)

<table>
<thead>
<tr>
<th>Test</th>
<th>Visual</th>
<th>Semantic</th>
<th>Modality-independent lexical access</th>
<th>Phonological word form</th>
<th>Orthographic word form</th>
<th>Motor speech</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>1</td>
<td>46</td>
<td>17</td>
<td>2</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>Oral picture naming</td>
<td>24</td>
<td>12–100</td>
<td>12–100</td>
<td>18–24</td>
<td>0–6</td>
<td>18–71</td>
</tr>
<tr>
<td>Oral tactile naming</td>
<td>0</td>
<td>12–100</td>
<td>12–100</td>
<td>24</td>
<td>0–6</td>
<td>18–71</td>
</tr>
<tr>
<td>Written picture naming</td>
<td>47</td>
<td>18–100</td>
<td>18–100</td>
<td>0–6</td>
<td>12–71</td>
<td>0–47</td>
</tr>
<tr>
<td>Oral reading</td>
<td>90</td>
<td>18–100</td>
<td>2–94</td>
<td>27</td>
<td>2–28</td>
<td>86</td>
</tr>
<tr>
<td>Repetition</td>
<td>8</td>
<td>0–100</td>
<td>0–16</td>
<td>0–10</td>
<td>0–8</td>
<td>18–68</td>
</tr>
<tr>
<td>Spelling to dictation</td>
<td>0</td>
<td>9–100</td>
<td>12–54</td>
<td>0</td>
<td>14–50</td>
<td>0–85</td>
</tr>
<tr>
<td>Spoken word comprehension</td>
<td>12</td>
<td>12–100</td>
<td>0–6</td>
<td>0–6</td>
<td>0–6</td>
<td>0–6</td>
</tr>
<tr>
<td>Written word comprehension</td>
<td>29</td>
<td>18–100</td>
<td>0–6</td>
<td>0–6</td>
<td>0–6</td>
<td>0</td>
</tr>
</tbody>
</table>

### Table 3
Structure matrix for the initial analysis

<table>
<thead>
<tr>
<th>Function 1 (highest in semantic group)</th>
<th>Function 2 (highest in modality-independent lexical access and phonological group)</th>
<th>Function 3 (highest in motor speech group)</th>
<th>Function 4 (highest in orthographic word form group)</th>
<th>Function 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>BA 22</td>
<td>0.899</td>
<td>0.271</td>
<td>0.232</td>
<td>0.021</td>
</tr>
<tr>
<td>BA 21</td>
<td>0.347</td>
<td>0.256</td>
<td>0.116</td>
<td>0.042</td>
</tr>
<tr>
<td>BA 37</td>
<td>0.092</td>
<td>0.823</td>
<td>0.038</td>
<td>0.182</td>
</tr>
<tr>
<td>BA 44</td>
<td>0.162</td>
<td>0.704</td>
<td>0.009</td>
<td>0.401</td>
</tr>
<tr>
<td>BA 39</td>
<td>0.032</td>
<td>0.089</td>
<td>0.870</td>
<td>0.061</td>
</tr>
<tr>
<td>BA 45</td>
<td>0.090</td>
<td>0.052</td>
<td>0.862</td>
<td>0.354</td>
</tr>
<tr>
<td>BA 38</td>
<td>0.194</td>
<td>0.031</td>
<td>−0.093</td>
<td>0.299</td>
</tr>
<tr>
<td>Cumulative percentage of variance</td>
<td>80.3%</td>
<td>89.8%</td>
<td>97.7%</td>
<td>99.9%</td>
</tr>
</tbody>
</table>

Pooled within-groups correlations between discriminating variables and standardized canonical discriminant functions. The highest absolute correlations between each variable (degree of hypoperfusion within each BA) and each function are displayed in bold print. Functions are identified by the analysis (not a priori). We have added in parentheses the group that has the highest value for each function.
Function 4 (most correlated with severity of hypoperfusion in left BA 39, angular gyrus) was highest. Figure 2 shows magnetic resonance DWI and PWI scans of two patients, with distinct regions of hypoperfusion associated with a deficit at the level of modality-independent lexical access (Panel A) versus a deficit at the level of accessing orthographic word forms (Panel B). There was only one patient with a deficit in visual recognition and only two patients whose 'earliest' (only) disruption in naming was in motor speech, so results are likely to be unreliable in these cases.

**Subsequent analyses**

As there were too few cases with deficits in access to visual/structural descriptions, modality-specific deficits in accessing phonological word forms, or isolated motor speech impairment to draw conclusions regarding these groups, we carried out two *post hoc* analyses with fewer classes of patients. Similar results were found. When we combined patients with impaired modality-independent lexical access (Group 3) with impaired access to phonological word forms (Group 4) or orthographic word forms (Group 5), two discriminant functions based on severity of hypoperfusion of the same seven BAs successfully distinguished the behaviourally-defined groups (Wilk’s lambda $= 0.274$; $I^2 = 137$; df=14, $P < 0.0001$). Function 1 was most correlated with severity of hypoperfusion in left BA 22 ($r = 0.965$), but also with hypoperfusion of left BA 21 ($r = 0.420$) and BA 38 ($r = 0.253$) and was highest in patients with semantic deficits. Function 2, which was highest in patients with deficits in lexical access (modality-independent lexical access or access to orthographic and/or phonological word forms) was more strongly correlated with the degree of hypoperfusion in left BA 37 ($r = 0.626$) and BA 44 ($r = 0.542$).

When patients were then reclassified as having no deficits, semantic deficits or post-semantic deficits, very similar results were obtained. Two functions, based on the severity of hypoperfusion in the same seven BAs were identified that distinguished between groups (Wilk’s lambda $= 0.238$; $I^2 = 142$; df=14, $P < 0.0001$). Table 4 displays the correlation coefficients for each independent variable for each function in the two *post hoc* analyses. Figure 3 displays the values of discriminant functions 1 ($x$ axis) and 2 ($y$ axis) for each case of semantic or post-semantic deficit, as behaviourally defined in this last analysis.

**Cross-Validation.** We ran a cross-validation using a leave-one-out procedure. The cross-validation for each analysis yielded identical or almost identical results for

---

**Table 4 Structure matrix for the subsequent analyses**

<table>
<thead>
<tr>
<th></th>
<th>Secondary analysis 1</th>
<th>Secondary analysis 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Function 1 (highest in semantic group)</td>
<td>Function 2 (highest in lexical access group)</td>
</tr>
<tr>
<td>BA 22</td>
<td>0.965</td>
<td>0.034</td>
</tr>
<tr>
<td>BA 21</td>
<td>0.420</td>
<td>0.171</td>
</tr>
<tr>
<td>BA 38</td>
<td>0.253</td>
<td>0.099</td>
</tr>
<tr>
<td>BA 37</td>
<td>0.305</td>
<td>0.626</td>
</tr>
<tr>
<td>BA 44</td>
<td>0.312</td>
<td>0.542</td>
</tr>
<tr>
<td>BA 45</td>
<td>0.339</td>
<td>0.397</td>
</tr>
<tr>
<td>BA 39</td>
<td>0.263</td>
<td>0.334</td>
</tr>
<tr>
<td>Cumulative percentage of variance</td>
<td>82.5%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Pooled within-groups correlations between discriminating variables and standardized canonical discriminant functions. The highest absolute correlations between each variable (degree of hypoperfusion within each BA) and each function are displayed in bold print. Functions are identified by the analysis (*not a priori*). We have added in parentheses the group that has the highest value for each function.
the new population as for the original population. For example, in the last analysis 80.0% of the original cases and 77.1% of the cross-validated cases were correctly classified. In the earlier analysis, 77.7% of the original group were correctly classified, and 76.8% of the cross-validated cases were correctly classified.

Linear regression analysis. The discriminant function analyses demonstrated that the distribution of tissue dysfunction across seven BAs distinguished between groups of patients behaviourally identified as having different levels of impairment in picture naming. However, these analyses do not directly reveal the independent contributions of each area to each type of impairment. To evaluate these contributions, we performed two separate linear regression analyses: one to determine the contributions of dysfunction in each of the seven BAs (as identified in the discriminant function analysis) to the severity of the lexical-semantic deficit (indicated by the error rate on auditory word/picture verification), and another to determine contribution of these BAs to severity of the naming deficit (indicated by error rate in oral naming of pictures).

The error rate in auditory word/picture verification was best predicted by the following model derived from linear regression, where VerifErr stands for verification error rate and HP stands for ‘severity of hypoperfusion of’ as defined earlier:

\[
\text{VerifErr} = \text{HP BA22} \times 8.6 + \text{HP BA 45} \times 5.0 \\
+ \text{HP BA 21} \times 1.9 + \text{HP 37} \times 0.16 \\
- \text{HP 38} \times 1.2 - \text{HP 39} \times 0.71 \\
+ 3.9 (r = 0.81; r^2 = 66; P < 0.0001)
\]

The coefficients indicate the ‘weight’ of the contribution to error rate in word/picture verification (a measure of lexical-semantics). This model indicates that hypofusion of left BA 22 (most of the superior temporal gyrus, extending to the superior temporal sulcus) was the strongest predictor of the severity of word comprehension impairment acutely after stroke. It was the only area where the severity of hypoperfusion independently predicted error rate \((P < 0.0001)\) after adjustment for the severity of hypoperfusion of the other areas.

Error rate in oral naming of pictures was best predicted by the following model derived from linear regression, where NE stands for naming error rate and HP stands for ‘severity of hypoperfusion of’ as defined earlier:

\[
\text{NE} = \text{HP BA22} \times 8.7 + \text{HP BA 45} \times 3.5 + \text{HP BA 37} \\
\times 3.3 + \text{HP 21} \times 1.7 - \text{HP 38} \times 1.6 - \text{HP 39} \\
\times 3.9 + 13 (r = 0.78; r^2 = 61; P < 0.0001)
\]

The areas where the degree of hypoperfusion independently contributed to the error rate in oral naming of pictures, after adjusting for the degree of hypoperfusion in the other areas, were: left BA 22 \((P < 0.0001)\), BA 37 (posterior middle and inferior temporal/fusiform gyrus; \(P = 0.019\)); and BA 39 (angular gyrus; \(P = 0.002\)).

**Discussion**

The results of this study provide evidence that distinct distributions of tissue dysfunction in seven cortical areas of the left hemisphere are associated with disruption of different components of the naming task. We did not find a one-to-one relationship between areas of tissue dysfunction and impaired components of naming. Instead, our results indicate that each component depends on the function of a number of areas in a network. Although certain areas were more heavily weighted than others in each discriminant function, all of the discriminant functions depended on the status of several regions. This finding is consistent with functional imaging studies that generally show several areas where activation is correlated with any component of the naming task (see introduction). It is also consistent with the proposal of ‘combinatorics’ by Price and colleagues (2005) that distinct cognitive processes emerge from the interactions between several regions that are specialized for particular inputs or outputs. Damage to a single part of the network would likely disrupt picture naming performance, but would differentially affect the various cognitive processes required for accurate naming.

The data from this study largely converge with evidence from other modalities investigating brain–language relationships. For instance, the severity of tissue dysfunction in left BA 22 had the greatest contribution in predicting the error rate in word/picture verification, a measure of the semantic deficit (lexical-semantics or possibly more broad deficits in semantics). Left BA 22 is sometimes referred to as Wernicke’s area (e.g. Kober et al., 2001), although others
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define Wernicke's area as a more limited area in posterior BA 22, and others define it as a broader area that includes part of angular gyrus. The role of BA 22 is consistent with results of functional imaging studies that demonstrate activation in left BA 22 during word comprehension tasks (Papathanassiou et al., 2000; Booth et al., 2002; Whatmough and Chertkow, 2002; Fridriksson and Morrow, 2005; Saur et al., 2006) and detecting semantic anomalies in sentences (Friederici et al., 2003; see also Maess et al., 2006). However, other functional imaging studies provide evidence for specialization within BA 22 (Wise et al., 2001; Scott et al., 2003) as well as other BAs (Poldrack et al., 1999). For example, there is converging evidence from several studies that more rostral areas of left lateral temporal cortex, linked via the uncinate fasciculus to ventrolateral prefrontal cortex, are engaged in processing word meaning; while caudal temporal regions, linked via the arcuate fasciculus to the dorsolateral prefrontal cortex, are engaged in processing phonetic and phonological structure (Wise, 2003; see also Hickok and Poeppel, 2000). We did not attempt to determine the areas within each BA that may have such specialized roles. Nevertheless, we did find evidence that at least part of left BA 22 is critical for accessing the type of semantic information needed to name pictures and to determine whether a word matches a picture, consistent with data from chronic stroke and direct cortical stimulation reviewed in the introduction showing that damage or temporary dysfunction of left BA 22 is associated with deficits in accessing word meaning.

The finding that severity of tissue dysfunction in left BA 37 correlated most strongly with the discriminant function that most contributed to classifying patients with impairment at the level of modality-independent lexical access also converges with evidence from functional imaging and chronic lesion studies. Left BA 37 includes part of posterior/lateral and ventral inferior temporal gyrus, which shows activation during word retrieval relative to later stages of picture naming (Kemeny et al., 2006) or during naming of tools in response to pictures or sounds (Tranel et al., 2005), or naming pictures relative to face orientation, more strongly in men than women (Grabowski et al., 2003). Left BA 37 also includes the mid fusiform gyrus, which reliably shows activation in reading words (Cohen et al., 1997, 2000, 2002), spelling words (Rapcsak et al., 2004), and naming objects (Abrahams et al., 2003; Price et al., 2005, Price et al., 2006). Price and Devlin (2003, 2004) have proposed that the left mid fusiform gyrus is important in modality-independent lexical processing, rather than specific to visual word forms. Cohen and colleagues (Cohen et al., 2004a, b) have argued that there are two distinct areas of the left fusiform gyrus, both in BA 37: one involved specifically in reading and one involved in modality-independent lexical processing. Our data cannot evaluate this hypothesis, since we did not look for distinct areas of tissue dysfunction within left BA 37, but our data do support the hypothesis that part of left BA 37 is important for modality-independent lexical processing.

In patients with disruption at the level of the orthographic word form, the discriminant function that was most correlated with severity of hypoperfusion in left BA 39 (angular gyrus) had the highest value. This finding is consistent with many lesion studies that show a strong association between chronic lesions involving left angular gyrus and impairment of both reading and writing (see Benson, 1979 or Hillis and Rapp, 2004, for review). Functional imaging studies show activation in left angular gyrus during spelling, at least in some patients (Beeson et al., 2003; Hsieh and Rapp, 2004). Together, these results indicate some role of the left angular gyrus in spelling. Although this area is plausibly involved in accessing orthographic representations, we did not attempt to distinguish this deficit from damage to sublexical phonology to orthography, which might affect spelling of words also. Functional imaging studies inconsistently show activation of left BA 39 during oral picture naming tasks (Farias et al., 2005; Fridriksson et al., in press; Harrington et al., 2006; Kemeny et al., 2006). Other functional imaging studies have revealed greater activation in BA 39 in response to semantic relative to phonological judgements (e.g. Mummery et al., 1998), semantically congruent sentences relative to incongruent or pseudoword judgements (Humphries et al., 2006); or cross-modal tasks (e.g. spelling judgements with auditory input or rhyming judgements with visual input; Booth et al., 2002b).

There were not enough patients with deficits in the other components of the naming process to comment on their relationship to dysfunction in particular BAs. Nevertheless, tissue dysfunction in left BA 38, anterior temporal cortex, BA 44 and 45, posterior inferior frontal gyrus and left BA 21, inferior temporal cortex, also contributed to severity of naming and comprehension error rates, and to distinguishing the level of impairment in picture naming. The severity of hypoperfusion in BA 38 and 21 were most correlated with the discriminant function that had a high value in patients with semantic deficits (see Table 4), while BA 44 and 45 correlated more strongly with the discriminant function that had a high value in patients with post-semantic deficits (and those with motor speech deficits in the initial analysis; Table 3). These findings are consistent with studies of progressive aphasic patients with atrophy in anterior temporal gyrus (BA 38) and inferior temporal cortex (BA 21) who initially present with spoken word retrieval deficits, but eventually develop semantic dementia or 'semantic' variety of primary progressive aphasia (Mummery et al., 1999; Gorno-Tempini et al., 2004). Patients with lesions in left BA 38 are impaired in naming famous landmarks, relative to patients with lesion in right BA 38, consistent with the hypothesis that this area may be critical in naming unique entities (Damasio et al., 2004; Tranel et al., 2006). Lesion studies also show chronic infarct or progressive atrophy involving BA 44 and 45 in patients...
with motor speech impairments (Mohr et al., 1987; Amici et al., 2006).

Likewise, several functional imaging studies reveal activation of left BA 38 (Grabowski et al., 2003), left BA 21 (Papathanassiou et al., 2000), and left BA 44/45 (Papathanassiou et al., 2000; Hirsch et al., 2001; Abrahams et al., 2003; Martin et al., 2005) in overt naming. Activation in left BA 21 and 38 (as well as posterior superior temporal sulcus) likely reflects semantic processing, compatible with our findings, because these areas are active in comprehension of normal discourse, apart from metalinguistic task demands (Crinion et al., 2000). Activation in left BA 44/45 was not seen in these normal comprehension tasks, but is seen during motor speech relative to non-speech articulatory movements (Bonilha et al., 2006).

Many of the cited functional imaging studies show bilateral activation in many of the regions we have discussed as well as in bilateral cingulate cortex. Damage to these right cortical regions does not normally interfere with naming common objects of the type used in this study. However, it is widely recognized that functional imaging studies reveal areas of the brain that are reliably engaged in a particular function, even if they are not essential for the function. For example, picture naming often elicits recollection of personal knowledge or emotions linked to the concept that might activate more widespread areas. Therefore, lesion studies like the current one can complement functional neuroimaging in exploring the neural regions necessary for a particular cognitive function or task (Chatterjee, 2005).

We should note that the network of regions we identified as important for naming may not include all of the areas that can support naming. Patients with damage to any of these regions may well recover naming over time, as the cognitive processes underlying naming begin to emerge from other ‘degenerate’ systems that can support naming (Price et al., 1999). This study only identified areas where tissue dysfunction was associated with acutely impaired picture naming, indicating that the area was necessary for the task before reorganization of structure/function relationships. Furthermore, this study revealed the areas where tissue dysfunction affects one cognitive process underlying naming more than it affects other components of naming. If tissue dysfunction in some other region were to affect all components equally, it might interfere with naming, but would not be identified in this analysis.

We should also note that analysis of regions of tissue dysfunction by Brodmann’s areas has limitations (e.g. known individual variability in cytoarchitectural fields). However, these limitations are not ameliorated or solved by using a voxel-based approach or analysis of the involved gyri, since areas with distinct functions likely correspond to regions with a particular cytoarchitecture within each individual brain. Use of BA templates (which estimate the location of distinct cytoarchitectural fields) has high interjudge reliability, some theoretical rationale, as well as some empirical support (because lesions involving specific BAs have been associated with various language deficits, and activation in particular BAs has been associated with particular language processes). Nevertheless, our references to particular BAs should be considered approximate, since we have no data on the cytoarchitecture of these areas. Furthermore, as discussed earlier, there may be specialization of distinct areas within each BA.

Another limitation of this study is that at least some of the patients had impairment involving more than one level of processing in the naming task. For example, many patients had mild impairments of motor speech in addition to a ‘primary’ deficit at the level of lexical-semantics, modality-independent lexical access, or orthographic/phonological word form. Such patients made recognizable semantic paraphasias, despite misarticulations (often self-corrected). Only two patients had a pure motor speech disorder, so we were unable to identify areas of tissue dysfunction that reliably discriminated motor speech deficits from other deficits. Nevertheless, this analysis was quite successful in discriminating patients with functional damage to different components of the naming task. Future studies are needed to confirm that these discriminant functions (using tissue dysfunction in the seven identified regions as the discriminant variables) applied sequentially can successfully classify an altogether new set of patients into the same groups defined by the primary impaired component of the naming process. Our cross-validation used a subset of the same patients, which provides a measure of reliability, but does not assure that these functions will be as successful in distinguishing the level of impairment in naming in other patients.

In summary, we have shown that each patient’s level of impairment in the naming process reflected the distribution of tissue dysfunction in particular regions of the left anterior, inferior, and posterior middle/superior temporal cortex, posterior inferior frontal, and inferior parietal cortex. These same regions show activation during propositional and non-propositional speech in functional imaging studies (Blank et al., 2002). While occipital cortex is also critical for picture naming, it is likely that bilateral occipital damage is necessary to disrupt visual recognition. Our results complement functional imaging studies by demonstrating which of the neural regions engaged in naming are also critical for naming.

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