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Semantic Interference during Object Naming in Agrammatic and Logopenic Primary Progressive Aphasia (PPA)

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Abstract

This study examined the time course of object naming in 21 individuals with primary progressive aphasia (PPA) (8 agrammatic (PPA-G); 13 logopenic (PPA-G)) and healthy age-matched speakers (n=17) using a semantic interference paradigm with related and unrelated interfering stimuli presented at stimulus onset asynchronies (SOAs) of -1000, -500, -100 and 0 ms. Results showed semantic interference (SI) (i.e. significantly slower RTs in related compared to unrelated conditions) for all groups at -500, -100 and 0 ms, indicating timely spreading activation to semantic competitors. However, both PPA groups showed a greater magnitude of SI than normal across SOAs. The PPA-L group and six PPA-G participants also evinced SI at -1000 ms, suggesting an abnormal time course of semantic interference resolution, and concomitant left hemisphere cortical atrophy in brain regions associated with semantic processing. These subtle semantic mapping impairments in non-semantic variants of PPA may contribute to the anomia of these patients.

Keywords

primary progressive aphasia; semantic interference; word interference paradigms; naming deficits in primary progressive aphasia; Free Surfer; cortical thickness

Introduction

Primary progressive aphasia (PPA) is a clinical dementia syndrome caused by neurodegenerative disease, which affects the language network and language functions while preserving attention, memory and other aspects of cognitive processing during the initial stages (Mesulam, 2003). One of the most prominent deficits seen in PPA is anomia manifested by word finding and object naming difficulty (Mesulam, 1982). The most severe anomia is seen in the semantic subtype of PPA (PPA-S), where word comprehension is also severely impaired (Adam, Patterson, Rogers, Nestor, Salmon, Acosta-Cabronero, et al.,

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2006; Gorno-Tempini, Dronkers, Rankin, Ogar, Phengrasamil, Rosen, et al., 2004; Mesulam, Rogalski, Wieneke, Cobia, Rademaker, Thompson, & Weintraub, 2009a; Mesulam, Wieneke, Rogalski, Cobia, Thompson, & Weintraub, 2009b; Neary, Snowden, Gustafson, Passant, Stuss, Black, et al., 1998). However, patients with agrammatic (PPA-G) and logopenic (PPA-L) variants of PPA, who have relatively spared word comprehension, also have naming impairments thought to stem from faulty word retrieval (e.g., phonological and/or articulatory deficits) rather than faulty semantic processes (Mesulam et al., 2009a, Mesulam et al., 2009b).

According to models of spoken word production, to name an object it is necessary to recognize the object, access the meaning or semantic representation of the object, selectively link the two representations, and activate the phonological form of the associated lexical item. These interrelated processes must unfold rapidly and in a manner that protects them from disruptive interference (Levelt 1992; Levelt, Roelofs, & Meyer, 1999; Rapp & Goldbrick, 2000; Roelofs 1992; also see Mesulam et al., 2009b). One method for investigating these aspects of naming is the picture-word interference paradigm, an adaptation of the Stroop task (Stroop 1935), which involves presentation of pictures to name coupled with lexical probes or interfering stimuli (IS, hereafter) presented with variable time relationships to the object. Normally, when the IS is semantically (categorically, but not associatively) related to the target picture, a semantic interference effect occurs. That is, picture naming is slowed compared to when the IS is unrelated to the target item. For example, naming a picture of a *fox* is slower in the presence of the IS *goat* compared to *globe*. This slowing occurs because the lexical-semantic network associated with the IS is automatically activated when it is encountered; in turn, the target picture activates its network, which includes the IS. Thus, competition occurs and the need to deactivate the IS is required (La Heif 1988; Schriefers, Meyer & Levelt, 1990; Starreveld & La Heij, 1995, 1996). Whether the source of the semantic interference effect is associated with semantic and/or lexical competition is unclear. Some suggest that both the IS and target are automatically lexicalized and, hence, available for production. The phonological form of the latter must, therefore, be inhibited in order for the target word to be produced (Bloem & La Heij, 2003; Bloem, van den Bogart, & La Heij, 2004; Finkbeiner & Caramazza, 2006; Janssen, Schrim, Mahon, & Caramazza, 2008; Mahon, Costa, Peterson, Vargas, & Caramazza, 2007). In either case, competition must be resolved before naming of the target item can be accomplished.

A parameter of importance for this task is the temporal relation between presentation of the probe and the picture to be named, that is, stimulus-onset asynchrony (SOA). At some SOAs semantically related IS hinder naming through the process of competitive interference as described above, whereas, at others the probe could conceivably facilitate naming by bringing the correct word closer to a retrieval threshold. Semantic interference effects are the most common and have been shown in healthy speakers when IS are presented at SOAs ranging from -300 ms to $+100$ ms (i.e., up to 300 ms prior to picture presentation or 100 ms following it) (Glaser & Dünghoff, 1984; La Heij, Dirx, & Kramer, 1990; Lupker, 1979; Rayner & Springer, 1986; Starreveld & LaHeij, 1995, 1996; Underwood, 1976).

Semantic interference is a normally occurring phenomenon. However, its magnitude and duration can be influenced by brain damage. In fact, the SI paradigm can be used to test the robustness of information processing routines that underlie object naming. Only a few studies have used the picture-word interference paradigm for this purpose in neurologically impaired patients with naming deficits. In a study by Hashimoto and Thompson (2010), involving 11 individuals with mild aphasia resulting from stroke, aphasic participants showed abnormally heightened semantic interference effects at SOAs of -300 and 0 ms. But at $SOA = +300$, semantic interference effects disappeared as in normal age-matched

speakers. In another study examining semantic interference with one aphasic individual, Wilshire, Keall, Stuart, and O'Donnell (2007) also found abnormal effects, albeit patterns that differed from those seen by Hashimoto and Thompson (2010). That is, the semantic interference effect was absent at SOA = 0 ms, but trends toward semantic interference were found at SOAs of +200 and +400 ms. Interestingly, none of the patients in Hashimoto and Thompson (2010) or in Wilshire et al. (2007) showed strong evidence pointing to semantic deficits in off-line testing.

Abnormal patterns of semantic interference also were seen in a group of individuals with primary progressive aphasia (PPA) studied by Vandenberghe, Vandenberghe, Weintraub, Johnson, Porke, Thompson, and Mesulam (2005). Like the stroke-induced aphasic speakers studied by Hashimoto and Thompson (2010) and Wilshire et al. (2007), abnormal semantic interference effects were found for the PPA speakers even though no word comprehension deficits were noted on behavioral testing. In contrast to unimpaired participants, who showed semantic facilitation (i.e., faster naming for related compared to unrelated words) at -750 ms SOA, the PPA group showed semantic interference in this condition. This pattern suggested that individuals with PPA successfully activate semantic representations in response to IS, however, deactivation is slowed compared to normal, leaving the competitor network active when the target is to be named. Alternatively, this pattern could suggest a delay in the time course of lexical activation, that is, later than normal rise time. In either case, the subsequent iterative process of linking the target object to its name was abnormally vulnerable to the interference of competing representations.

Priming studies provide some insights into how lexical-semantic activation proceeds in aphasic speakers. Individuals with Broca's aphasia resulting from stroke, typically involving anterior brain tissue, have shown reduced levels of activation and/or slow rise time; whereas, those with Wernicke's aphasia, associated with posterior brain lesions, show greater activation than normal as well as delayed deactivation (Blumstein, & Milberg, 2000; Janse, 2006; Prather, Zurif, Love, & Brownell, 1997; Swinney, Zurif, & Nicol, 1989; Yee, Blumstein, & Sedivy, 2008). Both priming and word-interference paradigms operate on the premise that the functional architecture of the lexical processing system involves spreading activation across linguistic units or nodes (Dell, 1986; Masson, 1995), which results in competition among potential candidates. Hence, activation of primes in priming paradigms and that for the IS presented in word-interference paradigms involve similar processes; however, the word-interference paradigm requires an addition step – naming of a related or unrelated competitor – following this activation.

The present experiment was designed to examine the effects of semantic interference on naming in individuals with PPA-G and PPA-Land to examine patterns of cortical atrophy in participants with abnormal semantic interference effects. We enrolled PPA patients and age-matched healthy controls in a word interference paradigm with SOAs of -1000, -500, -100, and 0 ms. Based on similarities between cerebrovascular lesion sites and the location of peak atrophy involving the inferior frontal gyrus, we hypothesized that reduced or delayed activation may be seen for the PPA-G group, akin to the performance of individuals with stroke-induced Broca's aphasia. In the case of reduced activation, semantic interference effects would be either absent or weak across all SOAs, whereas a pattern of delayed activation would result in semantic interference effects only in SOA = -500 and/or -1000 ms conditions. Conversely, we conjectured that PPA-L participants, who often show involvement of posterior brain structures (Gorno-Tempini et al., 2004; Gorno-Tempini, Brambati, Ginex, Ogar, Dronkers, Marcone et al., 2008; Mesulam et al., 2009b), may show patterns of excessive IS-induced activation, or delayed deactivation, similar to those observed in patients with stroke-induced Wernicke's aphasia. In the former case, the magnitude of semantic interference would exceed that of normal control participants across

conditions, whereas in the latter, semantic interference effects would be present in longer SOA conditions, i.e., at -1000 ms. We also entertained the possibility that both patient groups would show normal patterns of semantic interference if the source of their naming deficit stemmed strictly from post-semantic phonological and/or articulatory impairments.

Method

Participants

Participants included 21 individuals with PPA (8 PPA-G and 13 PPA-L) and 17 cognitively intact volunteers. All were recruited through the Cognitive Neurology and Alzheimer's Disease Center (CNADC) at Northwestern University (Chicago, IL) and tested in the Aphasia and Neurolinguistics Research Laboratory at Northwestern (Evanston, IL). The three participant groups were matched for age (PPA-G: \underline{M} = 62 years, \underline{sd} = 6.13; PPA-L: \underline{M} = 64 years, \underline{sd} = 7.29; control group: \underline{M} = 63 years; \underline{sd} = 6.4) ($\chi^2(2, N = 38) = .626; p = .731$, Kruskal-Wallis Test) and education (PPA-G: \underline{M} = 17 years, range = 14–20; PPA-L: \underline{M} = 16 years, range = 12–20; controls: \underline{M} = 16 years, range = 11–20) ($\chi^2(2, N = 38) = .353; p = .838$, Kruskal-Wallis Test). All were monolingual English-speaking, passed a pure-tone audiometric hearing screening, and were right handed, with the exception of two participants with PPA who were left handed (PPA-G1 and PPA-L8). All also presented a negative history of prior neurological or psychiatric deficits. Compensation for participation in the study was provided and informed consent was obtained prior to participation. The Institutional Review Board at Northwestern University approved this study.

The diagnosis of PPA was based on neurological, neuropsychological and neurolinguistic testing, showing an absence of neurological signs other than progressive language deficits. Symptom onsets ranged from 2 – 10 years prior to testing, however, the two PPA groups were matched for symptom duration (PPA-G: \underline{M} = 4 years, range = 2–5; PPA-L: \underline{M} = 4 years, range = 2–10) ($Z = -.876, p = .381$, Mann-Whitney U Test) (see Table 1).

To rule out memory, attention, and executive function deficits the Mini-Mental State Examination (MMSE) (Folstein, Folstein, & McHugh, 1975), Wechsler Memory Scales-III (Faces I and II) (Wechsler, 1997), Facial Recognition Test (Benton, Hamsher, Varney, & Spreen, 1998), Trail Making Test (Partington & Leiter, 1949), and a 10-item version of the Visual Verbal Test (Feldman & Drasgow, 1959; also see Wickland, Johnson, & Weintraub, 2004) were administered (see Table 2 for participant scores). Both PPA groups generally performed within normal limits on these measures, with no significant differences found between them and the control groups based on the Kruskal-Wallis Test, with the exception of the MMSE ($\chi^2(2, N = 38) = 18.160; p = .05$). On this test, both PPA groups performed more poorly than the controls, likely due to the patients' compromised language ability (Golper, Rau, Erskine, Langhans, & Houlihan, 1987; Osher, Wicklund, Rademaker, Johnson, & Weintraub, 2008). A motor speech examination also was administered; only four participants (PPA-G6, PPA-G8; PPA-L7, PPA-L11) presented with mild impairments, which did not affect speech intelligibility or ability to perform the experimental task.

To detail the language impairment of the PPA participants, a battery of neurolinguistic tests was administered. See Tables 3 and 4 for a summary of results. Aphasia Quotients (AQs) derived from administration of the Western Aphasia Battery (WAB, Kertesz, 2006) ranged from 73.9 to 85 (\underline{M} = 79.5) for the PPA-G participants, which was significantly lower than those for the PPA-L participants, ranging from 78.6 to 97.1 (\underline{M} = 90.2) ($Z = -3.259, p < .01$, Mann-Whitney U Test). WAB fluency scores also differed between groups: fluency scores for the PPA-G group ranged from 4 to 6 (\underline{M} = 5.1) and for the PPA-L group from 5 to 10 (\underline{M} = 8.2) ($Z = -3.232, p < .01$, Mann-Whitney U Test).

Confrontation naming was evaluated using the Boston Naming Test (BNT, Kaplan, Goodglass, & Weintraub, 2001) and the Northwestern Naming Battery, a test of category-specific naming and word processing (NNB, Thompson & Weintraub, experimental version). On both tests, all participants showed naming difficulty. Scores ranged from 45% to 98.3% ($M = 81.9\%$) for the PPA-G group and from 35 to 98.3% ($M = 83.2\%$) for the PPA-L group on the BNT ($Z = -.511, p = .609$, Mann-Whitney U Test) and from 85 to 100% ($M = 93.9\%$) for the PPA-G group and 73.3 to 100% ($M = 91.8\%$) for the PPA-L group on the noun naming subtest of the NNB ($Z = -.474, p = .636$, Mann-Whitney U Test). Noun to verb ratios also were calculated based on a subset of items from the NNB noun and verb naming subtests, with results showing significantly greater ratios for the PPA-G compared to the PPA-L participants, indicating greater difficulty naming verbs compared to nouns.

Both PPA groups showed relatively preserved single word comprehension tested using a 36-item subset of the Peabody Picture Vocabulary Test (PPVT, Dunn & Dunn, 2007) (i.e., moderately difficult items, #157–192). Scores ranged from 89.9 to 100% ($M = 95.1\%$) for the PPA-G group and from 83.3 to 100% ($M = 96\%$) for the PPA-L group ($Z = -.695, p = .487$, Mann-Whitney U Test). To evaluate semantic knowledge the Pyramids and Palm Trees Test (PPT; Howard & Patterson, 1992) was administered, (both word and picture versions). On the word version, scores ranged from 88.5 to 100% correct ($M = 94\%$) and 92.3 to 100% correct ($M = 97\%$) for the PPA-G and PPA-L groups, respectively ($Z = -1.292, p = .196$, Mann-Whitney U Test); scores on the picture version ranged from 94.2 to 100% correct ($M = 96.6\%$) and from 78.8 to 100% correct ($M = 95.7$) for the two groups, respectively ($Z = -.223, p = .824$, Mann-Whitney U Test). Performance on the picture version was within normal limits for both patient groups ($\chi^2(2, N = 38) = .828; p = .661$, Kruskal-Wallis Test), however, the PPA-G group performed significantly more poorly than the control group on the word version ($Z = -2.380, p < .05$, Mann-Whitney U Test).

Sentence comprehension and production were tested using the Northwestern Assessment of Verbs and Sentences (NAVS, Thompson, experimental version). The Sentence Comprehension Test (SCT) and the Sentence Production Priming Test (SPPT) of the NAVS examined comprehension and production, respectively, of both canonical and noncanonical sentence structures. Both production and comprehension of noncanonical sentences were more difficult for the PPA-G participants (SCT: $M = 74.2\%$; SPPT: $M = 41.1\%$) compared to PPA-L group (SCT: $M = 89.2\%$; SPPT: $M = 88.2\%$) (SCT: $Z = -2.055, p < .05$; SPPT: $Z = -2.456, p < .05$, Mann-Whitney U Test). The Northwestern Anagram Test (NAT) (Thompson, Mesulam & Weintraub, 2009, <http://www.soc.northwestern.edu/NorthwesternAnagramTest/>; also see Weintraub, Mesulam, Wieneke, Rademaker, Rogalski, & Thompson, 2009) also was administered to evaluate sentence production. Like the NAVS SPPT, the NAT examines production of both canonical and noncanonical sentences; however, rather than spoken responses, participants are required to create sentences that match pictures by ordering randomly presented word cards. Results showed patterns similar to those derived from the SPPT; the PPA-G, compared to the PPA-L, group performed significantly worse on noncanonical sentences ($M = 32.2\%$ vs. 81.7%) ($Z = -3.071, p < .01$, Mann-Whitney U Test), but there was no significant group difference in performance on canonical sentences ($Z = -1.314, p = .189$, Mann-Whitney U Test).

Finally, aspects of spontaneous speech were evaluated by collecting and analyzing narrative language samples derived by asking participants to tell the story of Cinderella from a wordless picture book (after Thompson, Ballard, Tait, Weintraub, & Mesulam, 1997; Thompson, Shapiro, Tait, Jacobs, Schneider, & Ballard, 1995). The narrative data showed that, although the PPA-G and PPA-L groups produced fewer words per minute than controls

participants, words per minute was lower in the PPA-G group ($M = 56.8$ vs. 94.8) ($Z = -2.317$, $p < .05$, Mann-Whitney U Test), who also produced fewer grammatically correct sentences ($M = 40.9\%$ vs. 80%) ($Z = -3.187$, $p < .01$, Mann-Whitney U Test).

Stimuli

Stimuli included forty black and white line drawings of either living ($n = 20$) or non-living items ($n = 20$). The living items were selected from the categories of birds/mammals or fruits/vegetables (10 each) and the nonliving items were either tools or clothing (10 each). An additional 10 filler items (also black and white line drawings), selected from a variety of other categories such as food items (e.g., pizza) and physical phenomenon (e.g., volcano) also were included for a total of 50 items. For each item, IS consisting of written words (all nouns) were selected, four of which were semantically related to the target (or filler) item and four that were not. For each of the four SOAs, one semantically related and one semantically unrelated IS was randomly selected and paired with each stimulus picture, for a total of 160 related target pairs, 160 unrelated target pairs, and 80 filler pairs (40 related and 40 unrelated). For example, for the target item *penguin*, *robin*, *goose*, *walrus*, and *seal* were selected as semantically related IS and *handle*, *weather*, *comic*, and *receipt* were selected as unrelated IS. Ten healthy volunteers (age 25 – 46) rated all word pairs for semantic, categorical rather than associative, relatedness (1 = not related; 7 = highly related). Only semantically related pairs with a mean ranking of 5.5 and above and unrelated pairs with a ranking of 2.5 or lower were used in the experiment. None of the IS overlapped phonologically with the target items. All items (both targets and IS) ranged from 1 – 3 syllables in length and were checked for frequency using the CELEX and MRC databases. Target (but not filler) items were matched for frequency by category (i.e., living and non-living things) (target picture: $t(38) = .899$, $p = .375$) and with IS across categories; ($t(318) = .062$, $p = .950$). However, overall, the mean frequency of the semantically related IS ($M = 0.6285$) was significantly lower than that of unrelated IS ($M = 1.1311$) across SOAs. See Appendix A for a complete list of stimuli.

The 400 stimulus pairs were pseudo randomly divided into 10 sets of 40 items each. Care was taken to ensure that each target item did not occur more than once per set. In addition, items from the same SOA condition were separated by at least three trials on each set. The picture and word stimulus pairs were entered into Super lab (version 4.0; Cedrus, Phoenix, AZ) in three versions, which varied the inter stimulus interval (ISI): 3500 ms, 5000 ms or 7000 ms ISI, to accommodate general naming delays evinced by some PPA participants. For all healthy participants the 3500 ms version was used; the version used for the PPA participants depended on naming latency observed during administration of the BNT: eight participants (five PPA-G and 3 PPA-L) were tested with the 5000 ms version and 4 PPA-L participants were tested with the 7000 ms version; for all others the 3500 ms version was used.

Procedures

Participants were tested on a Macintosh (20 inch, iMac 5, 1) HD Version 10.4.10. They were seated at a distance of approximately 2 feet from the computer screen on which the IS and target pictures were presented. Each trial began with presentation of a cross fixation (500 ms.), followed by an IS and target picture in the four SOA conditions (see Figure 1). Participants were asked to name each picture as quickly as possible and ignore the IS to the extent possible. The acoustic waveform of each response produced was recorded through a computer microphone using Praat 5.0 software (Boersma & Weenink 2010). Prior to

¹Filler items were higher in frequency than the experimental targets, however, all items (both experimental and filler) were matched for number of syllables and picturability.

beginning the experiment, participants were provided with pre-training to familiarize them with all picture stimuli (both target and filler items) and to ascertain their ability to name them. We also tested all written IS to determine reading ability. Each picture was presented for naming with no response contingent feedback provided. Items that could not be named correctly within a 5 second response time were presented a second time. All participants included in the study were able to name at least 80% of the pictures on either the first or second trial. The written IS were then presented one at a time for participants to read aloud; all showed good reading ability with performance ranging from 92% to 100%. Erred items were presented a second time, with feedback provided. Finally, practice trials were presented, which required participants to name target pictures overlaid with written words. These trials used stimuli similar, but not identical, to the experimental items.

Data Analysis

Naming responses that matched the target picture were considered correct. This included responses phonologically related to the target (e.g., *pinkquin* for *penguin*) as well as false starts and self-corrections, occurring within the allotted response time. All other responses were considered incorrect. Correct responses then were analyzed for reaction time (RT), measured from picture onset (marked with an inaudible beep) to production of the first phoneme of the target word marked in the acoustic waveform. Thirty percent of the data were rescored for both accuracy and RT by an independent coder for scoring reliability purposes; overall point-to-point agreement between the primary and secondary coders was 97%. Any disagreements were resolved by consensus. Mean accuracy and RTs derived from each SOA condition were computed for related and unrelated trials for each participant group.

Cortical Thickness Measurement: Data Acquisition and Analysis

Magnetic resonance (MR) imaging, performed at the Northwestern University Department of Radiology Center for Advanced MRI (CAMRI), was undertaken for both the PPA and control participants. T1-weighted images, using 3D MP-RAGE sequences (TR = 2300 ms, TE = 2.86 ms, flip angle = 9°, FoV = 256 mm) recording 160 slices at a thickness of 1.0 mm were acquired on a 3T Siemens TRIO system using a 12-channel birdcage head coil. MR images were processed using the image analysis suite Free Surfer (version 4.5.0), which is documented and freely available for download online (<http://surfer.nmr.mgh.harvard.edu/>). Cortical thickness estimates were calculated by measuring the distance between representations of the white-gray and pial-CSF boundaries across each point of the cortical surface (see Fischl, Sereno, Tootell, & Dale, 1999, for details). Statistical surface maps then were generated using a general linear model (GLM) that displayed differences in cortical thickness between PPA and control groups for each vertex along surface representations.

Results

Naming accuracy

Table 5 provides the mean percentage correct naming for the control, PPA-G, and PPA-L groups by condition. Overall, groups showed good ability to name. The mean of semantically related and unrelated trials was 97.6% and 97.9% correct, respectively, for the controls; 94.4% and 95.5% correct, respectively for the PPA-G group; and 89.5% and 91% correct, respectively, for the PPA-L group. A 3 (group) × 4 (SOA) × 2 (relatedness) ANOVA indicated a significant main effect of group ($F(2, 35) = 6.694, p < .01$), but not SOA ($F(3, 105) = .299, p = .826$). Pairwise comparisons for individual groups revealed that the PPA-L group performed statistically more poorly than the control group ($p < .01$), but not the PPA-G group ($p = .27$). A main effect of relatedness approached significance ($F(1,$

35) = 3.838, $p = .058$), with semantically related trials being more difficult, that is less accurate, than unrelated trials. There were no significant interaction effects.

Reaction time analyses

Only correct responses were analyzed for RT, which required removal of 2.2% (118/5440), 4.84% (124/2560), and 9.43% (377/40002) of the data from the control, PPA-G, and PPA-L groups, respectively. Furthermore, outliers (RTs greater than two standard deviations above the group mean) were replaced with the group mean. Less than 2% of the data for the patient groups and none for the controls were outliers.

Table 6 provides the mean RTs for related and unrelated trials at each SOA for each participant group. Because we were unable to completely control for frequency of occurrence of the related and unrelated IS, i.e., the semantically related IS were significantly lower in frequency than the unrelated stimuli, we first examined the relation between IS word frequency and RT using the Pearson test (2-tailed), with results showing no significant correlation between them for either the control or PPA groups (controls: $r = .064$, $p = .418$; PPA: $r = .107$, $p = .180$). Analysis of homogeneity of variance of the RT data also showed no significant differences ($p > .05$). The RT data were, therefore, first analyzed using a 3 (group) \times 4 (SOA) \times 2 (Relatedness) \times 2 (living versus non-living things) repeated measures ANOVA, which revealed main effects of group ($F(2, 35) = 33.611$, $p < .000$), SOA ($F(3, 105) = 79.035$, $p < .000$), relatedness ($F(1, 35) = 41.796$, $p < .000$), and living versus non-living things ($F(1, 35) = 17.410$, $p < .000$). Follow-up pairwise comparisons indicated that naming RTs were significantly longer for both PPA groups compared to the control group (p 's $< .001$) and RTs for living things were significantly longer than for non-living things for the control participants ($p < .001$), but not for either PPA group. In addition, there were interactions between relatedness and group ($F(2, 35) = 6.163$, $p < .01$) and between SOA and relatedness ($F(3, 105) = 14.981$, $p < .001$). In order to determine how relatedness affected groups and SOAs, a 3 (group) \times 4 (SOA) ANOVA was conducted with differences between related and unrelated naming RTs as the dependent variable. Results showed a main effect of SOA ($F(3, 105) = 14.981$, $p < .001$), with SI effects in the SOA = 0 ms condition being greater than those seen at the all other SOAs (p 's $< .01$). In addition, there was a main effect of group ($F(2, 35) = 6.163$, $p < .01$), with both PPA-G and PPA-L groups demonstrating significantly greater naming RTs for related compared to unrelated trials, that is, overall greater SI effects, than the normal controls (p 's $< .01$). Figure 2 displays the percentage of RT latency differences between groups, calculated using the following formula: $[(\text{unrelated} - \text{related}) / \text{unrelated}] \times 100$ ³, showing that at all SOAs the magnitude of SI effects was greater for both PPA groups compared to the healthy control participants.

In order to determine whether or not the overall magnitude of SI was related to performance on neuropsychological or language tests administered prior to the study, we undertook correlational analysis, using Pearson tests. Results showed no significant correlations between the magnitude of SI (calculated by computing the mean magnitude of SI across all SOAs for each participant) and performance on any of these tests. These data are presented in Table 7.

Additional analyses were undertaken to examine SI effects within each participant group using a 4 (SOA) \times 2 (Relatedness) ANOVA. For the control group, significant main effects of SOA ($F(3, 48) = 44.480$, $p < .001$) and Relatedness ($F(1, 16) = 8.986$, $p < .01$) and an interaction between SOA and Relatedness ($F(3, 48) = 7.418$, $p < .001$) were found. Post-hoc

²For one logopenic subjects, one script (160 responses) could not be analyzed due to computer error.

³After Wilshire et al. (2007).

analyses using a paired t-test (one-tail) revealed SI effects, that is, significantly slower naming RTs for semantically related compared to unrelated trials, at SOAs of 0 ($p < .01$), -100 ($p < .01$), and -500 ms ($p < .01$), but not at SOA -1000 ms. Inspection of the individual data derived from the SOA = -1000 ms condition showed that none of the control participants demonstrated slower mean RTs in the related compared to the unrelated condition, with 10 (of 17) showing the opposite pattern: faster RTs in the semantically related compared to the unrelated condition, which was significant for three participants ($p < .01$). No significant RT differences between related and unrelated conditions were found for the remaining control participants ($p > .05$). For the PPA-G group, there also were main effects of SOA ($F(3, 21) = 10.400, p < .001$) and Relatedness ($F(1, 7) = 5.678, p < .05$) as well as an interaction between SOA and Relatedness ($F(3, 21) = 6.510, p < .01$). Post-hoc analyses indicated significant SI at SOAs of 0 ($p < .01$), -100 ($p < .05$) and -500 ms ($p < .05$) but not at SOA -1000 ms ($p = .089$). Notably, however, six of the eight PPA-G participants (all but PPA-G1 and PPA-G5) showed semantic interference effects at -1000 ms (i.e., greater mean RTs in the related compared to the unrelated condition, ranging from 11.78 ms (PPA-G3; RT related = 1340.96 ms; unrelated = 1329.18 ms) to 282.08 ms (PPA-G2; RT related = 1553.59 ms; unrelated = 1271.51 ms) (PPA-G group mean RT difference = 55.94 ms). These RT differences were significant for all participants ($p < .05$), with the exception of PPA-G3, which approached significance ($p = .0654$).

For the PPA-L group, main effects of SOA ($F(3, 36) = 39.628, p < .001$) and Relatedness ($F(1, 12) = 49.613, p < .001$) and a significant interaction between SOA and Relatedness ($F(3, 36) = 3.997, p < .05$) also were found, with post-hoc analyses indicting SI effects for the PPA-L group at all SOAs: SOA 0 ($p < .001$), -100 ($p < .05$), -500 ($p < .001$), and -1000 ms ($p < .01$). Importantly, a SI effect at -1000 ms was found for 10 of the 13 PPA-L participants (all except for PPA-L2, PPA-L6, and PPA-L10). That is, mean RTs for related trials were longer than for unrelated trials for these participants, ranging from 8.01 ms (PPA-L3; related = 1084.52 ms; unrelated = 1076.51 ms) to 144.69 ms (PPA-L4; related = 1177.28 ms; unrelated = 1032.59 ms) (PPA-L group mean RT difference = 60.9 ms). For all participants RTs for related trials were significantly slower than unrelated trials ($p < .05$). SI affects at each SOA (calculated by subtracting RTs for unrelated trials from related trials) for participant group are shown in Figure 3.

Once again, we examined for correlations between SI and the PPA participants' performance (both PPA-G and PPA-L) on our pre-test neuropsychological and language measures. Results revealed no significant correlations between these variables (see Table 7). We also queried whether symptom duration or age were correlated with SI effects at SOA = -1000 ms and found no significant correlations for either (symptom duration: $r = .173, p = .453$; age: $r = .051, p = .828$). In addition, in order to determine that the abnormal SI effects seen at -1000 ms were not driven by disease severity we compared WAB AQ scores for those who did ($n = 16$) and did not ($n = 5$) show this effect. Results indicated no significant differences between groups ($M = 85.13$ and 86.72 for participants with normal and abnormal semantic interference, respectively; $p = .840$ (Mann-Whitney U Test)).

Cortical Thinning

Because participants from both the PPA-G and PPA-L groups evinced abnormal SI effects at -1000 ms, we examined atrophy patterns for patients who showed abnormal effects ($n = 13$; five PPA-G and eight PPA-L participants⁴). Two participants were left-handed (PPA-G1, PPA-L8) and therefore were not included in this analysis and an MR scan was not obtained for two of the participants with abnormal effects (PPA-G4, PPA-L5). Notably, because of

⁴Participants PPA-G2, 3, 6, 7, and 8; PPA-L1, 3, 4, 7, 9, 11, 12, and 13.

the low number of PPA participants with no semantic interference at -1000 ms and the fact that MR scans were obtained for only three of them (one PPA-G and two PPA-L participants⁵) we did not perform cortical thickness analysis for this small group. Figure 4 shows the regional distribution of cortical thinning (atrophy) for the participants showing abnormal SI compared to controls (FDR, $p = 0.01$). Results showed asymmetric cortical thinning, with atrophy constrained to the left hemisphere, most severely in the perisylvian region, with extensive atrophy in the lateral temporal cortex. Notably, significant cortical thinning also was found in the left inferior frontal gyrus, parahippocampal gyrus and in the posterior fusiform gyrus.

Discussion

In this experiment we examined the effects of semantic interference on object naming by presenting semantically related and unrelated interfering stimuli or word probes at SOAs of -1000 , -500 , -100 , and 0 ms. For the control group, statistically significant semantic interference effects were found at SOAs of 0 , -100 , and -500 ms, but not at -1000 ms. Previous studies also have found such effects in normal speakers at SOAs up to -300 ms (Glaser & Dünghoff, 1984; Hashimoto & Thompson, 2010; Starreveld & LaHeij, 1996). However, studies have reported no semantic interference at earlier SOAs (see, for example, Glaser and Dünghoff (1984) who found no semantic interference at $SOA = -400$ ms). We suggest that the semantic interference effect found in the present study at $SOA = -500$ ms likely relates to the age of our control participants (mean age = 63 years; $SD = 6$ years) compared to those in most studies of semantic interference effects, which have included younger participants (age range approximately 18 to 30 years). Indeed, Taylor and Burke (2002) found greater SI effects for older participants (age 62–85), similar in age to our control cohort, compared to younger speakers (age 18–29 years). Semantic priming studies also show greater priming effects for older compared to younger speakers, likely due to their extensively developed lexical-semantic networks (Laver & Burke, 1993).

Another possibility is that we found semantic interference at -500 ms for the healthy control participants because of frequency differences between our related and unrelated interfering stimuli. That is, the semantically related probes were significantly lower in frequency than our unrelated pairs, which may have inflated semantic interference effects. Indeed, Miozzo and Caramazza (2003) found longer RT latencies associated with lower distractor word frequency in word-interference paradigms. However, they found no interaction between frequency and semantic relatedness. Importantly, we also found no correlation between the frequency of our interfering stimuli and reaction time for either the control or PPA participants.

In keeping with previous studies we did not find interference effects in the $SOA -1000$ ms condition for the control participants. In fact, in this condition, naming was faster when distractors were semantically related (967.9 ms) compared to when they were unrelated (978.9 ms), albeit not significantly so for the group. Vandenberghe et al. (2005) and La Heij et al. (1990) found similar semantic facilitation effects in neurologically intact participants at SOAs of -750 and -800 ms, respectively. These data, considered collectively, suggest that activations triggered by a semantically related interfering stimulus normally cease to exert a competitive influence on object naming within approximately 750 seconds of presentation, at which time the residual activation trace appears to facilitate naming.

Turning to the results from our PPA participants, both PPA groups evinced significant semantic interference effects at -500 , -100 , and 0 ms, consistent with control participants,

⁵Participants PPA-G5, PPA-L 6, and PPA-L10.

indicating that exposure to a semantically related interfering stimulus induced spreading activation to related items that competitively interfered with subsequent naming of an object in that category. However, both PPA groups showed heightened activation, that is, a larger magnitude of semantic interference compared to age-matched controls at all SOAs. These greater semantic interference effects are similar to those found by Hashimoto and Thompson (2010). In addition, abnormal semantic interference in the -1000 ms SOA condition was noted for both logopenic and agrammatic PPA participants. For the logopenic group, the speed of object naming was slowed by a mean of 60.9 ms by a semantically related (compared to unrelated) word presented 1000 ms prior to object presentation. Interestingly, most of the agrammatic participants (six of eight) also showed this pattern, although the group effect was not significant ($p = .089$), with a mean RT difference between the two trial types of 55.9 ms. This finding supports those reported by Vandenberghe et al. (2005) who found semantic interference effects for PPA patients at -750 ms.

These abnormal semantic interference effects suggest excessive activation of semantic networks in aphasic individuals compared to normal speakers as well as greater vulnerability to distractor interference than normal. Interestingly, vulnerability to distractor interference has been shown to be particularly pronounced in individuals with the semantic variant of PPA, where a blurring of semantic distinctions among members of semantic categories becomes a major factor contributing to anomia, leading to characteristic semantic paraphasias and coordinate errors in word-object matching tasks (Mesulam et al., 2009a). Although the performance of individuals with the semantic variant of PPA was not examined in the present study, because their characteristically poor naming ability precluded participation, there is considerable overlap of symptoms among PPA variants. Therefore, it is possible that the abnormal semantic interference effects found in both agrammatic and logopenic participants stem from semantic mapping deficits characterized by difficulty in rapidly dissociating the interfering stimulus from the target when the two are semantically related and hence more likely to be blurred or confused. As discussed in the introduction, we point out once again that the source of such semantic mapping deficits may derive from impairments at the semantic or lexical, phonological level of word processing (or both). On Levelt's model of lexicalization (e.g., Levelt 1992; Levelt et al., 1999), for example, when an interfering stimulus is encountered, spreading activation to semantically related items occurs automatically and, in turn, lexical detail associated with both the IS and its semantic network are accessed. Hence, inhibition of semantic competitors is required at the semantic as well as the phonological level. Where in this path processing goes awry in individuals with PPA is, however, unclear.

Interestingly, the naming impaired participants in the present study performed well on tests of single word comprehension and semantic knowledge, as did the PPA individuals studied by Vandenberghe et al (2005), on the face of it suggesting that that the source of these individuals' naming deficits related more to word-retrieval difficulty, rather than to semantic deficits. The abnormal semantic interference effects found here, however, suggest otherwise – that naming deficits in PPA derive at least in part from impairments associated with subtle semantic processing deficits, which may not be detectable using off-line testing methods. In fact, in the present study, we found no significant correlations between any of our pre-test language measures and either the overall magnitude of semantic interference across SOAs or abnormal semantic interference at -1000 ms. Other work in our laboratories also has shown subtle abnormalities of semantic processing in PPA subtypes (e.g., PPA-G and PPA-L) that are not associated with overt abnormalities of word comprehension or object identification (Rogalski, Rademaker, Mesulam, & Weintraub, 2008).

Notably, the abnormal semantic interference effects found in the present study could not be attributed to general cognitive deficits, such as memory or executive function, in that pre-

testing of these functions showed that the PPA participants performed well across all measures. In addition, no significant correlations were found between performance on any of the neuropsychological tests administered and the magnitude of semantic interference across SOAs or abnormal semantic interference at -1000 ms. Notably, we also found no significant correlations between chronological age or PPA symptom duration and abnormal semantic interference. These findings indicate that the semantic mapping deficits found in our PPA participants cannot be explained by any general cognitive compromise or decline.

The patterns of cortical atrophy found for the PPA-G and PPA-L participants who showed abnormal semantic interference effects at -1000 ms also are in line with the semantic processing deficits noted. This group of individuals showed extensive atrophy in the left lateral temporal cortex, including the superior, middle, and inferior temporal gyri as well as the temporo-parietal junction. Notably, previous studies with non-semantic variants of PPA also have found atrophy in these regions. For example, Wilson, Henry, Besbris, Ogar, Dronker, Jarrold et al. (2010) and Gunawardena, Ash, McMillan, Avants, Gee, & Grossman (2010) reported temporal atrophy in their cohort of logopenic and agrammatic PPA participants, respectively. In the present study we also found atrophy in the parahippocampal gyrus on the ventral surface of the brain as well as in the ventral temporal occipital region (i.e., posterior fusiform gyrus) and in portions of the inferior frontal gyrus, also in the left hemisphere. Each of these regions has been implicated in semantic processing and could provide substrates for the SI effects we observed. In addition to research associating the lateral temporal cortex with semantic processing deficits (Gorno-Tempini et al., 2004; Hodges, Patterson, Oxbury, & Funnell, 1992; Mesulam, et al., 2009a; Mesulam et al., 2009b; Mummery, Patterson, Wise, Vandenberghe, Price & Hodges, 1999; Rosen, Kramer, Gorno-Tempini, Schuff, Weiner, & Miller, 2002), several studies indicate that the ventral occipitotemporal region, including the fusiform gyrus, is involved in processing of visual word forms (Devlin, Jamison, Gonnerman, & Matthews, 2006; Hillis, Newhart, Heidler, Barker, Herskovits, & Degaonkar, 2005; Kronbichler, Bergmann, Hutzler, Staffen, Mair, Ladurner et al., 2007; Simmons, Koutstaal, Prince, Wagner, & Schachter, 2003) as well as visual objects (Haxby, Gobbini, Furey, Ishai, Schouten, & Pietrini, 2001). Price and Devlin (2011) suggest that this region is engaged in both bottom-up and top-down processing, integrating visuospatial features abstracted from sensory input with higher-level associations, including meaning representations. The IFG also is engaged for semantic processing, with numbers of neuroimaging studies using a variety of tasks, including making semantic decisions about words and generating words based on semantic relationships, reporting significant activation in this region (Costafreda, Fu, Lee, Everitt, Brammer & David, 2006; Demb, Desmond, Wagner, Vaidya, Glover, & Gabrieli, 1995; Fiez, 1997; Gabrieli, Desmond, Demb, Wagner, Stone, Vaidya et al., 1996; Kapur, Craik, Tulving, Wilson, Houle, & Brown, 1994; Klein, Milner, Zatorre, Meyer, & Evans, 1995; Peterson, Fox, Posner, Mintun, & Raichle, 1988; Poldrack, Wagner, Prull, Desmond, Glover, & Gabrieli, 1999; Wagner, Paré-Blagoev, Clark, & Poldrack, 1998). Thompson-Schill, D'Esposito, Aguirre, and Farah (1977) also found greater IFG activation associated with the selection demands of neuroimaging tasks, suggesting a role of this region is selection of competing alternatives from semantic memory. In addition, the left IFG has been implicated in response inhibition (Swick, Ashley, & Turken, 2006). These latter roles fit well with the present findings in that the abnormal SI effects may result at least in part from an inability to select from (and deactivate or inhibit) activated semantically interfering related items.

Regardless of the precise role of these regions in semantic processes associated with either normal or disordered naming, the present findings indicate that agrammatic and logopenic PPA participants show similar automatic lexical-semantic processing routines. Hence our prediction that their performances would mirror those of stroke-induced anterior and posterior aphasias was not completely supported. Priming studies show that Broca's aphasia,

which in clinico anatomical terminology is associated with a prototypical anterior aphasia with necrosed tissue in the inferior frontal region, leads to an under activation of lexical competitors and/or delayed activation; whereas, Wernicke's aphasia, the prototypical posterior aphasia, with posterior perisylvian brain damage, leads to over activation as well as delayed deactivation of lexical competitors (Blumstein, & Milberg, 2000; Janse, 2006; Prather et al., 1997; Swinney, et al., 1989; Yee et al., 2008)⁶. However, neither the agrammatic or logopenic PPA individuals in the present study showed evidence of under activation. Rather both groups showed spreading activation to semantically related items, with semantic interference effects noted at all SOAs, with the exception of -1000 ms for some participants. They also did not show performance patterns suggestive of delayed activation of semantic networks in that both PPA groups showed semantic interference effects in the SOA = 0 ms and -100 ms conditions. However, the magnitude of semantic interference was abnormal for both PPA groups across all SOAs, an effect associated with over activation of semantic competitors, expected for patients with posterior but not anterior lesions. In addition, both groups showed evidence of delayed deactivation, as seen in Wernicke's aphasia, in that semantic interference effects persisted to the SOA = -1000 ms condition, indicating a failure to completely inhibit the lexical-semantic network associated with interfering stimuli in a timely manner, leaving them active during attempts to name target pictures.

The lack of clear-cut distinctions in lexical-semantic processing routines for the two PPA groups may reflect the nature of the clinical pathology associated with PPA compared to vascular aphasia. In aphasias caused by cerebrovascular lesions, portions of the brain are completely and permanently destroyed. In contrast, neurodegenerative disease that causes PPA leads to a gradual and partial loss of neurons at sites of atrophy. Hence, the remaining neurons, even at sites of maximal atrophy, continue to participate in relevant language tasks (Sonty, Mesulam, Weintraub, Johnson, Parrish, & Gitelman, 2007). The deficits in these patients, therefore, may reflect contributions from the residual functioning of atrophied tissue, resulting in blurred distinctions between PPA subtypes at least in early stages of language decline.

Further research using, for example, an eye-tracking paradigm similar to that used by Yee et al. (2008), may help to clarify the nature of lexical-semantic processing deficits in PPA and perhaps elucidate differences between PPA subtypes. The time course of activation and resolution of semantic competitors can be tracked by monitoring participant's eye movements, elucidating either over or under activation of semantic competitors as well as any delays in activation or abnormal resolution of semantic competition. A failure to resolve lexical competition would show a pattern of timely, but abnormally long-lasting, fixations on competitor items, whereas, a deficient activation pattern would show delayed fixations on competitor items. Regardless of which is correct, however, the abnormal semantic interference effects found for patients with PPA (both agrammatic and logopenic variants) suggest that naming difficulty in these patients does not result only from phonological encoding problems. Rather, faulty semantic processing is implicated as well.

Conclusion

Both agrammatic and logopenic PPA and healthy age-match participants show slowed object naming speeds when exposed to semantically related interfering stimuli 500 or 100 ms prior to or simultaneously with presentation of an object to be named. However, this semantic interference effect was greater in magnitude and also lasted longer, detectable even

⁶Studies showing differential priming effects for individuals with stroke-induced Broca's and Wernicke's aphasia provide only gross descriptions of patient lesions, therefore, they only estimate the neural correlates of these lexical-semantic processes.

in the -1000 ms SOA condition. These results show that individuals with non-semantic forms of PPA are able to activate appropriate semantic fields in response to experimental lexical probes but that they are excessively vulnerable to interference by semantic competitors during the subsequent iterative process that links an object to its name. Even PPA patients with intact word comprehension may thus have a perturbation of semantic processing that compromises naming ability.

- A semantic interference paradigm examined the time course of naming in PPA.
- Semantic interference at SOA = 0, -100 , and -500 ms was seen in PPAs and controls.
- Only PPA participants evinced abnormal SI at -1000 ms.
- A greater magnitude of SI was found for PPAs compared to controls across all SOAs.
- Atrophy in left perisylvian cortex was found for PPAs with abnormal SI effects.

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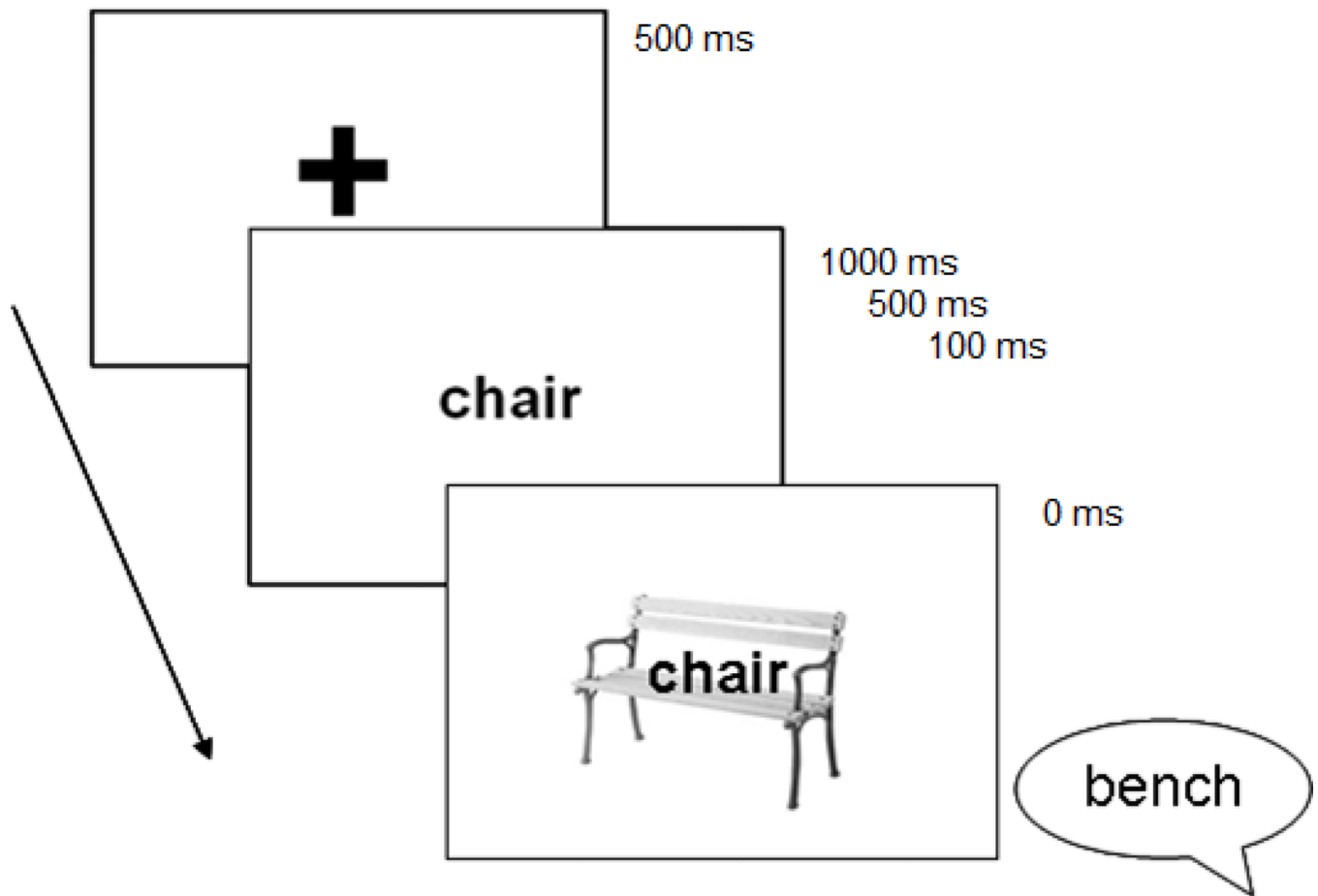
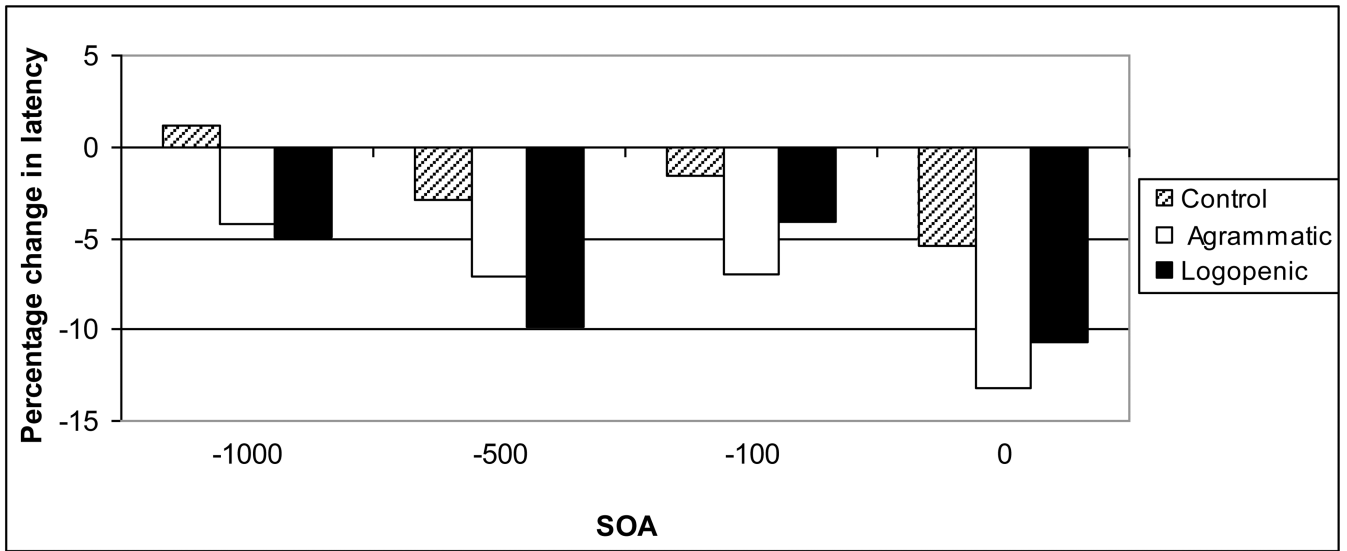
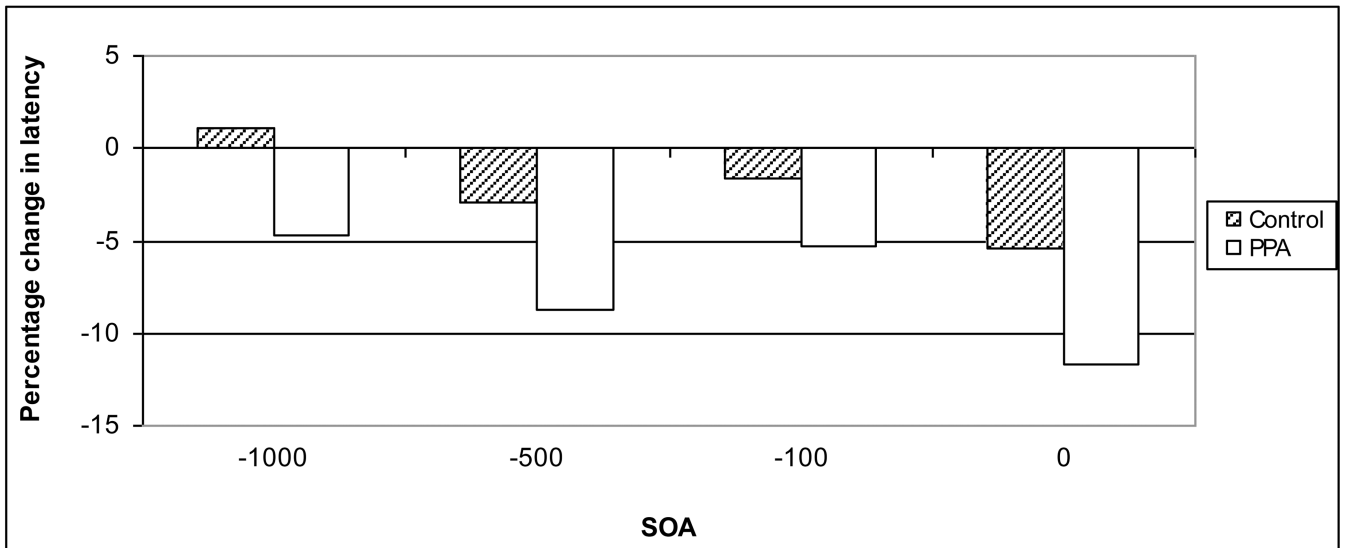


Figure 1. Cartoon of stimulus trials. On each trial a 500 ms. cross fixation preceded presentation of an interfering stimulus (IS) and target picture to be named in each SOAs condition.

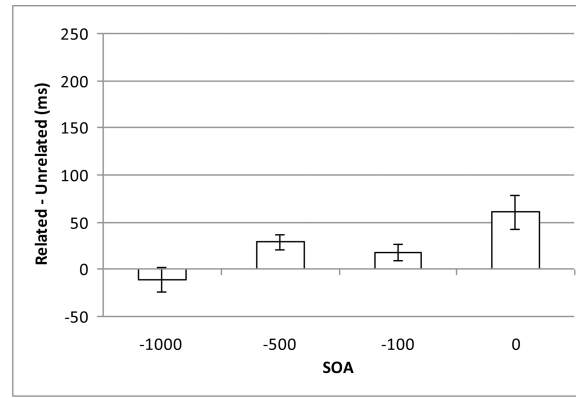


2a

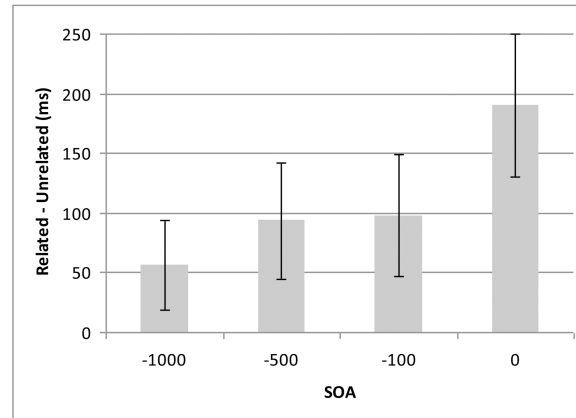


2b

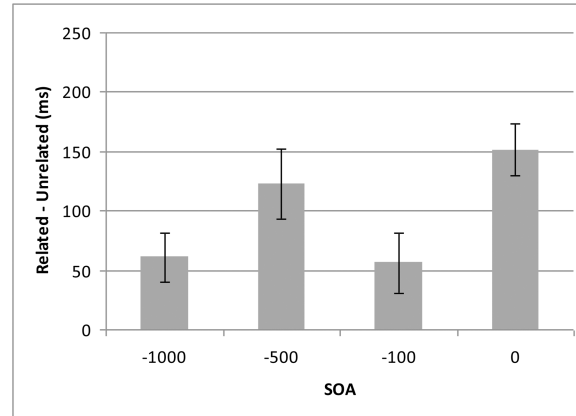
Figure 2.
 (a) Magnitude of semantic interference effect (RT latency differences between related and unrelated trials) at each SOA for control, agrammatic (PPA-G), and logopenic (PPA-L) participant groups; (b) Magnitude of semantic interference effect for control and PPA groups (PPA-G and PPA-L) combined.



3a



3b



3c

Figure 3. Semantic interference effects (mean RT for related-unrelated trials) for the (a) control group, (b) agrammatic (PPA-G) group, and (c) logopenic (PPA-L) group.

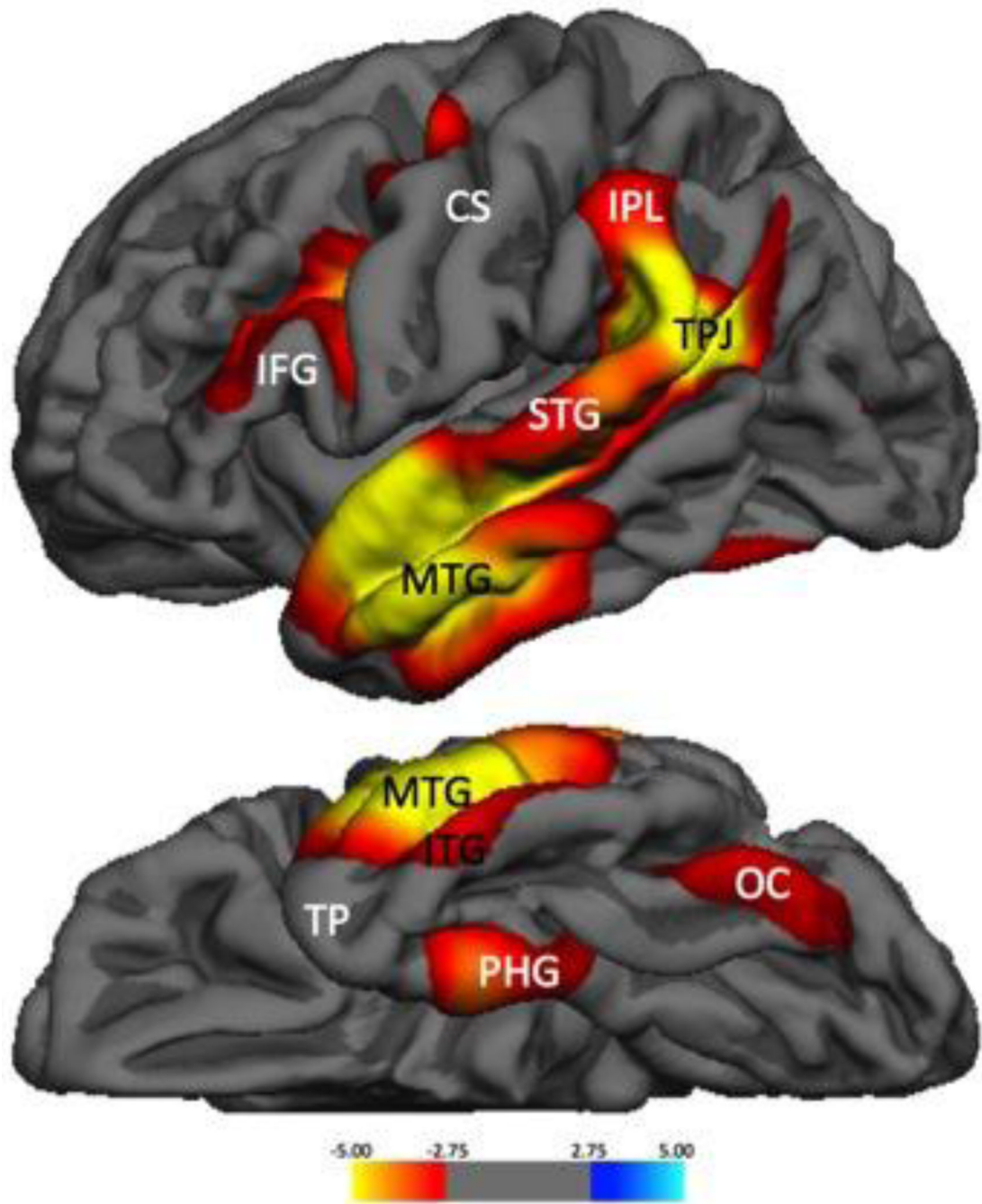


Figure 4.

Distribution of cortical thinning of the lateral (top) and ventral (bottom) left hemisphere pial surface for PPA individuals showing abnormal semantic interference effects in the SOA -1000 ms. condition. Yellow indicates regions of greatest thinning – compared to a normal cohort. Significance is displayed as a $\log_{10} p$ -value. IFG: inferior frontal gyrus, CS: central sulcus; IPL: inferior parietal lobule; TPJ: temporoparietal junction; STG: superior temporal gyrus, MTG: middle temporal gyrus, ITG: inferior temporal gyrus; TP: temporal pole; PHG: parahippocampal gyrus; OC: occipital cortex (posterior fusiform gyrus).

Table 1

Summary of PPA participant demographic data.

Participant	Age	Gender	Education	Handedness	Symptom Duration (years)
PPA-G 1	60	M	15	L	4.5
PPA-G 2	62	M	20	R	5
PPA-G 3	59	M	12	R	3.1
PPA-G 4	52	F	18	R	1.5
PPA-G 5	61	F	18	R	5
PPA-G 6	72	M	20	R	5
PPA-G 7	62	F	16	R	3
PPA-G 8	69	F	14	R	3.5
PPA-L 1	69	M	15	R	2.5
PPA-L 2	66	M	19	R	9.5
PPA-L 3	63	M	18	R	2.5
PPA-L 4	64	F	16	R	2.8
PPA-L 5	59	M	14	R	7
PPA-L 6	58	M	16	R	2
PPA-L 7	65	F	13	R	5
PPA-L 8	66	M	12	L	2.5
PPA-L 9	75	F	16	R	2.5
PPA-L 10	60	M	18	R	2
PPA-L 11	48	M	16	R	6
PPA-L 12	62	M	20	R	3
PPA-L 13	76	F	16	R	2
Mean (SD)					
PPA-G	62 (6)		17 (3)		3.8 (1.3)
PPA-L	64 (7)		16 (2)		3.8 (2.4)
Control	63 (6)		16 (3)		N/A

Note: A = Agrammatic; L = Logopenic

Table 2

Summary of neuropsychological test scores for agrammatic (PPA-G 1 – PPA-G 8) and logopenic (PPA-L 1 – PPA-L 13) participants across measures.

Participant	MMSE (30)	WMS-III Immediate (48)	Delayed (48)	Visual Perception Facial Recognition (54)	Processing Speed Trail Test A	Visual Verbal Shift (10)	Visual Verbal Sort (20)
PPA-G 1	28	N/A	N/A	48	41	10	20
PPA-G 2	28	39	39	48	44	10	20
PPA-G 3	20	28	31	51	108	8	18
PPA-G 4	30	37	39	45	25	8	18
PPA-G 5	30	31	38	42	64	6	16
PPA-G 6	28	35	41	52	34	10	20
PPA-G 7	26	34	36	53	28	6	16
PPA-G 8	28	41	36	52	55	7	17
PPA-L 1	30	N/A	N/A	45	37	9	18
PPA-L 2	24	N/A	N/A	N/A	48	N/A	N/A
PPA-L 3	27	N/A	N/A	48	29	8	18
PPA-L 4	26	N/A	N/A	46	28	8	18
PPA-L 5	24	31	48	39	87	8	18
PPA-L 6	23	42	44	44	49	9	19
PPA-L 7	19	26	29	41	N/A	N/A	N/A
PPA-L 8	29	38	39	47	36	9	19
PPA-L 9	28	30	37	49	17	N/A	N/A
PPA-L 10	28	37	40	50	35	9	19
PPA-L 11	29	39	39	50	33	7	17
PPA-L 12	29	38	37	48	31	10	20
PPA-L 13	24	33	37	47	25	10	20
Mean (SD)							
PPA-G	27.3 (3.2)	35.0 (4.5)	37.1 (3.2)	48.9 (3.9)	49.9 (26.9)	8.4 (1.7)	18.4 (1.7)
PPA-L	26.2 (3.2)	34.9 (5.2)	38.9 (5.2)	46.2 (3.4)	37.9 (17.8)	8.7 (0.9)	18.6 (1.0)
Control	29.7* (0.6)	37.25 (3.8)	39.1 (3.0)	46.9 (3.9)	30.4 (8.9)	9.0 (0.8)	18.9 (1.0)

Table 3
Summary of language test scores for agrammatic (PPA-G 1 – PPAG 8) and logopenic (PPA-L 1 – PPA-L 13) participants.

Participant	Western Aphasia Battery										PPVT	PPT
	AQ (100)	F (10)	Comp (10)	Rep (10)	Nam (10)	BNT (%)	Noun (%)	N:N	N:N	N:N		
PPA-G 1	80.4	6	9.6	7.2	8.4	98.3	100.0	1.1	97.2	N/A	100.0	
PPA-G 2	82.3	4	9.1	8	10	98.3	93.3	1.5	100.0	100.0	100.0	
PPA-G 3	79.9	4	8.85	7.8	9.3	81.7	95.0	1.1	94.4	90.4	94.2	
PPA-G 4	78.8	5	8.5	7.6	9.3	76.7	93.3	1.4	97.2	98.1	98.1	
PPA-G 5	75.3	4	8.25	8.8	8.6	88.3	98.3	1.0	100.0	88.5	96.2	
PPA-G 6	80.6	6	9	5.9	9.4	73.3	85.0	1.5	88.9	98.1	96.2	
PPA-G 7	73.9	6	7.85	5	9.1	45.0	86.0	1.2	94.4	94.2	94.2	
PPA-G 8	85	6	10	8.6	8.9	93.3	100.0	1.1	88.9	88.5	94.2	
PPA-L 1	92	9	9.2	9	9.8	98.3	96.7	0.9	97.2	98.1	98.1	
PPA-L 2	85.6	8	10	6.6	9.2	93.3	90.0	1.0	NA	NA	100.0	
PPA-L 3	97.1	10	9.85	8.9	9.5	96.7	100.0	1.0	100.0	100.0	96.2	
PPA-L 4	93	9	9.2	9	9.3	90.0	83.3	1.1	N/A	N/A	96.2	
PPA-L 5	90.5	9	9.85	7.4	9	86.7	96.7	1.0	97.2	98.1	100.0	
PPA-L 6	86.9	6	9.45	9	10	90.0	95.0	1.1	97.2	100.0	100.0	
PPA-L 7	78.6	6	7.4	8.8	8.1	83.3	83.3	1.2	83.3	94.2	78.8	
PPA-L 8	90.4	9	9.8	9	7.4	35.0	73.3	0.9	97.2	92.3	92.3	
PPA-L 9	97.2	10	10	9	9.4	88.3	98.3	1.1	97.2	94.2	94.2	
PPA-L 10	93.2	9	9.7	8.9	9	98.3	100.0	1.1	100.0	96.2	96.2	
PPA-L 11	83.2	5	9.8	9	8.8	98.3	91.7	1.1	100.0	96.2	96.2	
PPA-L 12	95.8	9	9.8	10	9.1	40.0	86.7	0.9	88.9	98.1	98.1	
PPA-L 13	88.8	8	9.6	7.2	9.6	83.3	98.3	1.0	97.2	100.0	98.1	
Mean (SD)												
PPA-G	79.5** (3.6)	5.1**** (1.0)	8.9* (0.7)	7.4* (1.3)	9.1 (0.5)	81.9 (17.6)	93.9 (5.8)	1.2* (0.2)	95.1 (4.4)	94.0 (4.9)	96.6 (2.5)	
PPA-L	90.2 (5.5)	8.2 (1.6)	9.5 (0.7)	8.6 (0.9)	9.1 (0.7)	83.2 (21.0)	91.8 (8.1)	1.0 (0.1)	96.0 (5.2)	97.0 (2.6)	95.7 (5.6)	
Control	99.8 (0.6)	10.0 (0.0)	10.0 (0.1)	10.0 (0.1)	9.6 (1.6)	98.2 (2.2)	99.5 (1.1)	1.0 (0.0)	99.0 (1.7)	98.9 (1.8)	98.1 (1.4)	

Note: AQ = Aphasia Quotient; F = Fluency; Comp = Auditory Comprehension; Rep = Repetition; Nam = Naming; BNT = Boston Naming Test; NNB = Northwestern Naming Battery; Noun = noun naming subtest; N:V = Noun:Verb ratio; PPVT = Peabody Picture Vocabulary Test; PPT = Pyramids and Palm Tree Test.

* $p < .05$,

** $p < .01$,

*** $p < .001$ (reflect significant differences between PPA-G and PPA-L groups).

Table 4

Summary of additional language test scores.

Participant	NAVS					NAT			Narrative Measures		
	SCT-C	SCT-NC	SPPT-C	SPPT-NC	C	NC	WPM	MLU	Prop. Gram. Sentences		
PPA-G 1	100.0	86.7	100.0	93.3	N/A	N/A	63.1	6.5	46.7		
PPA-G 2	66.7	60.0	66.7	6.7	80.0	33.3	25.2	4.0	10.0		
PPA-G 3	93.3	66.7	N/A	N/A	N/A	N/A	55.4	5.0	60.0		
PPA-G 4	60.0	66.7	80.0	26.7	100.0	33.3	110.3	7.6	57.5		
PPA-G 5	73.3	73.3	100.0	13.3	100.0	33.3	36.0	5.4	58.3		
PPA-G 6	86.7	53.3	80.0	20.0	100.0	33.3	77.1	11.3	21.8		
PPA-G 7	93.3	86.7	N/A	N/A	33.3	0.0	47.6	7.1	10.7		
PPA-G 8	100.0	100.0	100.0	86.7	66.7	60.0	40.0	6.8	62.5		
PPA-L 1	93.3	86.7	100.0	100.0	86.7	66.7	104.5	9.5	92.0		
PPA-L 2	100.0	100.0	100.0	80.0	N/A	N/A	100.8	7.9	72.0		
PPA-L 3	100.0	100.0	100.0	100.0	N/A	N/A	141.1	7.9	88.2		
PPA-L 4	100.0	93.3	100.0	93.3	N/A	N/A	98.1	7.8	94.7		
PPA-L 5	100.0	80.0	66.7	53.3	100.0	53.3	86.0	6.3	85.7		
PPA-L 6	100.0	73.3	100.0	86.7	100.0	73.3	118.7	10.5	78.1		
PPA-L 7	86.7	66.7	86.7	100.0	86.7	46.7	19.1	5.4	84.6		
PPA-L 8	100.0	100.0	100.0	100.0	100.0	100.0	83.0	7.6	54.6		
PPA-L 9	100.0	100.0	100.0	86.7	100.0	93.3	157.7	13.9	70.4		
PPA-L 10	80.0	60.0	86.7	66.7	86.7	80.0	58.9	8.6	88.9		
PPA-L 11	100.0	100.0	100.0	80.0	100.0	100.0	64.3	9.2	57.1		
PPA-L 12	100.0	100.0	100.0	100.0	100.0	100.0	105.8	10.1	92.3		
PPA-L 13	100.0	100.0	100.0	100.0	100.0	93.3	94.1	10.7	81.3		
Mean (SD)											
PPA-G	84.2* (15.5)	74.2* (15.7)	87.8 (14.2)	41.1* (38.5)	80.0 (26.7)	32.2* (19.1)	56.8* (27.0)	6.7* (2.2)	40.9*** (22.9)		
PPA-L	96.9 (6.4)	89.2 (14.5)	95.4 (10.0)	88.2 (14.9)	96.0 (6.4)	80.7 (20.0)	94.8 (35.5)	89.2 (14.5)	80.0 (13.1)		
Control	100.0 (0.0)	100.0 (0.0)	100.0 (0.0)	100.0 (0.0)	100.0 (0.0)	100.0 (0.0)	131.8 (19.6)	11.1 (2.1)	93.8 (43.7)		

Note: NAVS = Northwestern Assessment of Verbs and Sentences; SCT-C = Sentence Comprehension Test, Canonical sentences; SCT-NC = Sentence Comprehension Test, Noncanonical sentences; SPPT-C = Sentence Production Priming Test, Canonical sentences; SPPT-NC = Sentence Production Priming Test, Noncanonical sentences; NAT = Northwestern Anagram Test; C = Canonical sentences; NC = Noncanonical sentences; WPM = Words per Minute; MLU = Mean Length of Utterance.

* $p < .05$,

** $p < .01$ (reflect significant differences between PPA-G and PPA-L groups).

Table 5

Mean percentage correct naming (and standard deviation) for control, agrammatic PPA (PPA-G), and logopenic PPA (PPA-L) groups at each SOA.

Group	Stimulus Onset Asynchrony			Total Accuracy	
	-1000 ms	-500 ms	-100 ms		0 ms
Control					
Related	97.4 (3.8)	98.0 (2.6)	97.7 (2.7)	97.3 (2.6)	97.6 (2.4)
Unrelated	97.7 (3.2)	98.1 (2.6)	98.2 (2.8)	97.7 (3.2)	97.9 (2.6)
PPA-G					
Related	92.8 (5.6)	95.0 (4.6)	94.1 (8.1)	95.6 (3.7)	94.4 (4.8)
Unrelated	95.3 (4.1)	95.9 (5.2)	96.3 (2.7)	94.7 (3.6)	95.5 (2.9)
PPA-L					
Related	90.8 (10.0)	89.0 (11.6)	88.7 (10.3)	89.5 (10.3)	89.5 (10.3)
Unrelated	92.0 (7.0)	90.6 (8.4)	92.0 (7.0)	89.5 (9.1)	91.0 (7.4)

Table 6

Mean reaction time for semantically related and unrelated trials for control, agrammatic PPA (PPA-G) and logopenic PPA (PPA-L) groups at each SOA.

	Stimulus Onset Asynchrony											
	-1000 ms			-500 ms			-100 ms			0 ms		
	RT	SD	RT	SD	RT	SD	RT	SD	RT	SD	RT	SD
Control												
Related	967.9	90.2	1024.1**	77.7	1072.7**	118.6	1183.4**	106.1				
Unrelated	978.9	98.8	995.2	76.3	1055.3	121.7	1123.1	137.4				
Difference	-11.0		28.9		17.4		60.3					
PPA-G												
Related	1368.3	199.9	1404.5*	207.9	1488.1*	215.5	1628.1**	181.0				
Unrelated	1312.4	199.3	1310.8	151.9	1390.3	122.0	1437.8	186.1				
Difference	55.9		93.7		97.8		190.3					
PPA-L												
Related	1298.8**	173.7	1364.2***	144.3	1416.8*	172.9	1562.2***	184.4				
Unrelated	1237.9	150.2	1242.0	102.1	1360.5	149.7	1410.7	143.7				
Difference	60.9		122.2		56.3		151.5					

Note: Mean reaction times (RT) in milliseconds (ms), and standard deviation (SD) by stimulus onset asynchrony (SOA).

* $p < .05$.

** $p < .01$.

*** $p < .001$.

Table 7

Correlations between (a) the overall magnitude of semantic interference, and (b) semantic interference at the SOA = -1000 ms and performance on pre-test neuropsychological and language measures.

	Magnitude of SI		SI at -1000 ms	
	r	P	r	P
Neuropsychological				
MMSE	-.037	.874	.080	.730
WMS-III				
Immediate	-.174	.519	-.035	.897
WMS-III Delayed	-.193	.474	.175	.516
Facial Recognition	.095	.690	-.042	.861
Trail Test A	-.052	.828	-.099	.679
Visual Verbal				
Shifts	-.161	.523	.226	.367
Visual Verbal				
Points	-.183	.468	.214	.394
Language				
WAB-AQ	.009	.969	.104	.652
WAB-F	.177	.443	.046	.844
WAB-AC	-.108	.643	.000	.999
WAB-R	.027	.907	-.090	.697
WAB-N	-.247	.281	.163	.479
BNT	-.193	.401	-.055	.814
NNB-Noun	.085	.715	-.286	.208
NNB-N:V	-.372	.096	.371	.098
PPVT	-.191	.434	-.007	.977
PPT-Word	-.252	.312	.373	.127
PPT-Picture	-.206	.370	.030	.898

Note: Pearson correlation (2-tailed)

Appendix A

Target and corresponding interfering stimuli (IS), with mean frequencies and standard deviations (SDs)

	Target-Living		Related IS		Unrelated IS							
	SOA -1000	SOA -500	SOA -100	SOA 0	SOA -1000	SOA -500	SOA -100	SOA 0	SOA -100	SOA -500	SOA -100	SOA 0
1	apple	kiwi	melon	mango	cherry	Battle	echo	jargon	parcel			
2	bear	elk	goat	moose	Ape	Stamp	lawn	clock	gust			
3	butterfly	centipede	locust	termite	mosquito	Museum	computer	recipe	invention			
4	carrot	spinach	lettuce	parsley	cauliflower	Sulfur	dinner	goggles	title			
5	corn	barley	pea	squash	wheat	Poem	ring	wax	guard			
6	cow	llama	yak	mule	Ram	Drain	rug	tent	spear			
7	dog	mink	weasel	hare	coyote	Grease	cave	pond	sphere			
8	eagle	turkey	condor	swan	quail	Villain	label	disco	token			
9	garlic	parsnip	lentil	dill	pepper	Partner	desert	terror	locker			
10	giraffe	cheetah	gazelle	buffalo	antelope	Novel	mantle	cabin	lotion			
11	monkey	kangaroo	gorilla	panda	Sloth	Halo	rifle	leather	thunder			
12	olive	plum	pickle	turnip	Bean	Easel	target	finish	comment			
13	onion	basil	ginger	cabbage	pepper	Gutter	fiddle	cartoon	record			
14	owl	stork	hawk	duck	wren	Gum	moon	pad	pass			
15	pear	yam	guava	beet	Lime	Loft	jar	wire	nest			
16	penguin	robin	goose	walrus	Seal	Handle	weather	comic	receipt			
17	pig	boar	mole	fox	Hog	Tape	yacht	text	key			
18	squirrel	weasel	gecko	hamster	gopher	Symbol	beauty	trophy	textile			
19	whale	trout	otter	squid	dolphin	Lodge	globe	skate	sweat			
20	worm	snake	eel	mite	cricket	Net	gem	coal	pole			
Frequency M (SD)	1.11 (0.40)	0.47 (0.48)	0.6 (0.4)	0.54 (0.42)	0.74 (0.51)	1.13 (0.44)	1.24 (0.48)	1.13 (0.43)	1.17 (0.45)			
Target-Nonliving												
1	blender	mixer	chopper	beater	juicer	Journey	sheriff	diaper	acorn			
2	broom	rake	shovel	plough	vacuum	Knoll	swell	neck	slang			
3	dresser	trunk	cabinet	hamper	closet	Flower	nomad	shadow	bunny			
4	fork	cleaver	cutlery	dagger	skewer	Thief	knee	toast	root			
5	glove	jacket	vest	parka	hood	Swamp	loot	lard	mud			

	Target-Living	Related IS					Unrelated IS				
		SOA -1000	SOA -500	SOA -100	SOA 0	SOA -1000	SOA -500	SOA -100	SOA 0	SOA -100	SOA 0
6	knife	sword	bayonet	lancet	scalpel	Swarm	log	sky	soup		
7	pliers	tongs	sander	mallet	funnel	Cripple	recess	tennis	hygiene		
8	saw	chisel	axe	hatchet	File	Ham	nod	jog	clam		
9	scissors	marker	razor	eraser	sharpener	Pardon	habit	juror	theater		
10	screw	nut	bolt	pin	Tack	Tag	grudge	thumb	nerve		
11	shirt	jersey	fleece	mitten	Hat	Gulf	lock	host	pain		
12	shoe	sneaker	heel	nylons	slipper	Glue	bay	oat	cake		
13	shorts	jeans	boxers	trousers	slacks	Fang	coin	rice	bug		
14	skirt	dress	kilt	sarong	Toga	Frost	bull	yeast	grave		
15	spoon	cup	pot	spatula	baster	Park	junk	fist	guest		
16	stapler	clip	binder	folder	Latch	Neighbor	kitten	hostage	nanny		
17	stove	griddle	dryer	furnace	heater	Guide	nose	frog	dad		
18	stroller	crib	wagon	carriage	buggy	Kidney	jungle	moustache	cafe		
19	taxi	jeep	carriage	train	caravan	Pilot	suspect	statue	jockey		
20	truck	bus	sedan	wagon	shuttle	Smile	notch	slum	wrist		
	Frequency M (SD)	0.95 (0.65)	0.57 (0.59)	0.62 (0.49)	0.85 (0.66)	1.01 (0.51)	1.12 (0.51)	1.17 (0.55)	1.08 (0.55)		
Filler											
1	bread	cereal	barley	oat	Rice	Ink	lung	mom	hut		
2	cheese	yogurt	cream	butter	Milk	Vat	jam	pearl	foam		
3	cookie	pie	pudding	candy	Cake	Menu	physics	fairy	ivy		
4	guitar	saxophone	flute	bell	clarinet	Maple	pavement	nectar	tyrant		
5	house	barn	shed	mall	garage	Waste	mask	tray	zoo		
6	letter	postman	mailbox	postcard	package	Snore	boss	cart	youth		
7	pizza	spaghetti	burrito	lasagna	Taco	Meadow	virus	nostril	whisker		
8	ring	anklet	necklace	gold	bracelet	Mat	cone	law	wave		
9	volcano	mountain	plateau	cliff	bluff	Offender	pioneer	lavender	ritual		
10	wreath	corsage	stick	fabric	bouquet	Jump	claw	breath	gun		
	Frequency M (SD)	1.33 (0.83)	0.85 (0.52)	1.08 (0.57)	1.02 (0.61)	0.92 (0.45)	1.16 (0.22)	1.13 (0.62)	1.21 (0.60)		