

Paradoxical Features of Word Finding Difficulty in Primary Progressive Aphasia

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Impaired word retrieval is a main symptom of primary progressive aphasia (PPA). The cognitive features of this impairment in PPA are poorly understood. We studied 12 patients with PPA (6 English-speaking and 6 Dutch-speaking), 7 patients with early-stage clinically probable Alzheimer's disease (PRAD), 5 patients with mild cognitive impairment (MCI), and 15 age-matched, cognitively intact, control subjects. Subjects had to name a picture (the probe), which was preceded by a written word (the prime) that could be the correct name of the picture, a noun belonging to the same semantic subcategory (related prime), a semantically unrelated noun (unrelated prime), or a pseudoword (neutral control). Naming latencies were longer in PPA and PRAD patients than in control subjects. Critically, the interaction between group and prime type was highly significant. PPA patients named the probe more slowly after a related compared with an unrelated prime. In contrast, PRAD patients, mild cognitive impairment patients, and healthy control subjects tended to name the probe faster when it was preceded by a related prime. The semantic interference effect in PPA generalized across languages and PPA subtypes. Selection among competing word forms sharing a same semantic field is abnormal in PPA. The semantic interference effect constitutes a positive distinguishing feature between PPA and PRAD.

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Primary progressive aphasia (PPA) is a progressive clinical syndrome characterized by language impairment as its predominant manifestation for at least 2 years after clinical onset.^{1–3} Difficulty finding words is the most frequent presenting symptom.^{1,2} With clinically probable Alzheimer's disease⁴ (PRAD), a much more prevalent disorder, naming difficulties are also common and sometimes dominate the clinical picture, especially in patients younger than 60 years.⁵ The discrimination between PPA and PRAD partially relies on the absence of major memory deficits in the former group.^{1–3} The search for features that positively distinguish PPA from PRAD is a clinically important endeavor⁶ because treatment, prognosis, and counseling differ substantially between the two disease entities.

In the intact brain, priming studies have provided insight into the time course and cognitive architecture of word retrieval.^{7–9} Subjects name a picture (the probe) more rapidly when a word (the prime) with an associated meaning is presented a few hundred milliseconds before picture onset.^{10,11} Under these conditions, activity propagates among the word forms belonging to the same lexical-semantic networks,^{12–15} the

target word form comes closer to retrieval threshold, and responses are facilitated.^{10,13} In PRAD, semantic priming has been reported to be preserved,¹⁶ decreased,¹⁷ or increased^{17,18} depending on disease stage and subtype,¹⁹ task, and stimulus characteristics²⁰ (for a review, see Salmon and Fennema-Notestine²¹).

We applied a primed picture naming paradigm to study semantic priming in PPA. According to our a priori hypothesis, the selection among competing neighboring word forms should be impaired in PPA. We predicted that this would lead to paradoxical semantic interference where healthy control subjects would show facilitation. To assess disease specificity of priming effects seen in PPA, we applied the same paradigm to patients with PRAD or amnesic mild cognitive impairment²² (MCI), a condition in which a relatively isolated memory impairment increases the risk for subsequent PRAD.

Subjects and Methods

Subjects

We studied 12 patients with PPA,³ 7 patients with PRAD,⁴ 5 patients with MCI,²² and 15 cognitively intact, age-matched, control subjects.

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Six PPA patients were English-speaking and were observed at the Cognitive Neurology and Alzheimer's Disease Center, Northwestern University (Chicago, IL); the other six PPA patients were Dutch-speaking and were observed at the Memory Clinic, University Hospital Gasthuisberg (Leuven, Belgium). Three female and nine male PPA patients, 57 to 77 (mean, 68.9; standard error [SE], 1.9) years of age with 10 to 24 (mean, 15.9; SE, 1.1) years of education, participated in this study. Disease duration varied between 1.5 and 10 years. The mean Mini-Mental State Examination²³ score was 26.8 (standard deviation [SD], 2.5). All patients underwent an extensive neuropsychological assessment, which allowed for exclusion of significant impairment in cognitive domains other than language in all subjects. Language assessment in the English-speaking patients included the Boston Naming Test²⁴ and the Western Aphasia Battery²⁵; assessment in the Dutch-speaking patients included the Dutch version of the Boston Naming Test,²⁶ the Aachen Aphasia Test²⁷ (Dutch version), and the verbal semantic associative task of the Psycholinguistic Assessment of Language Processing in Aphasia²⁸. Seven PPA patients (Cases 1–3 and 7–10) had nonfluent progressive aphasia, characterized by effortful, agrammatic speech with short phrase length and distorted articulation; the other five patients had fluent progressive aphasia, characterized by effortless grammatical or paragrammatic speech with normal phrase length and normal articulation but limited content (Cases 4–6, 11, and 12).³ Cases 11 and 12 also could be classified as semantic dementia patients according to the consensus criteria that Neary and colleagues²⁹ reported. These two patients showed evidence of word comprehension deficit on clinical examination, as well as on the Akense Afasia Test comprehension subtest,²⁷ and were impaired on the Psycholinguistic Assessment of Language Processing in Aphasia word association task, which probes explicit associative-semantic judgments.²⁸ Their performance on the pseudo-object task of the Birmingham Object Recognition Battery³⁰ suggested a mild degree of associative visual agnosia, which is compatible with a diagnosis of semantic dementia.^{29,31}

Three control groups underwent the same neuropsychological and neurolinguistic protocol:

(1) the first group included 7 Dutch-speaking patients with early-stage PRAD,⁴ 3 men and 4 women, between 63 and 78 years of age (mean, 73.2; SE, 1.9), with a Clinical Dementia Rating score³² of 1 and a Mini-Mental State Examination of 22.7 (SE, 1.1), and with disease duration varying between 1 and 4 years; (2) the second group included 5 Dutch-speaking patients with MCI,²² 3 men and 2 women, between 55 and 75 years of age (mean, 65.0; SE, 3.8), with a Clinical Dementia Rating of 0.5 and a Mini-Mental State Examination score of 27.0 (SE, 0.4); and (3) the third group included 15 (10 English-speaking and 5 Dutch-speaking) cognitively intact control subjects, 6 men and 9 women, 56 to 91 years of age (mean, 69.4; SE, 2.2), with 9 to 20 years of education (mean, 15.4; SE, 0.9).

This study was approved by the Institutional Review Board at Northwestern University and the Ethics Committee of the University Hospital Gasthuisberg. Informed consent was obtained from all participants before the study.

Stimuli and Tasks

Subjects were tested in their native language. Stimuli were presented using SuperLab software (Cedrus, Phoenix, AZ). Colored pictures and written names of 60 different items, 30 animals and 30 manipulable objects, were used. Animals and objects were further subdivided into 3 semantic subcategories consisting of 10 items each: animal subcategories were domestic animals, wild and large animals, and tiny animals (insects and small amphibians); object subcategories were large tools (chisel, shovel, hammer, and so on), household items (telephone, typewriter, ruler, and so on), and utensils (spoon, corkscrew, funnel, and so on). Word frequency ranged between 1 and 117 (mean, 19; SE, 3.37) in the English version³³ and between 1 and 168 (mean, 20.7; SE, 4.2) in the Dutch version.³⁴

Before the main experimental task (primed picture naming), we tested confrontation naming and word comprehension for our stimuli. In the *confrontation naming task*, subjects were instructed to name the pictures. No primes were used. The *word comprehension task* consisted of a visual word–picture matching task. A printed word was presented together with four pictures: the target, a picture from the same subcategory, a picture from a different subcategory within the same supraordinate category, and a picture from the other supraordinate category. Subjects were instructed to indicate which picture matched the word.

For the main experimental task, the primed picture naming task, subjects were instructed to watch the screen during word presentation and to name the picture. In each trial, a written word was presented for 250 milliseconds in white capitals on a black background. This was followed by a 500-millisecond delay (total stimulus onset asynchrony [SOA], 750 milliseconds) and subsequent presentation of a colored picture. The picture remained on the screen until the subject provided a name or until 20 seconds had elapsed. The next trial started 5 seconds after the offset of the target picture. The written word preceding the picture could be the correct name of the picture (identity prime), a noun belonging to the same semantic subcategory (semantically related prime), a noun belonging to a different semantic category (semantically unrelated prime), or a nonword. The semantically related prime came from the same semantic subcategory as the target stimulus, whereas the semantically unrelated prime was an animal for a manipulable object and vice versa. Primes of the four different types were selected for each picture from among the appropriate stimulus set. For each of the subjects, the selection of primes was done pseudorandomly with the constraint that for each subject a given word was used once as an identity prime, once as a semantically related prime, and once as a semantically unrelated prime and with the additional constraint that each nonword was used once only.

A total of 240 trials were administered in 3 different blocks of 80 trials each. Each block was defined as a continuous series of 80 trials with a short pause every 20 trials. In each of the 3 blocks, 20 pictures were shown in total: 10 pictures from one animal subcategory and 10 from one inanimate subcategory. Each picture was shown four times, once with each prime type. In the Dutch-speaking subjects, verbal responses were recorded using SoundEdit (Cool Edit 2000, Sintrillium Software Cooperation, Phoenix, AZ), and

voice key latencies were determined digitally. In the English-speaking subjects, the experimenter, who was blinded for the prime, pressed the response bar at the onset of a correct response so that response times could be obtained; naming responses were recorded, stored on tape, and analyzed off-line.

Response times and accuracy were analyzed using a repeated-measures analysis of variance with group as between-subject factor (four levels: PPA, PRAD, MCI, and cognitively intact control subjects) and prime type as within-subject factor (four levels: identity, semantically related, semantically unrelated, and nonword). Only correct responses were used for further analysis. We applied an *F* test to assess main and interaction effects and performed planned comparisons of least squares means to compare the difference between semantically related and unrelated priming trials between groups (PPA vs PRAD, PPA vs MCI, and PPA vs healthy control subjects).

Results

Confrontation Naming and Visual Word–Picture Matching

PPA patients named, on average, 67.8% (SE, 5.0) of the animals and 68.1% (SE, 6.6) of the manipulable objects (Student's *t* test = 0.03 [22df]; *p* = 0.9). Errors during confrontation naming consisted principally of omissions, circumlocutions, and within-category substitutions (Table 1). Word retrieval was affected significantly more than word–picture matching (see Table 1).

Primed Picture Naming

Reaction time data are shown in Table 2 and in the Figure. Statistically, no outliers were detected within the three groups.

The main effect of group was significant ($F(3,35)$, 17.3; $p < 0.00001$): Patients with PPA (mean, 2,787 milliseconds; SE, 129) or with PRAD (mean, 2,151 milliseconds; SE, 170) responded significantly more

slowly than cognitively intact control subjects (1,484 milliseconds; SE, 116). PPA patients also responded significantly more slowly than PRAD and MCI patients. There was no significant difference between healthy control subjects and MCI patients (mean, 1,884; SE, 201) or between MCI patients and PRAD patients.

The main effect of prime type also was significant ($F(3,105)$, 18.7; $p < 0.00001$): Subjects were significantly faster after the identity prime than in any other condition (identity prime: 1,720 milliseconds; SE, 60; semantically related prime: 2,275 milliseconds; SE, 119; semantically unrelated: 2,150 milliseconds; SE, 93; nonword: 2,136 milliseconds; SE, 88).

Critically, the interaction between group and prime type was significant ($F(9,105)$, 7.4; $p < 0.00001$; see Fig. A). According to planned comparisons, the reaction time difference between semantically related and unrelated primes differed significantly between PPA patients and healthy control subjects ($F(1,35)$, 9.7; $p < 0.005$), between PPA and PRAD patients ($F(1,35)$, 7.4; $p < 0.05$), and between PPA and MCI patients ($F(1,35)$, 4.6; $p < 0.05$; see Fig. A): PPA patients were significantly slower after a semantically related prime compared with a semantically unrelated prime ($p < 0.000005$; see Table 2 and Fig. A), in contrast to cognitively intact control subjects, PRAD patients, and MCI patients. During semantically related priming trials, reaction times were significantly longer in PPA patients than in PRAD patients ($p < 0.02$), MCI patients ($p < 0.01$), or cognitively intact control subjects ($p < 0.00001$), whereas reaction times during the semantically unrelated priming trials did not differ significantly between the PPA and PRAD or MCI patients ($p = 0.1$).

Table 1. Confrontation Naming and Word–Picture Matching in Primary Progressive Aphasia Patients

Measure	Case No.												Proportion ^a
	1	2	3	4	5	6	7	8	9	10	11	12	
Confrontation naming ^b													
Omissions	5	12	14	2	2	2	1	1	3	1	19	35	39%
Substitutions													
Within category	9	5	6	6	2	7	10	5	7	4	6	1	28%
Between category	1	2	0	0	0	0	0	0	1	0	3	0	2.8%
Circumlocution	0	19	10	5	1	9	1	1	1	1	4	6	23%
Phonemic paraphasias	0	2	2	1	0	0	0	1	3	1	0	0	4.0%
Neologisms	4	1	0	0	0	0	0	0	0	2	0	0	2.8%
Total correct (%)	68	32	47	77	92	70	80	87	75	85	47	30	
Word–picture matching													
Total correct responses (%)	73	95	85	97	98	95	97	97	98	97	87	88	

Cases 1–6 were English-speaking and Cases 7–12 were Dutch-speaking patients with primary progressive aphasia (PPA). Cases 1–3, 8–10: nonfluent PPA; Cases 4–6, 11, and 12: fluent PPA.

^aProportion of errors of a given type for the total number of errors across all subjects.

^bTotal number of errors of a given type over the 60 trials for each of the subjects.

Table 2. Reaction Times in Milliseconds in the Four Types of Priming Trials (Mean and SD) and the Four Subject Groups

Case No.	Identity	Semantically Related	Semantically Unrelated	Nonword
PPA				
1	2,226 (405)	5,764 (853)	2,446 (289)	3,119 (477)
2	2,285 (326)	4,614 (643)	4,373 (686)	3,787 (498)
3	1,882 (244)	2,047 (327)	3,054 (605)	2,519 (459)
4	1,487 (108)	2,615 (448)	2,167 (202)	2,114 (162)
5	1,457 (135)	1,874 (154)	1,945 (279)	2,242 (481)
6	1,572 (143)	3,756 (531)	2,631 (294)	2,698 (338)
7	2,222 (59)	2,547 (80)	2,500 (78)	2,399 (85)
8	2,092 (160)	3,179 (261)	2,538 (173)	2,840 (230)
9	2,340 (126)	3,357 (240)	3,091 (153)	3,187 (304)
10	1,739 (59)	2,516 (321)	2,032 (110)	2,289 (155)
11	2,477 (197)	4,857 (433)	3,485 (301)	4,139 (457)
12	2,022 (198)	4,170 (701)	3,223 (589)	3,940 (474)
Mean (SE)	1,981 (98)	3,440 (216)	2,790 (149)	2,939 (144)
Clinically probable Alzheimer's disease				
1	1,977 (113)	3,001 (200)	3,129 (427)	2,916 (373)
2	1,746 (351)	1,629 (58)	1,797 (141)	1,677 (102)
3	1,333 (40)	1,784 (125)	1,785 (161)	1,688 (120)
4	2,038 (146)	2,141 (95)	2,480 (270)	2,386 (260)
5	1,755 (102)	2,152 (135)	2,024 (138)	2,469 (325)
6	2,378 (184)	2,675 (220)	2,877 (262)	2,403 (165)
7	1,694 (90)	2,218 (209)	2,282 (437)	1,801 (66)
Mean (SE)	1,845 (128)	2,228 (283)	2,339 (195)	2,191 (189)
Mild cognitive impairment				
Mean (SE)	1,691 (152)	1,942 (335)	1,965 (231)	1,938 (224)
Cognitively intact controls				
Mean (SE)	1,363 (87)	1,489 (193)	1,553 (133)	1,533 (129)

Cases 1–6: English-speaking PPA patients; Cases 7–12: Dutch-speaking PPA patients. Cases 1–3, 8–10: nonfluent PPA; Cases 4–6, 11, 12: fluent PPA.

PPA = primary progressive aphasia; SE = standard error.

We performed three subgroup analyses. First, we performed a repeated-measures analysis of variance with group as between-subject factor (two levels: Dutch- vs English-speaking PPA patients) and prime type as within-subject factor (four levels: identity, semantically related, semantically unrelated, and pseudoword). As panel B of the Figure indicates, Dutch- and English-speaking PPA patients showed the same semantic interference effect ($F(3,30)$, 0.37; $p = 0.7$). This also implies that the findings are independent of the two different ways in which responses were recorded (manual vs digital). Second, we performed a repeated-measures analysis of variance with group (two levels: fluent and nonfluent PPA patients) and prime type. As panel C of the Figure indicates, fluent and nonfluent PPA patients showed the same semantic interference effect ($F(3,30)$, 0.39; $p = 0.7$). Third, we performed a linear regression analysis with disease duration as explanatory variable and priming effect as dependent variable. There was no correlation between disease duration and priming effect ($r = 0.25$; $p = 0.4$).

In PPA patients, the total number of errors was also influenced by the type of prime. PPA patients made significantly more errors after a semantically related (32%; SE, 7) compared with a semantically unrelated

prime (27%; SE, 6.9) (Student's paired t test = 2.6 [11df]; $p < 0.05$). The proportion of errors consisting of a repetition of the prime or of the first syllable of the prime was also significantly larger after a semantically related prime (21.7%; SE, 7.1) compared with a semantically unrelated prime (1.5%; SE, 1.0) (Student's paired t test = 2.77 [5df]; $p < 0.05$). In MCI and PRAD patients, the total number of errors was approximately equal after semantically related (15.2%; SE, 2.8) and unrelated primes (15.9%; SE, 3.4) (Student's paired t test = 0.5 [11df]).

Discussion

In PPA patients, word retrieval was significantly slower and more error prone after a semantically related prime than a semantically unrelated prime (see Table 2 and Fig. A). This paradoxical negative priming effect generalized across different languages (see Fig. B) and PPA subtypes (see Fig. C). It was highly consistent among subjects, despite heterogeneity in disease duration and the wide range of severity of anomia (see Table 2). A different pattern of priming was obtained in PRAD patients, MCI patients, and healthy control subjects who showed faster word retrieval in response to a semantically related prime (see Table 2 and Fig. A). The dif-

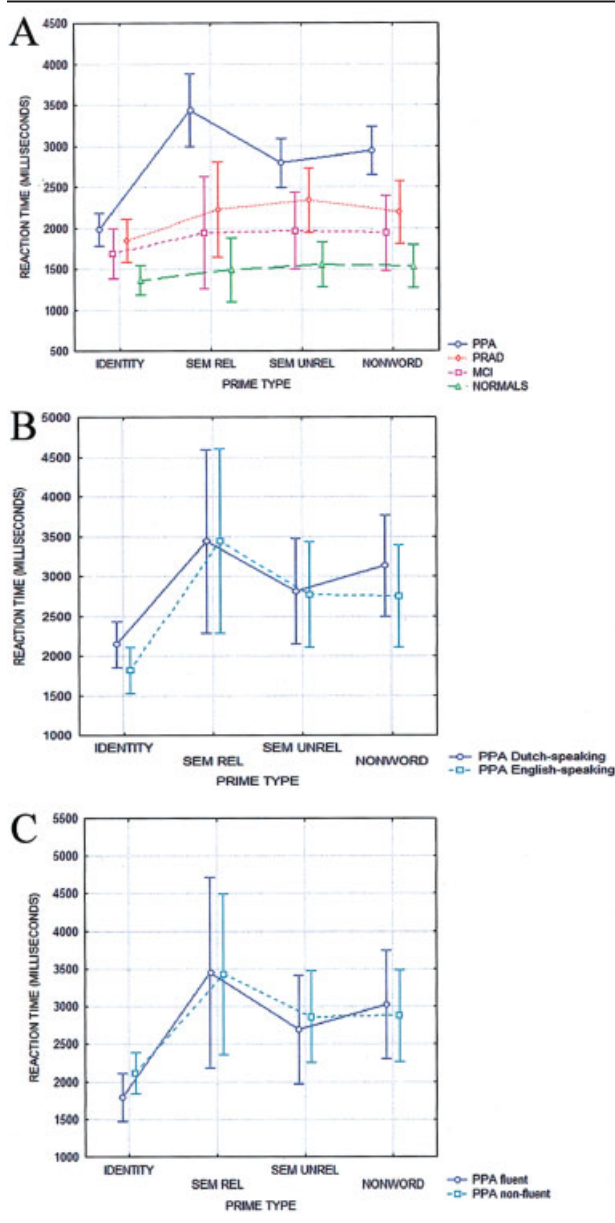


Fig. Primed picture naming. Reaction times (mean and standard error) plotted as a function of prime type. (A) PPA patients were significantly slower after a semantically related prime compared with a semantically unrelated prime. The cognitively intact control subjects and the patients with clinically PRAD and MCI tended to be faster after a semantically related prime compared with a semantically unrelated prime. Blue solid line indicates PPA; red dotted line indicates PRAD; magenta triangles indicate MCI; green diamonds indicate healthy control subjects. (B, C) PPA subgroup analysis. (B) Effect of language. Dark blue solid line indicates Dutch-speaking patients; cyan dashed line indicates English-speaking patients. (C) Effect of fluency. Dark blue solid line indicates fluent PPA; cyan dashed line indicates nonfluent PPA patients. MCI = mild cognitive impairment; PPA = primary progressive aphasia; PRAD = clinically probable Alzheimer's disease; SEM REL = semantically related; SEM UNREL = semantically unrelated.

ference between PPA and PRAD patients indicates that the semantic interference pattern is not a nonspecific consequence of “general cognitive loss.”

The facilitatory priming by semantically related items in healthy control subjects is expected given the long SOA¹⁰ and that we did not explicitly exclude semantically related primes with a high degree of associative linkage to the probe.¹¹ The preservation or augmentation of this semantic priming in early-stage PRAD also replicates previous findings^{17–19} (see Table 2).

Our findings in PPA differ from a semantic priming study of auditory lexical decision in a single case of semantic dementia³⁵ in whom semantic priming did not differ from that found in healthy control subjects. Two of our patients, Cases 11 and 12, fulfilled the criteria for semantic dementia,²⁹ yet showed a strong interference effect. One possible explanation is the SOA difference between the two studies (200–250 milliseconds³⁵ vs 750 milliseconds in this study). Further studies are required to examine the effect of parametric variations of SOA or proportion of different prime types to tease apart reflexive and cognitive components^{36,37} in different PPA subgroups.

Semantic interference has been described previously in neurological patients. In Broca aphasics, “inhibitory semantic priming” was found in a lexical decision task when the list contained a high proportion of semantically related primes.³⁸ An analogous process of “retrieval inhibition” also has been described in a picture naming task in amonic temporal lobe epilepsy patients.³⁹

The pathological interference seen in PPA can be understood in analogy with models for attentional search.^{40,41} The Theory of Visual Attention^{40,41} offers a mathematical account of why subjects spend more effort searching for a target within a stimulus array as the similarity between the target and the distractors increases. It explains patterns of attentional search in terms of discriminability and behavioral pertinence.^{40,41} We postulate that PPA interferes with the discriminability of semantically related word forms during lexical retrieval even at stages when semantic processing is relatively spared. According to this scenario, the prime activates the proper semantic field and paradoxically slows the naming of semantically related probes because the correct choice becomes embedded in a field of semantically related lexical items with similar activity levels. Impaired selection among word forms that are connected to the same semantic field can be caused by degradation of a semantic field,^{31,42} changes in the connections of the semantic field with word form networks,¹⁵ or changes within the word form networks themselves.^{15,43–45} The actual locus of impairment may vary among PPA patients.⁴⁵

In conclusion, naming is impaired in PPA because of alteration of the process of selecting among competing word codes belonging to the same semantic field.¹⁵ This

selection deficit generalizes across language groups, PPA subtypes, and disease stages and constitutes a positive feature distinguishing PPA from PRAD and MCI.

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References

1. Mesulam MM. Slowly progressive aphasia without generalized dementia. *Ann Neurol* 1982;11:592–598.
2. Mesulam MM. Primary progressive aphasia. *Ann Neurol* 2001; 49:425–432.
3. Mesulam MM. Current concepts: primary progressive aphasia: a language-based dementia. *N Engl J Med* 2003;349: 1535–1542.
4. McKhann G, Drachman D, Folstein M, et al. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA work group under the auspices of Department of Health and Human Services Task Force on Alzheimer's disease. *Neurology* 1984;34:939–994.
5. Emery VOB. Language functioning. In: Morris RG, ed. *The cognitive neuropsychology of Alzheimer-type dementia*. Oxford: Oxford University Press, 1996:166–192.
6. Kertesz A, Orange JB. Primary progressive aphasia: the future of neurolinguistic and biologic characterisation. *Brain Lang* 2000;71:116–119.
7. Meyer DE, Schvaneveldt RX. Facilitation in recognizing pairs of words: evidence of a dependence between retrieval operations. *J Exp Psychol* 1971;90:227–234.
8. Glaser W. Picture naming. *Cognition* 1992;42:61–105.
9. Levelt W. Producing spoken language: a blueprint of the speaker. In: Brown C, Hagoort P, eds. *The neurocognition of language*. Oxford: Oxford University Press, 1999:84–122, 1999.
10. Glaser W, Dungenhoff FJ. The time course of picture-word interference. *J Exp Psychol Hum Percept Perform* 1984;10:640–654.
11. Alario FX, Segui J, Ferrand L. Semantic and associative priming in picture naming. *Q J Exp Psychol* 2000;53A:741–764.
12. Collins AM, Loftus EF. A spreading-activation theory of semantic processing. *Psychol Rev* 1975;82:407–428.
13. Dell GS. A spreading-activation theory of retrieval in sentence production. *Psychol Rev* 1986;93:283–321.
14. Roelofs A. A spreading-activation theory of lemma retrieval in speaking. *Cognition* 1992;42:107–142.
15. Caramazza A. How many levels of processing are there in lexical access? *Cognitive Neuropsychology* 1997;14:177–208.
16. Park SM, Gabrieli JDE, Reminger S, et al. Preserved priming across study-test picture transformations in patients with Alzheimer's disease. *Neuropsychology* 1998;12:340–352.
17. Giffard B, Desgranges B, Nore-Mary F, et al. The nature of semantic memory deficits in Alzheimer's disease. New insights from hyperpriming effects. *Brain* 2001;124:1522–1532.
18. Chertkow H, Bub D. Priming and semantic memory loss in Alzheimer's disease. *Brain Lang* 1989;36:420–446.
19. Giffard B, Desgranges B, Nore-Mary F, et al. The dynamic time course of semantic memory impairment in Alzheimer's disease: clues from hyperpriming and hypoprimering effects. *Brain* 2002;125:2044–2057.
20. Auchterlonie S, Phillips NA, Chertkow H. Behavioral and electrical brain measures of semantic priming in patients with Alzheimer's disease: implications for access failure versus deterioration hypothesis. *Brain Cogn* 2002;48:264–267.
21. Salmon DP, Fennema-Notestine C. Implicit memory. In: Morris RG, ed. *The cognitive neuropsychology of Alzheimer-type dementia*. Oxford: Oxford University Press, 1996:105–127.
22. Petersen RC. *Mild cognitive impairment: aging to Alzheimer's disease*. Oxford: Oxford University Press, 2003.
23. Folstein MF, Folstein SE, McHugh PR. Mini-mental state: a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;12:189–198.
24. Kaplan E, Goodglass H, Weintraub S. *The Boston Naming Test*. Philadelphia: Lea and Febiger, 1983.
25. Kertesz A. *Aphasia and associated disorders*. New York: Grune and Stratton, 1979.
26. Marien P, Mampaey E, Vervaeke A, et al. Normative data for the Boston Naming Test in native Dutch-speaking Belgian elderly. *Brain Lang* 1998;65:447–467.
27. Graets P, DeBleser R, Willmes K. *Akense Afasie Test*. Lisse, the Netherlands: Swets and Zeitlinger, 1992.
28. Kay J, Lesser R, Coltheart M. *Psycholinguistic assessment of language processing in aphasia*. Hove, UK: Lawrence Erlbaum Associates, 1992.
29. Neary D, Snowden DS, Gustafson L, et al. Frontotemporal lobar degeneration: a consensus on clinical diagnostic criteria. *Neurology* 1998;51:1546–1554.
30. Riddoch MJ, Humphreys GW. *Birmingham Object Recognition Battery*. Hove, UK: Lawrence Erlbaum Associates, 1993.
31. Warrington E, Shallice T. Category specific semantic impairments. *Brain* 1984;107:829–853.
32. Morris JC, Ernesto C, Schafer K, et al. Clinical dementia rating training and reliability in multicenter studies: the Alzheimer's Disease Cooperative Study experience. *Neurology* 1997;48: 1508–1510.
33. Kucera F, Francis WN. *Computational analysis of present-day American English*. Providence, RI: Brown University Press, 1967.
34. Baayen HR, Piepenbrock R, Van Rijn H. *The CELEX lexical database (CD-ROM)*. Philadelphia: Linguistic Data Consortium, 1993.
35. Tyler LK, Moss HE, Patterson K, Hodges J. The gradual deterioration of syntax and semantics in a patient with progressive aphasia. *Brain Lang* 1997;56:426–476.
36. Neely JH. Semantic priming and retrieval from lexical memory: roles of inhibitionless spreading activation and limited-capacity attention. *J Exp Psychol Gen* 1977;106:226–254.
37. Rossell SL, Price CJ, Nobre AC. The anatomy and time course of semantic priming investigated by fMRI and ERPs. *Neuro-psychologia* 2003;41:550–564.
38. Bushell CM. Dissociated identity and semantic priming in Broca's aphasia: how controlled processing produces inhibitory semantic priming. *Brain Lang* 1996;55:264–288.
39. Blaxton T, Bookheimer S. Retrieval inhibition in anomia. *Brain Lang* 1993;44:221–237.
40. Duncan J, Humphreys GW. Visual search and stimulus similarity. *Psychol Rev* 1989;96:433–458.
41. Bundesen C. A theory of visual attention. *Psychol Rev* 1990; 97:523–547.
42. Hodges JR, Patterson K, Oxbury S, Funnell E. Semantic dementia: progressive fluent aphasia with temporal lobe atrophy. *Brain* 1992;115:1783–1806.
43. Hillis AE, Rapp BC, Caramazza A. When a rose is a rose in speech but a tulip in writing. *Cortex* 1999;35:337–356.
44. Hillis AE, Tuffiash E, Caramazza A. Modality-specific deterioration in naming verbs in nonfluent primary progressive aphasia. *J Cogn Neurosci* 2002;14:1099–1108.
45. Hillis AE, Oh S, Ken L. Deterioration of naming nouns versus verbs in primary progressive aphasia. *Ann Neurol* 2004;55: 268–275.