The Word Processing Deficit in Semantic Dementia: All Categories Are Equal, but Some Categories Are More Equal than Others

Friedemann Pulvermüller[1], Elisa Cooper-Pye[1], Clare Dine[1], Olaf Hauk[1], Peter J. Nestor[2], and Karalyn Patterson[1]

Abstract

■ It has been claimed that semantic dementia (SD), the temporal variant of fronto-temporal dementia, is characterized by an across-the-board deficit affecting all types of conceptual knowledge. We here confirm this generalized deficit but also report differential degrees of impairment in processing specific semantic word categories in a case series of SD patients ($N = 11$). Within the domain of words with strong visually grounded meaning, the patients' lexical decision accuracy was more impaired for color-related than for form-related words. Likewise, within the domain of action verbs, the patients' performance was worse for words referring to face movements and speech acts than for words semantically linked to actions performed with the hand and arm. Psycholinguistic properties were matched between the stimulus groups entering these contrasts; an explanation for the differential degrees of impairment must therefore involve semantic features of the words in the different conditions. Furthermore, this specific pattern of deficits cannot be captured by classic category distinctions such as nouns versus verbs or living versus nonliving things. Evidence from previous neuroimaging research indicates that color- and face/speech-related words, respectively, draw most heavily on anterior-temporal and inferior-frontal areas, the structures most affected in SD. Our account combines (a) the notion of an anterior-temporal amodal semantic "hub" to explain the profound across-the-board deficit in SD word processing, with (b) a semantic topography model of category-specific circuits whose cortical distributions reflect semantic features of the words and concepts represented. ■

INTRODUCTION

Meaning, the complex mapping between signs and symbols and their related objects, actions, and concepts appears to be processed in the human brain by a number of specific cortical structures. Neuroimaging evidence indicates that the brain areas activated depend in part on the type of meaning under processing. Perceiving, thinking of or reading about tools activates different areas in inferotemporal cortex from those that respond to animal concepts (Barsalou, 2008; Martin, 2007; Chao, Haxby, & Martin, 1999). Category-specific differences in brain processes have been proposed for gross category distinctions, such as nouns versus verbs or living versus nonliving entities, focusing largely on various types of sensorimotor information critical for the linkage between words and their referent objects and actions (Barsalou, 2008; Martin, 2007; Humphreys & Forde, 2001; Pulvermüller, 1996; Warrington & McCarthy, 1987). Recently, more fine-grained category distinctions have been reported, for example, between visually related words that denote a color versus a shape, which activated different areas in temporal cortex (e.g., Moscoso Del Prado Martin, Hauk, & Pulvermüller, 2006; Simmons et al., 2007; Pulvermüller & Hauk, 2006). In the fronto-central cortex, words related to actions involving specific parts of the body activate the motor areas that control movements with that body part (Kemmerer, Castillo, Talavage, Patterson, & Wiley, 2008; Aziz-Zadeh, Wilson, Rizzolatti, & Iacoboni, 2006; Tettamanti et al., 2005; Hauk, Johnsrude, & Pulvermüller, 2004; Pulvermüller, Härle, & Hummel, 2000). A recent trend in cognitive neuroscience is therefore to replace broad category distinctions such as living/nonliving by word types defined along more fine-grained semantic distinctions (for a discussion, see Pulvermüller, 1999, 2005). At the same time, experiments ground the fine-grained semantic distinctions in behavioral-cognitive data (e.g., semantic ratings; Pulvermüller, Lutzenberger, & Preissl, 1999).

Fine-grained category-specific patterns of cortical activation reflecting the meaning of words and concepts call for an explanation in brain theoretical terms. Such semantic topographies seem best explained by semantic binding circuits that reach into sensory and motor areas and reflect action- and perception-related features of lexical and conceptual meaning. A word such as "grass," referring to an object with a characteristic color, would accordingly be processed by inferior- and anterior-temporal networks

[1]MRC Cognition and Brain Sciences Unit, Cambridge, UK, [2]University of Cambridge

that underpin object and color knowledge, and an action word related to the hand, such as "grasp," would activate a circuit reaching into hand motor cortex (Figure 1A). Neural models of semantic topography and category-specific semantic networks in the human brain have, of course, been challenged. For example, the specific activations in sensory and motor areas might somehow be irrelevant epiphenomenal by-products of tasks such as picture naming, lexical decision, or silent reading rather than an index of semantics (for discussion, see Mahon & Caramazza, 2008; Oliveri et al., 2004). There are, however, good reasons for trusting the semantic topography account. First, the truthful reflection of semantic features in predefined sensory and motor areas argues in favor of a semantic explanation of category-specific brain activation and against a secondary process (Kemmerer et al., 2008; Simmons et al., 2007; Aziz-Zadeh et al., 2006; Tettamanti et al., 2005; Hauk et al., 2004). Second, the rapid spread of activation to motor and visual areas within ~200 msec provides direct support for early semantic rather than for late epiphenomenal processes (Hauk, Shtyrov, & Pulvermüller, 2008; Moscoso Del Prado Martin et al., 2006; Hauk & Pulvermüller, 2004; Shtyrov, Hauk, & Pulvermüller, 2004; Pulvermüller et al., 2000). Third, sensorimotor brain activation has been shown to correlate with semantic stimulus properties, another feature that argues against an epiphenomenon (Hauk, Davis, Kherif, & Pulvermüller, 2008; Pulvermüller, Shtyrov, & Ilmoniemi, 2005). Fourth, sensorimotor activations reflecting category-specific semantics persist even when subjects are instructed to ignore spoken language input and even under subliminal stimulation, providing further strong evidence against secondary strategy-related effects (Boulenger, Silber, et al., 2008; Pulvermüller et al., 2005; Shtyrov et al., 2004). These results

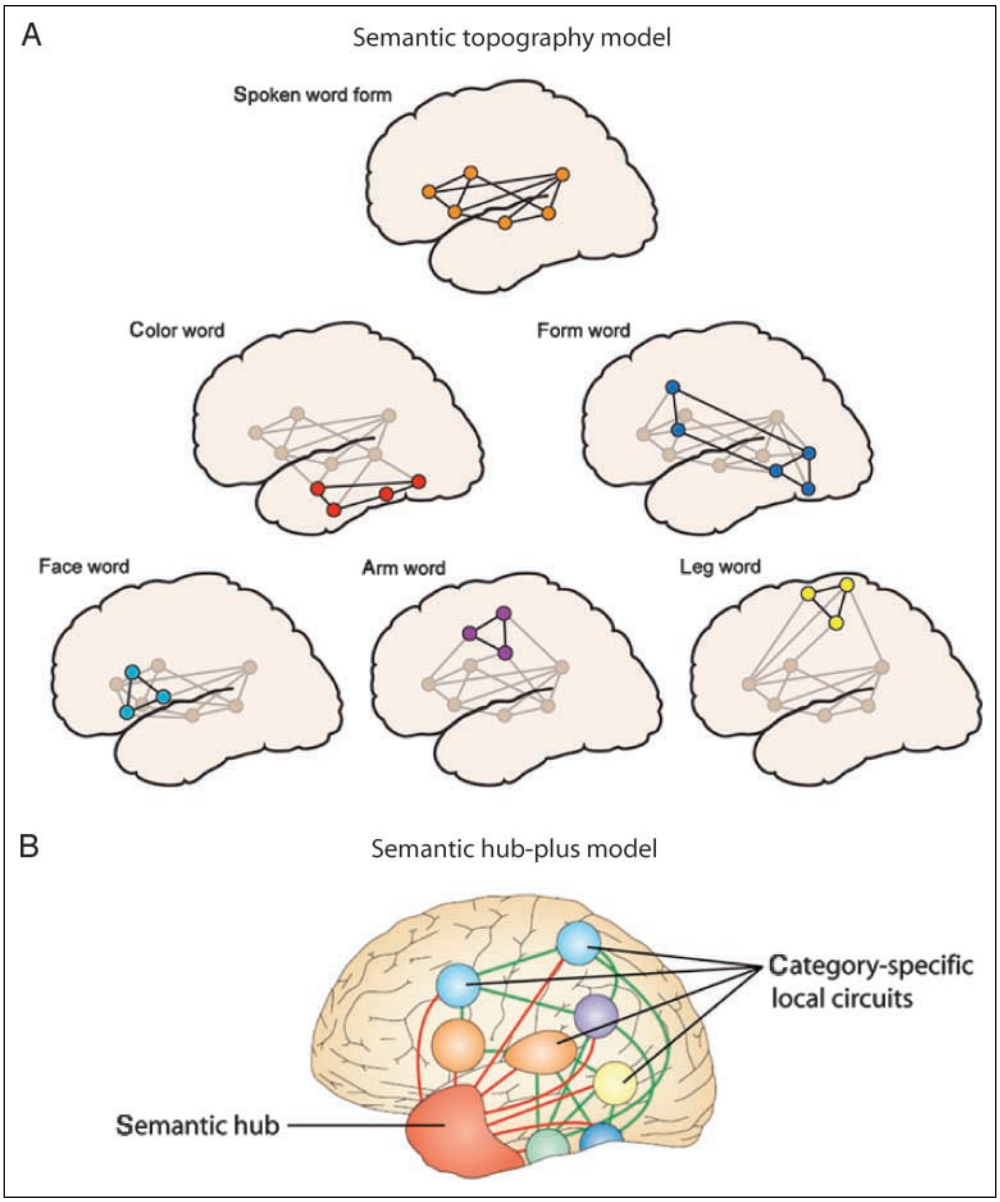


Figure 1. (A) Semantic topography model proposing word-form representations in peri-sylvian cortex (top diagram) bound to category-specific semantic circuits in different areas. Visually related color words use semantic circuits in anterior-temporal structures, whereas for form words more posterior temporal structures are relevant (middle row). Action word circuits link with different parts of motor and premotor cortex, depending on whether reference actions are performed with face, arm, or leg (bottom row). For abstract word processing, anterior-temporal and frontal structures are relevant. The model predicts category-specific deficits specifically for those word types whose semantic circuits fall into the brain areas typically affected by SD, that is, for color, face, and abstract items. (B) Semantic hub model assuming a semantic convergence zone in temporal pole for all kinds of concepts and semantics. The model also includes category-specific circuits in sensorimotor areas.

are consistent with the claim that semantic processing is reflected at least in part by category-specific cortical activation.

The case based on findings from functional imaging would be greatly bolstered by converging evidence from neuropsychology: If semantic circuits in cortex have category-specific distributions, there must be focal lesions that affect the processing of different conceptual categories to different degrees. Such specific impairments have, of course, been reported in the neuropsychological literature for a range of category sets, which are only partially congruent with each other. Verb and noun processing are reported to be differentially affected after lesions in fronto-parietal versus temporal cortex (Boulenger, Mechtouff, et al., 2008; Bak et al., 2006; Neininger & Pulvermüller, 2001, 2003; Bak, O'Donovan, Xuereb, Boniface, & Hodges, 2001; Daniele, Giustolisi, Silveri, Colosimo, & Gainotti, 1994; Damasio & Tranel, 1993; Miceli, Silveri, Villa, & Caramazza, 1984). Animal versus tool names and the more general categories of living versus nonliving thing labels can be affected differentially as a consequence of stroke or herpes simplex virus encephalitis (Gainotti, 2004; Warrington & McCarthy, 1983, 1987; Warrington & Shallice, 1984). Although not all of these differences are easily explained by a sensorimotor account (see, e.g., Crepaldi et al., 2006; Luzzatti et al., 2001), these results have been interpreted as support for category-specific sensorimotor networks for semantic conceptual processing.

Unsurprisingly, this interpretation has also been criticized. First, some of the studies did not control for important cognitive and psycholinguistic stimulus features (see, e.g., Pulvermüller, 1999), including length of words and physical makeup of pictures, frequency of occurrence, and imageability. Second, there are systematic confounds associated with the stimulus categories that support alternative explanations. Most nouns and verbs are indeed related to objects and actions, respectively, but imageability is usually higher for nouns than for verbs (Bird, Lambon-Ralph, Patterson, & Hodges, 2000). As the noun–verb distinction is lexical syntactic in nature, additional nonsemantic features distinguish the two categories. Verbs carry much syntactic information as they usually define the syntactic frame of a sentence; nouns merely fill the slots required by the verb. Verbs come (at least in most European languages) in a larger number of inflected variants than nouns, and therefore even if word-form frequency is matched perfectly, word-stem frequency will typically be higher for verbs than nouns. The noun/verb distinction is therefore codetermined by grammatical, lexical, and semantic properties (Bird et al., 2000; Pulvermüller, Lutzenberger, et al., 1999). Similar confounds hold for other categories, including living versus nonliving things and animals versus tools. Typical animals are similar to each other, with considerable overlap between their visual and semantic feature sets; in contrast, tools are more dissimilar and their feature correlation is therefore reduced compared with that of animals (Rogers et al., 2004; Tyler, Moss, Durrant-Peatfield, & Levy, 2000; Lambon Ralph, Graham, Ellis, & Hodges, 1998; Humphreys & Riddoch, 1987). Category-specific dissociations between nouns and verbs or animals and tools, along with concordant differences in brain activation, therefore do not provide unambiguous evidence for category-specific semantic circuits but could rather be due to associated differences of syntax, frequency, feature correlation, or the like.

If category-specific impairments—whatever their explanation—can result from stroke or herpes simplex virus encephalitis, what about the neurological condition that most selectively impairs semantic memory, semantic dementia (SD)? SD is part of the spectrum of fronto-temporal dementias and is sometimes referred to as temporal-variant fronto-temporal dementia because the degeneration especially affects the anterior- and inferior-temporal lobes (Drzezga et al., 2008; Desgranges et al., 2007; Nestor, Fryer, & Hodges, 2006; Diehl et al., 2004). SD results in a gradual but eventually profound deterioration of knowledge for all kinds of semantic concepts that have been assessed to date and across all tested modalities of input (spoken words, written words, objects, pictures, sounds, etc.) and output (speaking, writing, drawing, nonverbal pointing, etc.; Patterson, Nestor, & Rogers, 2007; Bozeat, Lambon Ralph, Patterson, Garrard, & Hodges, 2000; Saffran & Schwartz, 1994). Only a few studies have investigated possible differences in the degree to which semantic categories are impaired in SD, and most of these have focused on the broad lexico-semantic categories of living and nonliving things. Although a few single cases of SD revealed an advantage for nonliving > living things, the great majority of SD patients evaluated in this fashion show no significant difference between these two broad domains of knowledge (Lambon Ralph, Lowe, & Rogers, 2007; Noppeney et al., 2007; Lambon Ralph, Patterson, Garrard, & Hodges, 2003; Lambon Ralph, Graham, et al., 1998; Lambon Ralph, Howard, Nightingale, & Ellis, 1998). Similarly, object and action naming were found to be impaired to the same degree in SD (Cotelli et al., 2006). The selective yet pervasive conceptual-semantic deficit in SD (Bozeat et al., 2000) has led some researchers to propose a "semantic hub," a region dedicated to semantic and conceptual binding (Patterson et al., 2007), underpinned by anterior-temporal cortex. This notion is further supported by recent TMS evidence suggesting that stimulation of the anterior-temporal lobe produces temporary but generalized, category-unspecific, semantic deficits (Lambon Ralph, Pobric, & Jefferies, 2009; Pobric, Jefferies, & Lambon Ralph, 2007). It is possible that the category-specific semantic circuits and the anterior-temporal semantic center interact in the processing of meaning in the brain (Figure 1B).

The absence of any persuasive evidence for category specificity in SD may be related to methodological issues. The categories of living and nonliving things may be too broad to reveal a coherent dissociation pattern because they are intrinsically heterogeneous. For example, there are fundamental differences in kind and, correspondingly, in the dissociation patterns after focal brain disease between subtypes of nonliving things, for example, tools, large man-made objects, and musical instruments (Warrington & McCarthy, 1987). A particular deficit for one subcategory could therefore be counteracted by better performance for other subcategories, and if specific fine subcategories of both action-related nonliving concepts and visually related living things were impaired, a large-category comparison would fail to reveal the specificity of the deficit. Similar concerns hold for any difference between nouns and verbs or between animals and tools.

Guided by the semantic topography model (Figure 1A), we hypothesized that a degree of category specificity might emerge in SD if the investigation focused on fine-grained differences in semantic concepts. This should be especially true if the categories selected could be specifically mapped to the regions most damaged in SD, the anterior-temporal and the adjacent inferior-frontal cortex. The fine word categories whose specific fMRI activation maps are closest to the SD-affected regions are face- and articulator-related words, which have been demonstrated to activate inferior-frontal cortex (Hauk et al., 2004), and words with strong color associations, where fMRI suggests the importance of anterior-temporal cortex (Pulvermüller & Hauk, 2006).[1] A relevant contrast for the former is provided by words relating to hand and arm movements that, like face-related words, evoke general features of action but yield fMRI activations in more dorsolateral fronto-central regions. A contrast germane to the color category would be words relating to object form: Color, shape, or form is a visual feature of objects, but it yields fMRI activations in more posterior temporal areas. Semantic topography therefore predicts that, if all other relevant variables are balanced, SD patients' performance in a lexico-semantic task should be more impaired for color words than for form words and more impaired for face words than for arm words. In contrast, a semantic hub model neglecting category-specific circuits would predict equally poor processing of all of these categories. A combination of semantic topography and hub models predicts general but also unequal degradation in SD.

Knowledge of words from different categories was assessed in a lexical decision task, where the words were intermixed with word-like but meaningless pseudowords. The disadvantage of other more obviously semantic tasks, such as naming, is that different semantic categories tend to place differential demands on specific perceptual and cognitive processes.[2] Furthermore, the profound anomia characteristic of SD makes naming a poor choice for such an assessment: Naming scores close to or at zero, which are not uncommon in more advanced SD, may be dramatic but would be uninformative in the current investigation. In lexical decision, stimuli can be controlled and matched for physical, cognitive, and psycholinguistic features, and the task stays constant over different conceptual categories whereas effects of semantic links can become manifest in behavioral responses. Note that not only behavioral evidence (Chumbley & Balota, 1984) but also neuroimaging results indicate access to semantic knowledge in the lexical decision task when word and pseudoword stimuli are matched closely for orthographic and phonological characteristics, and the task instructions emphasize accuracy (see, e.g., Binder, Westbury, McKiernan, Possing, & Medler, 2005; Binder et al., 2003; Pulvermüller, Lutzenberger, et al., 1999; Pulvermüller, Mohr, & Schleichert, 1999). It is already well established that, with proper design of pseudoword foils, success in lexical decision is substantially reduced in SD patients relative to controls (Patterson, 2007; Rogers et al., 2004; Diesfeldt, 1992). If words and meanings are linked reciprocally by topographically specific circuits, a focal lesion should exacerbate the lexical decision deficit for words from semantic categories especially reliant on the affected circuits (Neininger & Pulvermüller, 2003; Pulvermüller, 1999).

METHODS

Participants

The patients participating in this study were 11 cases who presented to Neurology Clinics at Addenbrooke's Hospital, Cambridge, and fulfilled standard criteria for a clinical diagnosis of SD (Hodges & Patterson, 2007). Figure 2 presents examples of structural MRI scans from three patients showing cortical atrophy mainly in rostral temporal cortex.

All patients were native speakers of British English; 10 of 11 patients were right-handed and all were male—neither by design nor in accord with any sex bias in the incidence of SD, but merely by chance of those in the testable Cambridge SD cohort at the time. Their vision was normal or corrected to normal. Table 1 provides the results of standard testing as well as demographic details for each of the patients. The table, arranged in descending order of Addenbrooke's Cognitive Examination (ACE) scores to reflect the general cognitive status of these particular patients, reveals a considerable range of severity/stage of progression across the 11 cases, from mild (e.g., DB) to moderate (e.g., JM) to severe (IB, DCJ).

The following description of the patients' performance is made with reference to control data from a group of normal individuals of similar age and education (see Woollams, Cooper-Pye, Hodges, & Patterson, 2008). The nonsemantic tests, Rey Figure and digit span, produced performance within the normal range with only one or two exceptions among the more severe cases (Rey for DCJ, digit span for DG). Scores on the semantic and language tests are presented as proportions of the maximum possible score for naming (the standard 64-item picture naming test used in Cambridge), word–picture matching (the same 64 items with 10 picture choices per spoken word target), and the Camel and Cactus test (again, the same 64 items, where the target picture is to be matched to one of four alternative response pictures with which it is associated). The most mildly affected patient, DB, was within the control range on these easy naming and word-to-picture matching tests,

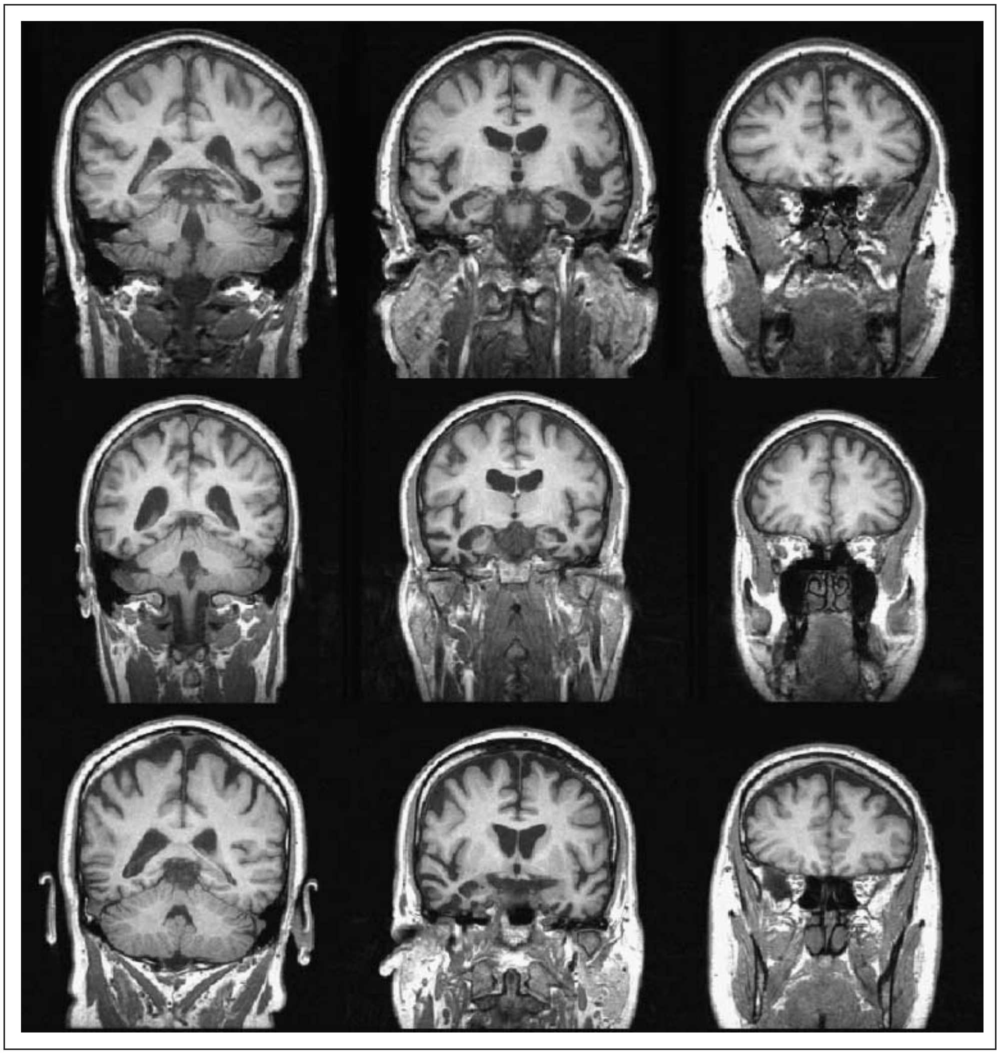


Figure 2. Typical structural brain abnormalities found in the patient population tested. Coronal sections of structural MRI scans from three patients are shown. From left to right, sections at the levels of the splenium, rostral hippocampus, and frontal lobes are shown; the left hemisphere is displayed on the left. Rostral temporal cortex was severely degenerated in all cases.

but the other 10 patients were impaired on both, most substantially so, and all 11 cases had abnormal scores on the Camel and Cactus test of semantic association. Scores on the two fluency tests are given as proportions of the mean score from healthy control subjects. Three of the milder cases (DB, BC, and JW) were good at producing words on the basis of initial letter, but on the sensitive category fluency measure, all 11 patients, even the mildest, were markedly abnormal.

For the lexical decision experiment, 10 male right-handed healthy individuals were selected from the MRC-CBU Participant Panel as suitable controls for the patients. For the two groups, mean (*SD*) age was 66.7 (6.9) years for the patients and 67.9 (6.4) years for the controls; mean (*SD*) years of education were 14.0 (3.3) years for the patients and 14.6 (3.6) years for the controls.

Procedure

Subjects were seated in front of a laptop computer with ~1 m distance from the screen. Written words and pseudowords were presented in large gray letters on a dark background and remained on screen until a response was obtained. Between stimuli, a fixation cross appeared in the middle of the screen for an interval randomly varying between 1.5 and 2.5 sec. Subjects were instructed to look constantly at the fixation cross and to decide, as quickly and accurately as possible, for each stimulus whether it was a "good meaningful English word" or a "meaningless letter string." In case of doubt, they were advised to guess. Our original intention was to use button press responses to obtain a measure of RT; but some of the more severely impaired patients had difficulty with the slightly "dual-task" nature of judging the lexicality of the letter strings while at the same time keeping track of the assignment of buttons to yes versus no responses. In the end, we therefore settled for the more natural verbal mode of responding ("yes" or "no" or, if the patient preferred, "word" or "no word"). As soon as a decision was expressed, the experimenter pressed a response button coding the type of response. As the experimenter's button presses only provide a delayed approximation of response times in the subjects, we primarily base our analysis on response accuracy.

Table 1. Individual Demographic Information and Neuropsychological Test Performance for 11 SD Patients, Ordered by ACE Scores as a Measure of General Cognitive Status

Patient	*Age*	*Years of Education*	*ACE (100)*	*MMSE (30)*	*Rey Copy (36)*	*Rey Delay Copy (36)*	*Digit Span F*	*Digit Span B*	*Picture Naming*	*Spoken WPM*	*CCT Pictures*	*Letter Fluency*	*Category Fluency*
DB	66	18	80	27	36	22.5	8	6	0.91	0.98	0.88	0.88	0.35
BC	60	16	70	28	35	15.5	8	6	0.64	0.80	0.61	1.00	0.32
PS	59	12	67	28	36	15.5	7	5	0.55	0.75	0.70	0.51	0.03
JW	75	16	66	27	36	23.5	8	4	0.70	0.86	0.70	0.93	0.42
JC	60	10	55	25	36	18	7	4	0.41	0.86	0.81	0.20	0.19
JM	70	15	51	24	36	4.5	6	5	0.30	0.84	0.81	0.59	0.03
BH	78	13	48	22	34	8	7	5	0.33	0.63	NT	0.24	0.06
AB	70	10	45	20	36	NT	5	4	0.36	0.59	0.59	0.32	0.16
DG	56	10	42	22	27.5	19	4	3	0.19	0.69	0.80	0.22	0.03
IB	61	11	30	17	28	NT	7	6	0.03	0.13	0.30	0.24	0.00
DCJ	70	19	22	9	20	0	5	3	0.09	0.81	0.36	0.02	0.00
Mean	66	14	52.36	22.64	32.77	14.06	6.55	4.64	0.41	0.72	0.66	0.47	0.14
SD	7	3	17.57	5.73	5.32	8.14	1.37	1.12	0.27	0.23	0.20	0.34	0.15
N	11	11	11	11	11	9	11	11	11	11	10	11	11

ACE, MMSE, Rey Copy and Delay Copy, and Digit Span are reported as whole scores.

Spoken WPM, picture naming, CCT pictures, and letter and category fluency are reported as proportions correct.

Letter and category fluency proportion scores were calculated using age-matched controls' average score as the standard of correct performance.

ACE = Addenbrooke's Cognitive Examination; MMSE = Mini-Mental State Exam; F = forward; B = backward; Spoken WPM = spoken word–picture matching; CCT = Camel and Cactus Test; NT = not tested.

Instructions were first given in writing and then repeated verbally. A practice block then followed to familiarize participants with the task. Questions were answered, and more instructions were given after the practice block; practice was repeated if required. The experiment was started only after participants were comfortable with the task. After every 42 items, participants were asked whether they would like a rest, and if so, a break was given.

Stimuli

The stimuli consisted of 210 meaningful English words and 210 orthographically well-formed pseudowords. Six different word groups, each consisting of 35 words, were selected as follows on the basis of semantic associations: words semantically related to (1) color knowledge (hereinafter COLOR), (2) form or shape (FORM), actions involving (3) the face and articulators (FACE), (4) the arms and hands (ARM), or (5) the legs and feet (LEG), and (6) abstract concepts (ABSTRACT). Ratings of the word stimuli, querying the extent to which they evoked semantic links to the five specific types of information (i.e., the six conditions minus abstract words), were also collected from a different population of normal individuals. These confirmed the semantic differences between the word groups (see Table 2). It was not possible to match the words across all six groups for all of the psycholinguistic variables known to affect lexical decisions—word length, bigram and trigram frequency, word frequency, and imageability—but subsets of these conditions, corresponding to sensible planned comparisons in the analysis, were well matched for these variables, in particular the two conditions emphasizing visual knowledge, COLOR and FORM, and then separately the three conditions emphasizing action, FACE, ARM, and LEG (see Table 2). All action words were verbs, and the number of noun–verb ambiguous items was matched over action word categories. Visually related words were nouns, adjectives, or occasionally both (e.g., gold), and the numbers of these three kinds were also matched. Six groups of pseudowords were created so that each matched the words from one of the six semantic word groups as closely as possible in length and bigram and trigram frequencies.

Data Analysis

Average hit rates, false-positive rates, and d' values were calculated for each subject and word/pseudoword category and entered into repeated measures ANOVAs including the within-group variable of word category and the between-group factor of patients versus controls. Follow-up planned comparison analyses were performed to detect

Table 2. Perceptual, Psycholinguistic, and Semantic Features of the Word and Pseudoword Stimuli Used in the Lexical Decision Task

Variable	*Abstract*	*Color*	*Form*	*Face*	*Arm*	*Leg*
Words						
Length (letters)	4.6 (0.98)	4.23 (0.81)	4.03 (0.62)	4.49 (0.66)	4.57 (0.74)	4.65 (0.73)
Bigram frequency	37031.25 (16260.38)	35944.53 (13444.73)	37075.21 (16284.16)	30514.15 (13954.83)	33001.8 (14615.7)	35852.3 (16141.41)
Trigram frequency	3398.69 (2132.79)	3193.08 (2095.91)	3272.2 (2189.88)	2798.11 (1961.47)	3076.92 (2043.77)	2912.55 (1632.10)
Word frequency	11.31 (14.85)	22.89 (23.85)	22.43 (22.15)	7.17 (9.97)	8.09 (9.83)	8.15 (11.24)
Concreteness	328.4 (24.19)	560.76 (64.09)	558.29 (49.32)	440.95 (67.96)	484.27 (50.28)	475.25 (66.09)
Imageability	382.7 (52.47)	558.16 (53.75)	568.43 (40.56)	497.15 (61.09)	499.09 (59.64)	508.17 (51.04)
Color	1.48 (0.52)	5.69 (1.01)	2.59 (1.15)	1.71 (0.66)	1.83 (0.82)	1.45 (0.39)
Form	1.7 (0.52)	3.35 (1.12)	4.99 (0.78)	2.1 (0.84)	2.77 (0.95)	2.55 (0.96)
Face	2.33 (1.09)	1.53 (1.01)	1.35 (0.54)	6.01 (0.60)	1.84 (0.76)	1.36 (0.42)
Arm	2.11 (1.04)	1.42 (0.40)	1.95 (0.92)	1.41 (0.57)	5.55 (0.72)	1.79 (0.60)
Leg	1.46 (0.59)	1.16 (0.21)	1.5 (0.7)	1.13 (0.16)	2.17 (0.84)	5.36 (1.22)
Pseudowords						
Length (letters)	4.63 (0.69)	4.37 (0.6)	4.11 (0.63)	4.37 (0.65)	4.51 (0.61)	4.59 (0.7)
Bigram frequency	36226.03 (14686.41)	34908.69 (13125.53)	36482.11 (16454.11)	31149.86 (14489.83)	31906.09 (15276.59)	34056.12 (16147.5)
Trigram frequency	3385.15 (2102)	3125.71 (2136.79)	3103.40 (2220.88)	2944.24 (1996.06)	2835.52 (1888.29)	2879.45 (1699.78)

For each feature and word category, mean and *SD* (in brackets) are given. Frequencies are given in occurrences per million words, indicating how many times a given item occurs in an average sample of 1 million words of standard text. Bigram, trigram, and word frequencies are taken from the CELEX Database; concreteness and imageability values form the MRC Psycholinguistic Database. Ratings of color-, form-, arm-, face-, and leg-related meaning immanent to the words were on 7-point scales (1 = *no relationship*, 7 = *strong*, see Hauk et al., 2004; 1 = *no relationship*, 7 = *strong*, see Pulvermüller, Lutzenberger, et al., 1999). Brackets at the top indicate that visually related words (color and form) were matched for length, bigram, trigram, and word frequency, imageability, and concreteness and that for action word subcategories (related to face, arm, and leg), the same matching was successful.

statistical differences between matched stimulus groups. Of particular interest was whether the comparisons of FACE versus ARM words and of COLOR versus FORM words yielded significant differences. Because patient performance was substantially below that of control participants, an attempt was made to remove the variance related to general between-group differences by normalizing performance within each group. To this end, scores obtained for each category were divided by the mean over all categories for that subject. This led to a second set of analyses.

RESULTS

Spearman correlation yielded significant linear correlations between the patients' severity of semantic impairment, as indicated by some of the neuropsychological test measures in Table 1, and their overall d' values in the lexical decision task (ACE: $r = 0.66$; naming: $r = 0.71$; both p values $<.05$). Correlations with d' were far from significant for age and education level.

SD patients' overall performance on the lexical decision task was substantially reduced compared with that of control subjects. This was revealed by all three measures: hit rate (79.9% vs. 95.1%), $F(1, 19) = 9.21$, $p < .0069$; false-positive rate (34.5% vs. 6.7%), $F(1, 19) = 10.69$, $p < .004$; and d' (1.49 vs. 3.38), $F(1, 19) = 35.17$, $p < .001$. This consistent difference is evidence that lexico-semantic processing was generally impaired—and substantially so—in the patients. Average values for the patient and control groups for hit rates and d' values, calculated on both raw and normalized data, are displayed in Figures 3 and 4. Planned comparison tests contrasting patient and healthy participant performance confirmed significant differences for each semantic category separately.

Analysis of performance on the six word categories across both participant groups revealed significant main effects on all measures: hit rates, $F(5, 95) = 14.36$, $p < .0001$; false-positive rates, $F(5, 95) = 5.09$, $p < .0004$; and d' values,

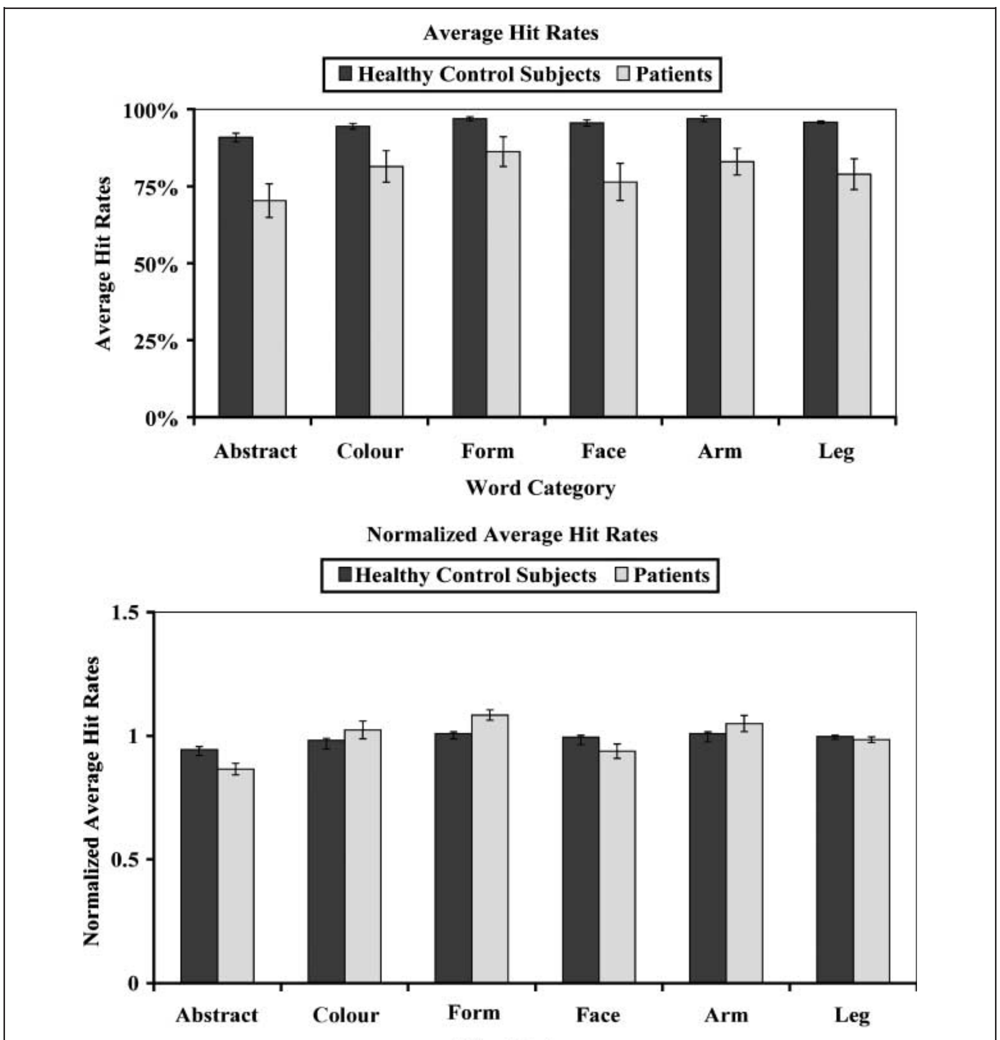
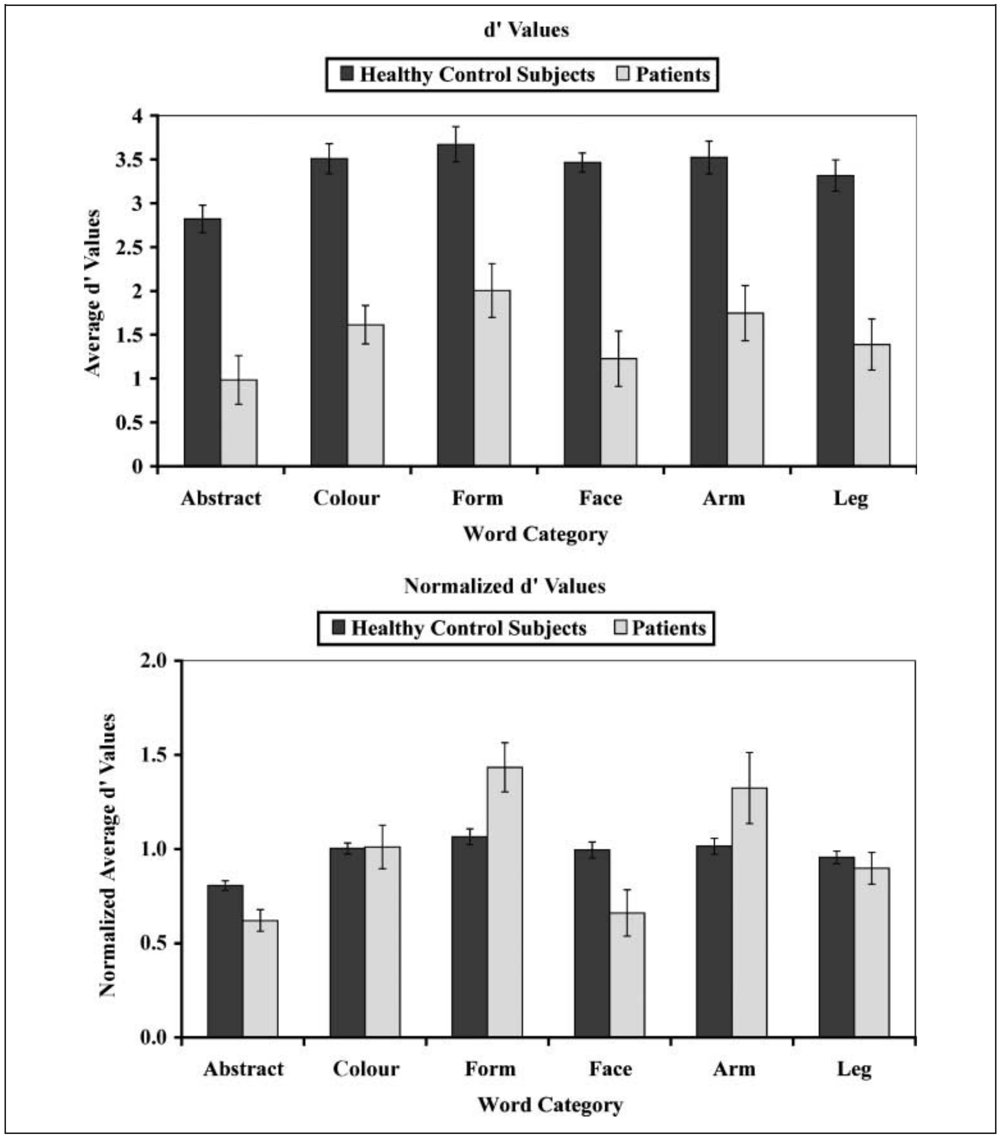


Figure 3. Performance on the lexical decision task. Hit rates are given for patients (black bars) and healthy control subjects (gray) for each of the six word categories: abstract words, color, form, face, arm, and leg. Raw results are displayed at the top, normalized data at the bottom.

Figure 4. Performance on the lexical decision task. d' results are given for patients (black bars) and healthy control subjects (gray) for each of the six word categories. Raw results are displayed at the top; normalized data are displayed at the bottom.



$F(5, 95) = 16.58$, $p < .0001$. ABSTRACT words led to generally reduced performance (combined hit rate = 80.5%) compared with other categories, and there were also some more subtle differences in hit rate between visually related words (COLOR = 87.9%, FORM = 91.6%) and action-related words (FACE = 86.0%, ARM = 89.9%, LEG = 87.4%).

Importantly, the analysis of hit rates revealed significant processing differences between word categories in the patients but not in healthy controls, resulting in a significant interaction of the Group and Word Category factors, $F(5, 95) = 3.54$, $p < .0056$. Whereas ABSTRACT words led to reduced performance in both groups, performance on other word groups was similar in the control participants but more variable in the patients. Between-category differences in the patients, but not in healthy control subjects, were most clearly visible after normalization in the patient group (Figure 3B). Critically, planned contrasts between categories matched for psycholinguistic variables demonstrated that the patients had higher hit rates for FORM than for COLOR words, $F(1, 19) = 7.69$, $p < .012$, and for ARM than for FACE words, $F(1, 19) = 8.27$, $p < .0096$. The Group × Word Category interaction remained significant after normalization of hit rates (see Methods), $F(5, 95) = 3.65$, $p < .0046$. It also persisted after removal of data for abstract words, $F(4, 76) = 2.62$, $p < .041$.

Analysis of d' scores largely confirmed the results obtained from the hit rates. Although raw scores (Figure 4A) yielded only a marginal interaction of Group and Word Category ($p < .1$), normalized data confirmed differential impairment of conceptual word categories in patients and healthy control participants (Group × Word Category), $F(5, 95) = 3.75$, $p < .0053$ (Figure 4B). The significant interaction persisted after removal of data for abstract words, $F(4, 76) = 3.28$, $p < .015$. Planned comparison F tests further confirmed differences between well-matched visually related and action-related words (FORM > COLOR and ARM > FACE; all F values >4, all p values <.05) in patients but not in healthy participants. Seven of 11 patients obtained lower d' values for COLOR as compared with FORM words, and for 10 of 11 patients, d' values were lower for FACE than for ARM words.

For the subset of the five most severely affected patients (bottom of Table 1), average d' values for face and arm action words were 0.85 and 1.55, respectively (difference = 0.70), suggesting a substantial discrepancy, whereas the corresponding values for the five most mildly impaired patients (top of Table 1) were more similar (1.67 vs. 1.98, difference = 0.32). More severely affected patients thus showed the stronger word category difference for action words. The opposite pattern emerged for the color/form distinction. In this case, the larger numerical discrepancy in average d' scores was present for the mild patients (2.09 vs. 2.71, difference = 0.62), whereas more similar results emerged for the advanced ones (1.21 vs. 1.42, difference = 0.21).

A final analysis of the patients' performance grouped words that, according to the topography model (Figure 1A), (a) are more or less dependent on areas affected in SD (factor Involvement) and (b) draw, respectively, more on frontal versus temporal lobe (factor Lobe) and then investigated the effect of these factors in mild and more severely affected patients (factor Severity). The analysis yielded a three-way interaction (Severity × Involvement × Lobe) that approached significance, $F(1, 8) = 3.52, p < .097$. This analysis further confirmed that patient performance was more markedly degraded on word kinds for which the model predicted such degradation (COLOR and FACE) as compared with words for which no additional defect had been predicted (FORM and ARM words), $F(1, 8) = 16.46, p < .0036$.

Although healthy control participants did not show category differences on accuracy measures (d', hit rates), one may ask whether their response times might indicate a pattern of category specificity that matches the one seen in accuracy measures obtained from the patients. Response times in healthy individuals did not reveal significant differences between the six word groups, $F(5, 45) = 1.56, p = .126$, *ns*, or between the five nonabstract word groups, $F(3, 36) = 1.49, p > .2$, *ns*. Because of the special procedure applied, however, response times were long (~1350 msec), and their variance was high, especially in one subject (average response time >3 sec). After removal of this slow responder's data from the analysis, RT differences between the six categories were significant, $F(5, 40) = 6.77, p < .001$, mainly because of slowed responses to abstract words. After removing abstract items, the word category main effect was at significance threshold, $F(4, 32) = 3.72, p < .047$, and appeared to be due to differences between action-related and visually related words (which, as we note again, were not exactly matched). Comparison of two "frontal" word groups (FACE and ARM) against "temporal" items (COLOR and FORM; factor Lobe) and distinguishing the categories most affected in the patients (FACE and COLOR) from the rest (factor Involvement), the Lobe factor yielded significance, $F(1, 8) = 10.22, p < .01$ (visually related words = 1119 msec, action-related words = 1163 msec), but the Involvement factor did not (FACE/COLOR = 1149 msec, ARM/FORM = 1133 msec). As this pattern of results is orthogonal to that seen in the patients, the observed semantic category deficits in SD appear unrelated to processing differences present in healthy control subjects. Analyses of response times in SD patients did not reveal significant effects.

DISCUSSION

SD produces a severe deficit in lexico-semantic processing that applies across the board to all semantic word categories. This was confirmed by the general performance reduction observed in the lexical decision experiment (average $d' = 1.5$ for the patients as compared with average $d' = 3.4$ for matched healthy participants). Importantly, however, and constituting a novel finding, there were significant differences in lexical decisions on words from different semantic categories, which were absent in matched healthy control subjects (significant Word Category × Group interactions). In SD patients, semantic word groups matched for a range of important psycholinguistic criteria led to significantly different processing success: Hit rates and d' values were lower for the COLOR condition than for the FORM condition, and action words in the FACE category produced lower hit rates and d' values than those in the ARM condition. Because of careful matching of other properties that affect lexical decision accuracy, we can assert with some confidence that these differences are best explained in terms of semantic features and corresponding category-specific topographies of the underlying cortical circuits. These findings have important implications for theories of semantic and conceptual processing and representation.

SD has been considered an across-the-board deficit in semantic processing (Patterson et al., 2007; Saffran & Schwartz, 1994). As mentioned in the Introduction section, previous group studies have failed to uncover category specificity of semantic deficits in SD in terms of the most commonly assessed distinctions: living versus nonliving concepts (Lambon Ralph, Graham, et al., 1998; Lambon Ralph et al., 2007) and objects versus actions (Cotelli et al., 2006). Our current findings suggest that the absence of any category differences in previous studies of SD might be due to the grain size of the categories under study. A contrast between the broad categories of living and nonliving things can be motivated on the basis that they are innate to the human cognitive system (Caramazza & Mahon, 2003). By contrast, if category differences result from differential grounding of semantics in sensory/motor versus functional knowledge (Warrington & McCarthy, 1983), then more fine-grained subdivisions of semantic space are required—separating, for example, large artifacts from tools, color from form, and action knowledge relating to different body parts (Barsalou, 2008; Pulvermüller, 2005; Humphreys & Forde, 2001; Farah & McClelland, 1991; Warrington & McCarthy, 1987). Consistent with this suggestion, the differential degrees of deficit in lexical decision revealed in SD patients by the present investigation cannot be explained by any domain-general principle. Although the larger categories of visually related and action-related words did not afford a well-matched contrast, it is nevertheless observable that the patients were not differentially impaired on one or other of these broad domains. The generally reduced performance on abstract words might suggest a general category difference (abstract vs. concrete), but as not all psycholinguistic confounds (e.g., word frequency) could be ruled out for this contrast, this conclusion is not fully endorsed by the data. Where a degree of category specificity emerged in the present work was between subtypes of action words and between subtypes of visually related words.

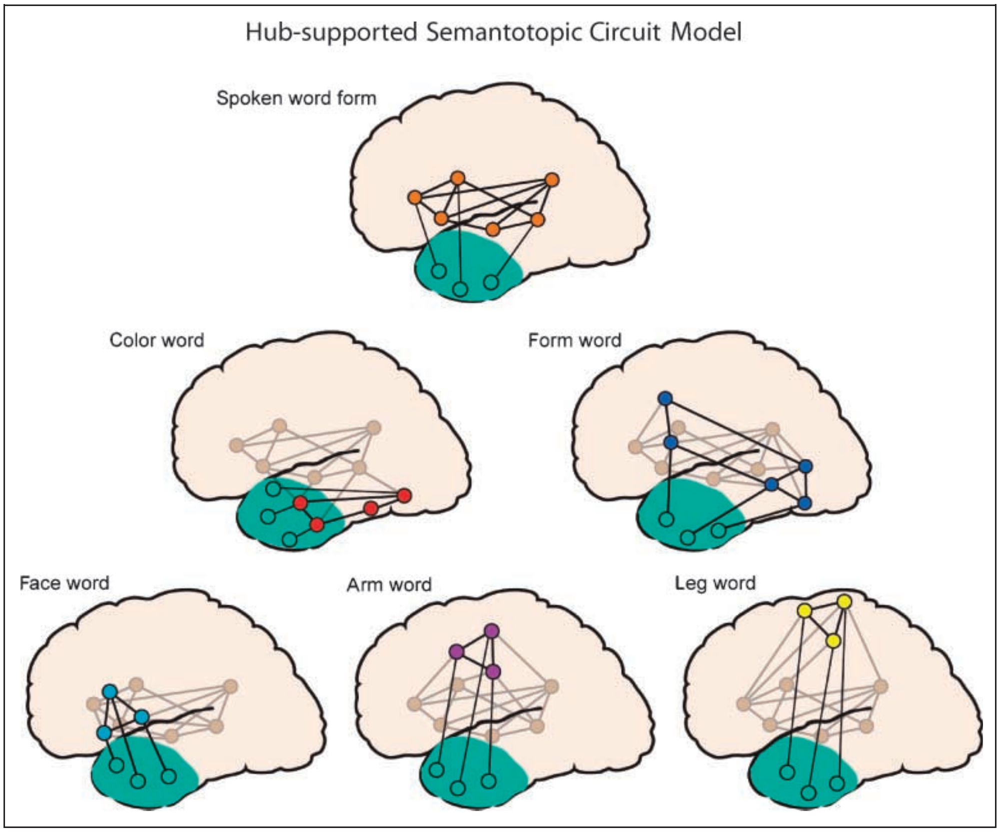
This pattern of results supports a distributed circuit model of lexico-semantic networks according to which knowledge of object color (relative to knowledge of object form) and knowledge about actions relating to the face and articulators (compared with those relating to hand and arm) draw more heavily on anterior-temporal and adjacent frontal structures. Considering the first of these contrasts, despite the fact that color processing areas in the occipito-temporal cortex are posterior to areas specializing in form analysis (Corbetta, Miezin, Dobmeyer, Shulman, & Petersen, 1991; Zeki et al., 1991), recent studies have indicated that processing of color concepts involves anterior-temporal structures (Miceli et al., 2001; Mummery, Patterson, Hodges, & Price, 1998), whereas form-related concepts and words activate posterior-lateral fusiform gyrus and, in addition, dorsolateral pFC (Moscoso Del Prado Martin et al., 2006; Pulvermüller & Hauk, 2006). Comparison of mildly and severely affected patients indicated that the difference between color and form word impairment was more pronounced at early (mild) stages of the disease, whereas later on the difference diminished, perhaps suggesting posterior spreading of the lesion. With regard to the second contrast: Action words and concepts elicit semantic somatotopy along the fronto-central cortex, with more ventral activation to FACE words and more dorsal activation to ARM words (Hauk et al., 2004; Pulvermüller et al., 2000). Although SD in the very early stages is associated with damage restricted to the temporal lobes (Nestor et al., 2006)—and the present population also showed most massive degradation there (Figure 2)—inferior-frontal atrophy and hypometabolism emerge with advancing disease (Drzezga et al., 2008; Mummery et al., 2000). The bigger numerical difference between action word category d' values seen in more severely affected patients of the present cohort is consistent with this observation. In conjunction with the semantic topography model, the functional deficit in inferior-frontal structures explains the specific deficit for face-related words.

Note that not all brain models of category specificity explain the pattern of deficits found here in SD. For example, Martin and Chao (2001) have proposed that the processing of color semantics is located posterior to form semantics in posterior temporal cortex. This proposal on its own does not account for the present differential deficit for color words in SD patients, which, similar to earlier results from patients (Miceli et al., 2001; Mummery et al., 1998) and the abovementioned imaging work, suggest a specific contribution of anterior-temporal cortex to color concept processing. Also, previous theories of category specificity did not reach the fine grain size to differentiate action word subcategories according to their body part reference. The semantic topography model in Figure 1A and its proposed extension (Figure 5) seem to provide the best explanation available to date of the pattern of lexico-semantic deficits seen in SD. Still, the model needs further specification to more fully account for the semantics of a wider range of words and concepts (e.g., prepositions, Kemmerer & Tranel, 2003; Noordzij, Neggers, Ramsey, & Postma, 2008).

In contrast to one prediction of the semantic topography model, SD patients' performance on leg words was not significantly better than that on face words, although the suggested cortical distribution of leg-action concepts should, by hypothesis, include neuronal assemblies in motor and premotor areas, which are not specifically affected in SD. Although this lack of significance does not constitute a strong finding falsifying the semantic somatotopy model, it still suggests that semantic circuits may be more complex than the sketches presented in Figure 1A would indicate. More specifically, the tendency toward an impairment of leg-word processing in SD patients may suggest that the processing of these words critically depends on the integrity of neuronal assemblies in anterior-temporal or inferior-frontal cortex, not just on leg motor and premotor regions. Direct brain imaging evidence for anterior-temporal contributions to leg-word processing has recently been revealed by cluster analysis performed on fMRI data from healthy subjects (Pulvermüller, Kherif, Hauk, Mohr, & Nimmo-Smith, 2009). These results revealed cell assemblies for leg words with both dorsal fronto-central (including motor) and anterior-temporal cortex contribution, therefore explaining why SD patients' performance on leg words was similar to that on the affected face words.

The present pattern of results refutes the suggestion outlined in the Introduction section that differential activations to various semantic kinds might be epiphenomenal rather than reflecting the operation of differently distributed semantic networks. Because the data come from patients with the most severe specifically semantic deficit known to date, there cannot be any doubt that the function of the damaged circuits is semantic conceptual in nature. In addition, the consistency between degrees of

Figure 5. Model unifying a semantic hub with category-specific semantic circuits. Widely dispersed interactive circuits reaching into anterior-temporal cortex are envisaged to form the cortical basis of semantic processes. The cortical topographies of these circuits reach into sensory and motor systems that ground concepts in actions and perceptions. This hub-supported somatotopic circuit model accounts for both general semantic deficit and semantic category differences observed in SD patients. Furthermore, the model is consistent with a range of neuroimaging findings about category-specific semantic activation of action-perception circuits.



deficit in SD for various semantic categories and the evidence from a range of regional functional activation studies in the healthy brain using well-matched word groups with different types of meaning support the semantic topography model.

A semantic hub model that denied a role of category-specific semantic networks would be unable to account for the present pattern of results. Similarly, the semantic topography model as shown in Figure 1A would not account for the massive general impairment in SD of all semantic classes as demonstrated in the present and earlier studies. The best account of the data therefore results from adding a semantic hub to the semantic topography model (Figure 1A and B). This results in a hub-supported model of semantotopic circuits (Figure 5). According to this model, an intact semantic hub in temporal poles is necessary for the functionality of the semantic system, possibly in ways made explicit in the computational model of Rogers et al. (2004), but semantic conceptual computations are being carried out in widespread brain areas. Importantly, these widespread areas are specific to different kinds of concepts and meanings, with form and face words drawing most heavily on anterior-temporal and inferior-frontal areas affected in SD. The general importance of anterior-temporal lobes in semantic processing may relate to their strategic placement as links between cortical and limbic structures (Pulvermüller & Schumann, 1994). A future target will be to define, more precisely, the functional roles of hub- and category-specific parts of semantic circuits.

Acknowledgments

The patients were recruited into this study with permission from the Consultant Neurologist in charge of their care, author P. J. N. The authors thank Dr. Anna Woollams for her help and advice at early stages of this project and Dr. Hilary Green for testing most of the SD patients. The work was supported by the Medical Research Council (UK) (U1055.04.003.00001.01 and U1055.04.003.00003.01) and by the European Community under the "New and Emerging Science and Technologies" Programme (NEST, Nestcom Project).

Reprint requests should be sent to Friedemann Pulvermüller, MRC Cognition and Brain Sciences Unit, 15 Chaucer Road, Cambridge CB2 7EF, UK, or via e-mail: friedemann.pulvermuller@mrc-cbu.cam.ac.uk.

Notes

1. Color and form words matched for psycholinguistic properties have only been investigated by a few studies, which indicated that both categories activate fusiform cortex and posterior middle temporal cortex but that this activation is generally stronger for form words (Simmons et al., 2007; Moscoso Del Prado Martin et al., 2006; Pulvermüller & Hauk, 2006). In contrast, color words more strongly activated anterior parahippocampal gyrus than matched form words (Pulvermüller & Hauk, 2006), a finding also consistent with some lesion evidence showing specific color-semantic deficits after anterior-mesial temporal lobe damage (Miceli et al., 2001).
2. Naming color, form and action, for example, requires either very different stimuli demanding naming at different description levels, or, if the same stimuli are presented for color/form/action naming, the amount of filtering and level of information extraction

would be different between categories. Picture judgments are problematic for investigating fine-grained category differences because action concepts are not easily depicted and, in case this is possible, the relationship between picture and concept (the picture always depicts an actor, possibly an object and the action) is very different from the simple relationship between a depicted object and the word referring to it.

REFERENCES

Aziz-Zadeh, L., Wilson, S. M., Rizzolatti, G., & Iacoboni, M. (2006). Congruent embodied representations for visually presented actions and linguistic phrases describing actions. *Current Biology, 16,* 1818–1823.

Bak, T. H., O'Donovan, D. G., Xuereb, J. H., Boniface, S., & Hodges, J. R. (2001). Selective impairment of verb processing associated with pathological changes in Brodmann areas 44 and 45 in the motor neurone disease–dementia–aphasia syndrome. *Brain, 124,* 103–120.

Bak, T. H., Yancopoulou, D., Nestor, P. J., Xuereb, J. H., Spillantini, M. G., Pulvermüller, F., et al. (2006). Clinical, imaging and pathological correlates of a hereditary deficit in verb and action processing. *Brain, 129,* 321–332.

Barsalou, L. W. (2008). Grounded cognition. *Annual Review of Psychology, 59,* 617–645.

Binder, J. R., McKiernan, K. A., Parsons, M. E., Westbury, C. F., Possing, E. T., Kaufman, J. N., et al. (2003). Neural correlates of lexical access during visual word recognition. *Journal of Cognitive Neuroscience, 15,* 372–393.

Binder, J. R., Westbury, C. F., McKiernan, K. A., Possing, E. T., & Medler, D. A. (2005). Distinct brain systems for processing concrete and abstract concepts. *Journal of Cognitive Neuroscience, 17,* 905–917.

Bird, H., Lambon-Ralph, M. A., Patterson, K., & Hodges, J. R. (2000). The rise and fall of frequency and imageability: Noun and verb production in semantic dementia. *Brain and Language, 73,* 17–49.

Boulenger, V., Mechtouff, L., Thobois, S., Broussolle, E., Jeannerod, M., & Nazir, T. A. (2008). Word processing in Parkinson's disease is impaired for action verbs but not for concrete nouns. *Neuropsychologia, 46,* 743–756.

Boulenger, V., Silber, B. Y., Roy, A. C., Paulignan, Y., Jeannerod, M., & Nazir, T. A. (2008). Subliminal display of action words interferes with motor planning: A combined EEG and kinematic study. *Journal of Physiology (Paris), 102,* 130–136.

Bozeat, S., Lambon Ralph, M. A., Patterson, K., Garrard, P., & Hodges, J. R. (2000). Non-verbal semantic impairment in semantic dementia. *Neuropsychologia, 38,* 1207–1215.

Caramazza, A., & Mahon, B. Z. (2003). The organization of conceptual knowledge: The evidence from category-specific semantic deficits. *Trends in Cognitive Sciences, 7,* 354–361.

Chao, L. L., Haxby, J. V., & Martin, A. (1999). Attribute-based neural substrates in temporal cortex for perceiving and knowing about objects. *Nature Neuroscience, 2,* 913–919.

Chumbley, J. L., & Balota, D. A. (1984). A word's meaning affects the decision in lexical decision. *Memory and Cognition, 12,* 590–606.

Corbetta, M., Miezin, F. M., Dobmeyer, S., Shulman, G. L., & Petersen, S. E. (1991). Selective and divided attention during visual discriminations of shape, color, and speed: Functional anatomy by positron emission tomography. *Journal of Neuroscience, 11,* 2383–2402.

Cotelli, M., Borroni, B., Manenti, R., Alberici, A., Calabria, M., Agosti, C., et al. (2006). Action and object naming in frontotemporal dementia, progressive supranuclear palsy, and corticobasal degeneration. *Neuropsychology, 20,* 558–565.

Crepaldi, D., Aggujaro, S., Arduino, L. S., Zonca, G., Ghirardi, G., Inzaghi, M. G., et al. (2006). Noun–verb dissociation in aphasia: The role of imageability and functional locus of the lesion. *Neuropsychologia, 44,* 73–89.

Damasio, A. R., & Tranel, D. (1993). Nouns and verbs are retrieved with differently distributed neural systems. *Proceedings of the National Academy of Sciences, U.S.A., 90,* 4957–4960.

Daniele, A., Giustolisi, L., Silveri, M. C., Colosimo, C., & Gainotti, G. (1994). Evidence for a possible neuroanatomical basis for lexical processing of nouns and verbs. *Neuropsychologia, 32,* 1325–1341.

Desgranges, B., Matuszewski, V., Piolino, P., Chetelat, G., Mezenge, F., Landeau, B., et al. (2007). Anatomical and functional alterations in semantic dementia: A voxel-based MRI and PET study. *Neurobiology of Aging, 28,* 1904–1913.

Diehl, J., Grimmer, T., Drzezga, A., Riemenschneider, M., Forstl, H., & Kurz, A. (2004). Cerebral metabolic patterns at early stages of frontotemporal dementia and semantic dementia. A PET study. *Neurobiology of Aging, 25,* 1051–1056.

Diesfeldt, H. F. A. (1992). Impaired and preserved semantic memory functions in dementia. *Advances in Psychology, 89,* 227–263.

Drzezga, A., Grimmer, T., Henriksen, G., Stangier, I., Perneczky, R., Diehl-Schmid, J., et al. (2008). Imaging of amyloid plaques and cerebral glucose metabolism in semantic dementia and Alzheimer's disease. *Neuroimage, 39,* 619–633.

Farah, M. J., & McClelland, J. L. (1991). A computational model of semantic memory impairment: Modality specificity and emergent category specificity. *Journal of Experimental Psychology: General, 120,* 339–357.

Gainotti, G. (2004). A metanalysis of impaired and spared naming for different categories of knowledge in patients with a visuo-verbal disconnection. *Neuropsychologia, 42,* 299–319.

Hauk, O., Davis, M. H., Kherif, F., & Pulvermüller, F. (2008). Imagery or meaning? Evidence for a semantic origin of category-specific brain activity in metabolic imaging. *European Journal of Neuroscience, 27,* 1856–1866.

Hauk, O., Johnsrude, I., & Pulvermüller, F. (2004). Somatotopic representation of action words in the motor and premotor cortex. *Neuron, 41,* 301–307.

Hauk, O., & Pulvermüller, F. (2004). Neurophysiological distinction of action words in the fronto-central cortex. *Human Brain Mapping, 21,* 191–201.

Hauk, O., Shtyrov, Y., & Pulvermüller, F. (2008). The time course of action and action–word comprehension in the human brain as revealed by neurophysiology. *Journal of Physiology (Paris), 102,* 50–58.

Hodges, J. R., & Patterson, K. (2007). Semantic dementia: A unique clinicopathological syndrome. *Lancet Neurology, 6,* 1004–1014.

Humphreys, G. W., & Forde, E. M. (2001). Hierarchies, similarity, and interactivity in object recognition: "Category-specific" neuropsychological deficits. *Behavioral and Brain Sciences, 24,* 453–509.

Humphreys, G. W., & Riddoch, M. J. (1987). On telling your fruit from your vegetables—A consideration of category-specific deficits after brain-damage. *Trends in Neurosciences, 10,* 145–148.

Kemmerer, D., Castillo, J. G., Talavage, T., Patterson, S., & Wiley, C. (2008). Neuroanatomical distribution of five semantic components of verbs: Evidence from fMRI. *Brain and Language, 107,* 16–43.

Kemmerer, D., & Tranel, D. (2003). A double dissociation between the meanings of action verbs and locative prepositions. *Neurocase, 9,* 421–435.

Lambon Ralph, M. A., Graham, K. S., Ellis, A. W., & Hodges, J. R. (1998). Naming in semantic dementia-What matters? *Neuropsychologia, 36,* 775–784.

Lambon Ralph, M. A., Howard, D., Nightingale, G., & Ellis, A. W. (1998). Are living and non-living category-specific deficits causally linked to impaired perceptual or associative knowledge? Evidence from a category-specific double dissociation. *Neurocase, 4,* 311–338.

Lambon Ralph, M. A., Lowe, C., & Rogers, T. T. (2007). Neural basis of category-specific semantic deficits for living things: Evidence from semantic dementia, HSVE and a neural network model. *Brain, 130,* 1127–1137.

Lambon Ralph, M. A., Patterson, K., Garrard, P., & Hodges, J. R. (2003). Semantic dementia with category specificity: A comparative case-series study. *Cognitive Neuropsychology, 20,* 307–326.

Lambon Ralph, M. A., Pobric, G., & Jefferies, E. (2009). Conceptual knowledge is underpinned by the temporal pole bilaterally: Convergent evidence from rTMS. *Cerebral Cortex, 19,* 832–838.

Luzzatti, C., Raggi, R., Zonca, G., Pistarini, C., Contardi, A., & Pinna, G. D. (2001). On the nature of the selective impairment of verb and noun retrieval. *Cortex, 37,* 724–726.

Mahon, B. Z., & Caramazza, A. (2008). A critical look at the embodied cognition hypothesis and a new proposal for grounding conceptual content. *Journal of Physiology (Paris), 102,* 59–70.

Martin, A. (2007). The representation of object concepts in the brain. *Annual Review of Psychology, 58,* 25–45.

Martin, A., & Chao, L. L. (2001). Semantic memory and the brain: Structure and processes. *Current Opinion in Neurobiology, 11,* 194–201.

Miceli, G., Fouch, E., Capasso, R., Shelton, J. R., Tomaiuolo, F., & Caramazza, A. (2001). The dissociation of color from form and function knowledge. *Nature Neuroscience, 4,* 662–667.

Miceli, G., Silveri, M., Villa, G., & Caramazza, A. (1984). On the basis of agrammatics' difficulty in producing main verbs. *Cortex, 20,* 207–220.

Moscoso Del Prado Martin, F., Hauk, O., & Pulvermüller, F. (2006). Category specificity in the processing of color-related and form-related words: An ERP study. *Neuroimage, 29,* 29–37.

Mummery, C. J., Patterson, K., Hodges, J. R., & Price, C. J. (1998). Functional neuroanatomy of the semantic system: Divisible by what? *Journal of Cognitive Neuroscience, 10,* 766–777.

Mummery, C. J., Patterson, K., Price, C. J., Ashburner, J., Frackowiak, R. S., & Hodges, J. R. (2000). A voxel-based morphometry study of semantic dementia: Relationship between temporal lobe atrophy and semantic memory. *Annals of Neurology, 47,* 36–45.

Neininger, B., & Pulvermüller, F. (2001). The right hemisphere's role in action word processing: A double case study. *Neurocase, 7,* 303–317.

Neininger, B., & Pulvermüller, F. (2003). Word-category specific deficits after lesions in the right hemisphere. *Neuropsychologia, 41,* 53–70.

Nestor, P. J., Fryer, T. D., & Hodges, J. R. (2006). Declarative memory impairments in Alzheimer's disease and semantic dementia. *Neuroimage, 30,* 1010–1020.

Noordzij, M. L., Neggers, S. F., Ramsey, N. F., & Postma, A. (2008). Neural correlates of locative prepositions. *Neuropsychologia, 46,* 1576–1580.

Noppeney, U., Patterson, K., Tyler, L. K., Moss, H., Stamatakis, E. A., Bright, P., et al. (2007). Temporal lobe lesions and semantic impairment: A comparison of herpes simplex virus encephalitis and semantic dementia. *Brain, 130,* 1138–1147.

Oliveri, M., Finocchiaro, C., Shapiro, K., Gangitano, M., Caramazza, A., & Pascual-Leone, A. (2004). All talk and no action: A transcranial magnetic stimulation study of motor cortex activation during action word production. *Journal of Cognitive Neuroscience, 16,* 374–381.

Patterson, K. (2007). The reign of typicality in semantic memory. *Philosophical Transactions of the Royal Society of London, Series B, Biological Sciences, 362,* 813–821.

Patterson, K., Nestor, P. J., & Rogers, T. T. (2007). Where do you know what you know? The representation of semantic knowledge in the human brain. *Nature Reviews Neuroscience, 8,* 976–987.

Pobric, G., Jefferies, E., & Lambon Ralph, M. A. (2007). Anterior temporal lobes mediate semantic representation: Mimicking semantic dementia by using rTMS in normal participants. *Proceedings of the National Academy of Sciences, U.S.A., 104,* 20137–20141.

Pulvermüller, F. (1996). Hebb's concept of cell assemblies and the psychophysiology of word processing. *Psychophysiology, 33,* 317–333.

Pulvermüller, F. (1999). Words in the brain's language. *Behavioral and Brain Sciences, 22,* 253–336.

Pulvermüller, F. (2005). Brain mechanisms linking language and action. *Nature Reviews Neuroscience, 6,* 576–582.

Pulvermüller, F., Härle, M., & Hummel, F. (2000). Neurophysiological distinction of verb categories. *NeuroReport, 11,* 2789–2793.

Pulvermüller, F., & Hauk, O. (2006). Category-specific processing of color and form words in left fronto-temporal cortex. *Cerebral Cortex, 16,* 1193–1201.

Pulvermüller, F., Kherif, F., Hauk, O., Mohr, B., & Nimmo-Smith, I. (2009). Distributed cell assemblies for general lexical and category-specific semantic processing as revealed by fMRI cluster analysis. *Human Brain Mapping, 30,* 3837–3850.

Pulvermüller, F., Lutzenberger, W., & Preissl, H. (1999). Nouns and verbs in the intact brain: Evidence from event-related potentials and high-frequency cortical responses. *Cerebral Cortex, 9,* 498–508.

Pulvermüller, F., Mohr, B., & Schleichert, H. (1999). Semantic or lexico-syntactic factors: What determines word-class specific activity in the human brain? *Neuroscience Letters, 275,* 81–84.

Pulvermüller, F., & Schumann, J. H. (1994). Neurobiological mechanisms of language acquisition. *Language Learning, 44,* 681–734.

Pulvermüller, F., Shtyrov, Y., & Ilmoniemi, R. J. (2005). Brain signatures of meaning access in action word recognition. *Journal of Cognitive Neuroscience, 17,* 884–892.

Rogers, T. T., Lambon Ralph, M. A., Garrard, P., Bozeat, S., McClelland, J. L., Hodges, J. R., et al. (2004). Structure and deterioration of semantic memory: A neuropsychological and computational investigation. *Psychological Review, 111,* 205–235.

Saffran, E. M., & Schwartz, M. F. (1994). Of cabbages and things: Semantic memory from a neuropsychological perspective. In C. Umilta & M. Moscowitch (Eds.), *Attention and performance XV: Conscious and nonconscious information processing* (pp. 507–536). Cambridge, MA: MIT Press.

Shtyrov, Y., Hauk, O., & Pulvermüller, F. (2004). Distributed neuronal networks for encoding category-specific semantic

information: The mismatch negativity to action words. *European Journal of Neuroscience, 19,* 1083–1092.
Simmons, W. K., Ramjee, V., Beauchamp, M. S., McRae, K., Martin, A., & Barsalou, L. W. (2007). A common neural substrate for perceiving and knowing about color. *Neuropsychologia, 45,* 2802–2810.
Tettamanti, M., Buccino, G., Saccuman, M. C., Gallese, V., Danna, M., Scifo, P., et al. (2005). Listening to action-related sentences activates fronto-parietal motor circuits. *Journal of Cognitive Neuroscience, 17,* 273–281.
Tyler, L. K., Moss, H. E., Durrant-Peatfield, M. R., & Levy, J. P. (2000). Conceptual structure and the structure of concepts: A distributed account of category-specific deficits. *Brain and Language, 75,* 195–231.
Warrington, E. K., & McCarthy, R. A. (1983). Category specific access dysphasia. *Brain, 106,* 859–878.
Warrington, E. K., & McCarthy, R. A. (1987). Categories of knowledge: Further fractionations and an attempted integration. *Brain, 110,* 1273–1296.
Warrington, E. K., & Shallice, T. (1984). Category specific semantic impairments. *Brain, 107,* 829–854.
Woollams, A. M., Cooper-Pye, E., Hodges, J. R., & Patterson, K. (2008). Anomia: A doubly typical signature of semantic dementia. *Neuropsychologia, 46,* 2503–2514.
Zeki, S., Watson, J. D., Lueck, C. J., Friston, K. J., Kennard, C., & Frackowiak, R. S. (1991). A direct demonstration of functional specialization in human visual cortex. *Journal of Neuroscience, 11,* 641–649.