Levels of Abstractness in Semantic Noun and Verb Processing

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Semantic and lexical features of words dissimilarly affected by non-fluent, logopenic, and semantic primary progressive aphasia

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Abstract

Objective: To determine the effect of three psycholinguistic variables—lexical frequency, age of acquisition, and neighborhood density—on lexical-semantic processing in individuals with non-fluent, logopenic, and semantic primary progressive aphasia (PPA). Identifying the scope and independence of these features can provide valuable information about the organization of words in our mind and brain.

Method: We administered a lexical-decision task—with words carefully selected to permit distinguishing lexical frequency, age of acquisition, and orthographic neighborhood density effects—to 41 individuals with the three variants of PPA (13 non-fluent, 14 logopenic, and 14 semantic) and 25 controls.

Results: Of the psycholinguistic variables studied, lexical frequency had the largest influence on lexical-semantic processing, but age of acquisition and neighborhood density also played an independent role. The effect of these latter two features differed across PPA variants and is consistent with the atrophy pattern of each variant. That is, individuals with non-fluent and logopenic PPA experienced a neighborhood density effect consistent with the role of inferior frontal and temporoparietal regions in lexical analysis and word form processing. By contrast, individuals with semantic PPA experienced an age of acquisition effect consistent with the role of the anterior temporal lobe in semantic processing.

Conclusions: The findings are in line with a hierarchical mental lexicon structure with a conceptual (semantic) versus lexeme (word-form) level, such that a selective deficit at one of these levels of the mental lexicon manifests differently in lexical-semantic processing performance, consistent with the affected language-specific brain region in each PPA variant.

Keywords: age of acquisition, lexical frequency, neighborhood density, psycholinguistics, word processing, mental lexicon, dementia

Introduction

Words are complex entities composed of various pieces of information, of which meaning is one and lexical label (i.e., word form) another. Various features of words have been proposed to affect processing at either the word form level or conceptual level. The most discussed feature is lexical frequency, how often a word occurs in a given language corpus. A long-lasting and unsettled debate revolves around if and how lexical frequency relates to the age at which a word is learned, or 'age of acquisition' (AoA). These features are highly correlated with each other; a high-frequency word is often acquired at an early age while a low-frequency word is usually acquired at a later age (e.g., Morrison, Ellis, & Quinlan, 1992). Another psycholinguistic feature—but bound to a word's lexical label—that influences lexical-semantic processing is orthographic neighborhood density. This feature quantifies how many close neighbors a word has by counting the number of words that differ orthographically by one letter from the target word. Determining the scope and independence of these psycholinguistic features in word processing can provide valuable information about the organization of words in our mind and brain, and in particular about how separate language aspects may be affected differently due to regional atrophy in individuals with brain damage.

Frequency and AoA are often investigated with various linguistic tasks such as naming and lexical decision with the intention of measuring which of the two features has a larger effect on accuracy and response time (RT). Notably, across studies AoA has been reported to have a larger effect than frequency, an equal effect, or a smaller effect (e.g., Brysbaert & Ghyselinck, 2006; Cortese & Khanna, 2007; Gilhooly & Logie, 1982; Treiman, Mullennix, Bijeljac-Babic, & Richmond-Welty, 1995). These contradictory results may be related to the methodological approach used. Many studies use multiple regression analyses to define each feature's influence (e.g., Brown & Watson, 1987; Cortese & Schock, 2013), but this statistical approach can be problematic because of high collinearity between frequency and AoA. To circumvent this statistical hurdle, some researchers manipulate one feature while

controlling for another, for example, comparing performance on early- versus late-acquired words with on average equal frequencies (e.g., Barry, Hirsh, Johnston, & Williams, 2001; Turner, Valentine, & Ellis, 1998). In this study, we have adapted this approach with an additional step, namely to not only control for the other variable but to contrast extreme values of one variable within a constant, extreme value of the other; for example, to analyze the effects of early versus late AoA within only low-frequency words, or high versus low frequency within only late AoA words (Gerhand & Barry, 1999).

The effects reported for orthographic neighborhood density are contradictory as well. High neighborhood density facilitates lexical decision in some studies (e.g., Pollatsek, Perea, & Binder, 1999; Sears, Hino, & Lupker, 1995), inhibits it in others (e.g., Carreiras, Perea, & Grainger, 1997), and an effect is absent in yet others (e.g., Coltheart, Davelaar, Jonasson, & Besner, 1977). This inconsistency may be explained by an interaction between neighborhood density and frequency, in which neighborhood density works in a facilitative manner for low-frequency words and in an inhibitive manner for high-frequency words (Balota, Cortese, Sergent-Marshall, Spieler, & Yap, 2004; Sears et al., 1995).

The mental lexicon is thought to be separated into a conceptual level, lemma level, and lexeme level. The conceptual level relates to semantics, the lemma level to syntax, and the lexeme level to aspects of word form in single-word processing (Bock & Levelt, 1994). AoA is considered to have a semantic locus, while neighborhood density applies to the word form level (e.g., Brysbaert, Van Wijnendaele, & De Deyne, 2000; Cortese & Khanna, 2007; Levelt, Roelofs, & Meyer, 1999; Roelofs, Meyer, & Levelt, 1996; Steyvers & Tenenbaum, 2005). These loci are exemplified by highly overlapping measures of AoA across languages for words and their translation equivalents, while values of neighborhood density for such word pairs differ dramatically across languages (see Lexicon Projects, e.g., Balota et al., 2007; Ferrand et al., 2010; Keuleers, Diependaele, & Brysbaert, 2010; Keuleers, Lacey, Rastle, & Brysbaert, 2012). The locus of frequency is debated but is proposed to relate to both levels (Vonk, 2017).

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Individuals with primary progressive aphasia (PPA) experience breakdown of language due to progressive cortical atrophy. While semantic impairment at a word-level is only a diagnostic deficit in individuals with the semantic variant of PPA (svPPA), in individuals with all three variants of PPA—non-fluent, logopenic, and semantic—words are affected in some way, namely the production, retrieval, or understanding of words, respectively. Individuals with the non-fluent variant of PPA (nfvPPA) are the least affected in semantic processing, with normal single-word comprehension and spared object knowledge, yet with variability among individuals with the non-fluent variant regarding the degree of word-finding difficulties. The hallmark of individuals with the logopenic variant of PPA (lvPPA) is anomia; although their single-word comprehension is preserved, they often experience effort finding the intended word for production. This deficit is not driven by impairment at a conceptual level, as shown by their ability to use instead simpler substitutions or circumlocutionary descriptions. By contrast, in individuals with svPPA, the conceptual level is inherently affected as these individuals lose the core knowledge of concepts; they may claim they have never known the name or use of a common object.

To determine how the conceptual and lexeme levels of the mental lexicon relate to lexical-semantic processing, this study investigated if and how the psycholinguistic features of frequency, AoA, and neighborhood density differently affect lexical decision accuracy and RT in individuals with PPA. The correspondence between the focal atrophy pattern of individuals with each variant of PPA on the one hand and the brain regions involved in word-form (at the lexeme level of the mental lexicon) or semantic (at the conceptual level of the mental lexicon) processing on the other hand leads to explicit hypotheses about the influence of psycholinguistic variables on lexical decision performance. The inferior frontal, temporoparietal, and occipitotemporal networks are involved in lexical analysis and word form processing in reading (e.g., Shaywitz et al., 1998). These areas are typically affected in individuals with either nfvPPA or lvPPA, but not in those with svPPA (e.g., Gorno-Tempini et al., 2011). Thus, we predicted an effect of neighborhood density in individuals with nfvPPA and lvPPA, but not in

those with svPPA. By contrast, individuals with svPPA experience semantic problems, caused by atrophy in the anterior temporal lobe. As the effect of AoA has a semantic locus, we predicted that AoA specifically influenced lexical decision performance in individuals with svPPA, but not in those with nfvPPA or lvPPA.

Method

Participants

The study sample included a group of 41 individuals with PPA (29 women; mean age = 68.2, SD = 6.7; mean years of education = 16.2, SD = 1.9; Table 1), classified as 13 individuals with nfvPPA, 14 with lvPPA, and 14 with svPPA at the University of California at San Francisco (UCSF) Memory and Aging Center. The clinical diagnosis of dementia and the specific syndrome of PPA for each individual were based on multidisciplinary criteria including clinical history, neurological examination, neuroimaging, and neuropsychological and language evaluation by a group of neurologists, neuroscientists, neuropsychologists, and speech-language pathologists. Neuroimaging confirmed atrophy of the left inferior frontal gyrus and insula in the nfvPPA group, of the left posterior temporal cortex and inferior parietal lobule in the lvPPA group, and of the bilateral anterior temporal lobes in the svPPA group. Neuroimaging was also used to exclude other causes of focal brain damage (e.g., tumor, white matter disease). Of the individuals with svPPA, eight were affected by more atrophy in their right hemisphere than their left hemisphere, yet all displayed substantial atrophy in their left hemisphere on structural MRI scans and exhibited language deficits consistent with svPPA.

Additionally, 25 age-matched controls (18 women; mean age = 69.6, SD = 7.6; mean years of education = 17.7, SD = 1.3) were tested. None of the control participants had a history of head injury or neurological or psychiatric disorders. Recent structural MRI scans (within one year of cognitive testing),

as well as scores on the Clinical Dementia Rating (CDR; Morris, 1993) and Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975) were available for 18 of the 25 control participants (Table 1).

All controls were monolingual speakers of American English. Among the 41 participants with PPA, all were native speakers of American English; of them, four were proficient in at least one other language. All reported having normal or corrected-to-normal vision. Hearing was screened in each ear at a level of 25 dB Hearing Level (HL) at octave frequencies between 250 and 8000 Hz; all participants passed the screening, indicating adequate sensitivity for the sounds presented in this study. Participants gave written consent in accordance with the Institutional Review Boards of UCSF and the City University of New York.

Stimuli

The materials consisted of two sets of 48 nouns each to contrast frequency with either AoA or neighborhood density, with three words overlapping between the sets. Each set was divided into four categories of 12 words following a 2x2 design (high/low frequency versus early/late AoA and high/low frequency versus high/low neighborhood density; see Appendix for all words). Familiarity ratings were available for 83 of the 93 unique words (Nusbaum, Pisoni, & Davis, 1984), with the words having high familiarity on a scale from 1-7 (mean = 6.95, SD = 0.11, range 6.5-7).

The four categories in Set 1 (frequency vs. AoA) each included 12 words that were either high frequency/early acquired, high frequency/late acquired, low frequency/early acquired, or low frequency/late acquired. Low-frequency words occurred 0.4-8.0 times per million words and high-frequency words occurred 20-560 times per million words (Brysbaert & New, 2009). Age of Acquisition was determined according to the ratings of Kuperman, Stadthagen-Gonzalez, and Brysbaert (2012). Words were considered early acquired 2.5-4.5 years of age and late acquired between 7-10 years of age.

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The categories were matched on letter length, phoneme length, syllable length, imageability, orthographic neighborhood density, phonological neighborhood density, and familiarity (Balota et al., 2007; Brysbaert, Stevens, De Deyne, Voorspoels, & Storms, 2014). When each of two categories was collapsed to be divided only by our target variables (either frequency or AoA), the two 24-word categories still matched on these additional variables.

The four categories in Set 2 (frequency vs. neighborhood density) included 12 words each that were either high frequency/high neighborhood density, high frequency/low neighborhood density, low frequency/high neighborhood density, or low frequency/low neighborhood density. As neighborhood density is highly influenced by a word's number of letters (the more letters, the fewer neighbors), only four-letter words—having 2-4 phonemes—were included in this set. Neighborhood density is measured by the Levenshtein distance to its 20 closest neighbors when performing the minimum number of changes (insertions, deletions or substitutions of single characters) to morph one word into another (Yarkoni, Balota, & Yap, 2008). For example, a Levenshtein distance of 1 (the smallest possible) means that the 20 closest words to the target word can all be formed by changing only one character. In this set, four-letter words are considered to have high neighborhood density with an orthographic Levenshtein distance of 1-1.1 and to have low neighborhood density with a distance of 1.45-1.9. The categories were matched on phoneme length, syllable length, AoA, and familiarity. All words in this set were relatively early acquired (AoA = 3.42-6.44 years). When each of two categories was collapsed to be divided only by our target variables (either frequency or neighborhood density), the two 24-word categories still matched on these additional variables.

Pseudowords were orthographically and phonologically plausible in English. Candidates for pseudowords were automatically created using Wuggy, a pseudoword generator (Keuleers & Brysbaert, 2010), followed by a manual selection and verification by a second reader who was a native speaker of American English. Pseudowords were based on real words used in the experiment; all pseudowords

were the same letter- and syllable-length as their base word, differed less than ±0.15 orthographic

Levenshtein distance from their base word, and had up to 2 neighbors at one edit-distance more or less

than their base word. Each pseudoword was generated for a different real word of the stimuli, i.e., no

pseudowords shared the same base word. No homophones of existing English words were included.

Procedure

A lexical decision task was administered in which participants had to identify whether the string

of letters on the screen formed a real word or not. Participants were tested individually in a quiet room

at a table with the investigator seated next to them. They indicated their answer by pressing a green

button on a keyboard for a real word (green sticker covered key /) and a red button for a pseudoword

(red sticker covered key z). The instructions specified to answer as accurately and as quickly as possible

but stressed that accuracy was more important than speed. This clause served the purpose to avoid

shallow lexical processing and to lessen the chance of a speed-accuracy trade-off that would negatively

affect accuracy (Pollatsek et al., 1999). Stimuli were simultaneously presented visually and auditorily to

avoid the measurement of task-input-related effects due to diagnosis (e.g., surface dyslexia in

individuals with svPPA and phonological loop deficits in individuals with lvPPA).

The task was divided into short blocks, with the first block being preceded by detailed

instructions and practice items to accustom the participants to the task. For similar reasons, unknown to

the participant, each block started with three filler items. Blocks, as well as words and pseudowords

within a block, were randomly presented. A fixation cross of 750 ms preceded the onset of a word.

Participants had to answer within six seconds after onset of the word; if no answer was given after six

seconds, the word would disappear and a new trial would appear—the item's accuracy would be scored

as incorrect. E-Prime 2.0 (2.0.10.356) was used to design and run the experiment, recording response

accuracy and RT in ms (Schneider, Eschman, & Zuccolotto, 2002).

Statistical analysis

Descriptive statistics were calculated for all variables. Items that received no response were scored as incorrect (0.1% of the responses; 8 out of 6337, all in individuals with PPA). Responses faster than 200 ms would have been excluded from analyses but did not occur in the data. Analyses with RT as the dependent variable included only items with correct responses. Due to the typical positively skewed distribution of RT, a natural logarithmic transformation was applied to render the data normally distributed.

Means were calculated for both accuracy and RT for each of four categories: high/low frequency versus early/late AoA in Set 1 and high/low frequency versus high/low neighborhood density in Set 2. The main analysis included models per diagnostic group to compare high versus low frequency while AoA (Set 1)/neighborhood density (Set 2) was controlled, and early versus late AoA/high versus low neighborhood density while frequency was controlled, and the interaction between frequency and AoA (Set 1)/neighborhood density (Set 2). Additional models per diagnostic group separated the effects of frequency and AoA (Set 1)/neighborhood density (Set 2) by analyzing differences in accuracy and RT among the four different categories of words: high frequency-early AoA (Set 1)/high neighborhood density (Set 2), high frequency-late AoA (Set 1)/low neighborhood density (Set 2), low frequency-early AoA (Set 1)/high neighborhood density (Set 2), and low frequency-late AoA (Set 1)/low neighborhood density (Set 2). Another series of models compared the effects of frequency and AoA (Set 1)/neighborhood density (Set 2) in each diagnostic group separately to the effects of these variables in the control group.

The data were analyzed with linear mixed models with maximum likelihood estimation adjusted for age, years of education, disease severity, and d' (positive response-bias). Models analyzing RT included a random intercept (categories nested within subjects) and fixed slope, while models analyzing

accuracy included a fixed intercept and fixed slope, as covariance estimates indicated that there was no unique variance to estimate among individuals above and beyond the residual variance per category. Disease severity was calculated as a composite score of CDR box score (Lynch et al., 2006) and MMSE in order to account for individual variances in severity of PPA; this composite score was the sum of the rescaled CDR box and MMSE scores, ranging from 0-2 in which a higher score signifies higher severity. Response bias on the lexical decision task was measured using the sensitivity index d', following Signal Detection Theory (Macmillan, 2002), in which the lower the value, the higher the response bias (e.g., Kielar, Deschamps, Jokel, & Meltzer, 2018; Nilakantan, Voss, Weintraub, Mesulam, & Rogalski, 2017).

Fixed variables for models within each diagnosis included age, years of education, disease severity, d', frequency, AoA (Set 1 only)/neighborhood density (Set 2 only), and the interaction term between frequency and either AoA or neighborhood density in the main analysis. Standardized effect sizes (Cohen's d) were calculated by dividing the mean difference between the factor's levels by the standard deviation ($\sqrt{N}$*standard error of the estimate, in which N is the number of levels per factor (2) times the group's participants) (Cohen, 1992; Taylor, 2015). Additional models within each diagnostic group to compare the four categories among each other included age, years of education, disease severity, d', and category as fixed variables. Pairwise comparisons were performed using the Šidák correction. Models that compared each PPA group to the control group included age, education, diagnosis, disease severity, d', category, diagnosis*frequency, and diagnosis*AoA (Set 1)/neighborhood density (Set 2). All data were analyzed in IBM SPSS Statistics Version 24 (IBM Corp, 2016).

Results

Frequency vs. Age of acquisition

Main effects including effect sizes are reported in Table 3. Overall lexical decision performance measured by accuracy and RT is presented in Table 2. In the control group, high frequency and early AoA resulted in more accurate and quicker responses than low frequency and late AoA for both measures. For individuals with nfvPPA, higher word frequency resulted in better accuracy and quicker response times, while early AoA did not affect accuracy but did lead to quicker responses. In the lvPPA group, frequency did not predict accuracy, but higher frequency items elicited quicker responses, while AoA predicted neither accuracy nor RT. In the svPPA group, high frequency and early AoA facilitated both accuracy and RT compared to low frequency and late AoA. None of the groups showed an interaction between frequency and AoA on either accuracy or RT, except for a trend for accuracy in the svPPA group, with a larger AoA effect for low-frequency words than for high-frequency words (Figure 1).

When contrasting extreme values of one variable within a constant value of the other variable in pairwise comparisons, the svPPA group showed separate effects of frequency and AoA, with better performance on both accuracy (p < .001) and RT (p = .033) on high- versus low-frequency words within late AoA words, and more accurate (p = .001) performance on early- than late-acquired words within low-frequency words. The nfvPPA group showed a frequency effect within early AoA words on accuracy (p = .026). The control and lvPPA groups did not show differences among any categories for either accuracy or RT measures.

Performance of each PPA group was also compared to that of the controls (Table 4). The nfvPPA group showed a stronger frequency effect than controls on accuracy, but not RT; the groups did not differ in the effect of AoA on either measure. The lvPPA group did not differ from controls on accuracy or RT measures in either frequency or AoA effects. The svPPA group demonstrated a stronger frequency effect and AoA effect than the control group on both measures.

Frequency vs. neighborhood density

Main effects including effect sizes are reported in Table 3. Controls responded more accurately and quickly to high-frequency than low-frequency words, but there was no effect of neighborhood density. Individuals with nfvPPA and lvPPA showed the same pattern: they answered high-frequency words more accurately and quicker than low-frequency ones and high neighborhood density words more accurately, but not quicker, than low neighborhood density ones. The svPPA group answered more accurately and quickly to high-frequency than low-frequency words; there was no effect of neighborhood density on accuracy, but there was on RT. Only the nfvPPA group showed an interaction between frequency and neighborhood density on their accuracy performance, with a larger neighborhood density effect within low-frequency words than within high-frequency words (Figure 2).

When contrasting extreme values of one variable within a constant value of the other variable in pairwise comparisons, the groups collectively showed a pattern of an independent frequency effect across accuracy and RT, present within both low neighborhood density and high neighborhood density words. Additionally, the nfvPPA group showed a neighborhood density effect within low-frequency words ($p = .004$).

Performance of each PPA group was also compared to that of the controls (Table 4). The nfvPPA group did not differ from controls on the frequency effect on either measure. However, the nfvPPA group demonstrated a stronger neighborhood density effect than did controls on accuracy, but not RT. In the lvPPA group, the frequency effect was stronger than in controls on both measures. Additionally, the neighborhood density effect was also stronger in individuals with lvPPA compared to controls on accuracy, but not RT. The svPPA group demonstrated a stronger frequency effect than controls on both measures, and no difference in neighborhood density effect for accuracy, but a stronger effect on RT.

Discussion

We investigated the effect of three psycholinguistic variables—lexical frequency, AoA, and neighborhood density—on lexical-semantic processing in individuals with the three variants of PPA: nfvPPA, lvPPA, and svPPA. The theoretically-based expectation was that the effects of AoA and neighborhood density in individuals with PPA would be different across variants because these variables are associated with the conceptual versus lexeme levels of the mental lexicon, respectively (e.g., Cortese & Khanna, 2007; Roelofs et al., 1996). Indeed, our results showed that some effects are substantially stronger in individuals with one variant than another. In particular, individuals with svPPA experience a strong AoA effect (i.e., better performance on early-acquired than late-acquired words) on both accuracy and RT measures, while accuracy performances of those with the nfvPPA and lvPPA are subject to an effect of neighborhood density (i.e., better performance on words with a high than low neighborhood density). These findings support the idea that psycholinguistic variables influence lexical-semantic processing at different levels of the mental lexicon.

Lexical frequency is one of the most investigated psycholinguistic variables and has been widely shown to affect RT and accuracy in lexical decision (e.g., Balota et al., 2007; Brown & Watson, 1987). In this study, as well, frequency had an effect on both accuracy and RT in individuals of all three PPA groups as well as in controls. Effect sizes of the impact of frequency on accuracy were medium in the control group, medium to large in the nfvPPA and lvPPA groups, and large to very large in the svPPA group. The size of each group's frequency effect corresponded to their overall accuracy score on the lexical decision task. In other words, errors and slower responses in lexical decision were specifically made on low-frequency words; the more errors one makes, the larger the performance gap between words with high versus low frequency becomes.

Our data demonstrate that frequency is not the only psycholinguistic variable to influence lexical-semantic processing. A topic of much debate is the relation between frequency and AoA: are

these variables measuring the same or distinct effects, are the effects of equal size or is one stronger

than the other, and are they related or independent of each other (e.g., Brysbaert & Ghyselinck, 2006;

Gerhand & Barry, 1998; Zevin & Seidenberg, 2002)? Our findings strongly suggest that frequency and

AoA measure two different features because with negligible variance in word frequency in the category

of low-frequency words, individuals with svPPA still show a solid AoA effect. In addition, the data show a

trend that the AoA effect is stronger for low-frequency words than high-frequency words in individuals

with svPPA, which is also reported in some studies of adults without dementia (Cortese & Schock, 2013;

Gerhand & Barry, 1999). This interaction further emphasizes that lexical frequency and AoA are most

probably two different features, both having independent influences on lexical-semantic processing.

The words in this dataset and the combination into categories were carefully controlled for a

broad range of psycholinguistic and semantic variables. Having done so counters claims in the literature

that finding an effect of frequency or AoA is actually a disguised effect of another variable; for example,

Gilhooly and Logie (1982) argued that reports of an AoA effect are in fact failures to control for word

familiarity. However, in the current study when familiarity was controlled for in the stimulus set that

investigated frequency versus AoA (in addition to letter length, phoneme length, syllable length,

imageability, orthographic neighborhood density, and phonological neighborhood density), the results

still showed independent effects of the two variables.

More specifically, in this study, the performance of the control group demonstrated that

frequency and AoA have a more or less comparable effect on lexical decision accuracy, consistent with

results by Brysbaert and Ghyselinck (2006). In individuals with PPA, however, the effect of AoA was

always smaller than the frequency effect. Individuals with nfvPPA and lvPPA showed virtually no effect

of AoA, while individuals with svPPA showed a solid medium to large effect of AoA on accuracy and RT.

The individuals with svPPA were also the only group to show a larger AoA effect compared to controls

on both accuracy and RT. These results confirm the prediction that the effect of AoA, given its strong

relation to semantics, would be particularly affected in individuals with svPPA having atrophy in the

anterior temporal lobe, which is known to be a semantic hub (e.g., Binney, Embleton, Jefferies, Parker, &

Lambon Ralph, 2010; Mummery et al., 2000; Pobric, Jefferies, & Ralph, 2010).

The second set of stimuli was designed to investigate effects of lexical frequency versus

orthographic neighborhood density. Investigating isolated effects of neighborhood density on lexical-

semantic processing can be challenging, as neighborhood density size is extraordinarily strongly linked

to word length—the more letters a word has, the harder it becomes to form another word by changing

only one character. In turn, word length is correlated with lexical frequency as formulated by Zipf's law

(Zipf, 1935), which demonstrated that the length of a word is inversely related to the frequency of its

use. To avoid potential contamination of word length-effects on neighborhood density values, all items

in this set were restricted to having four letters in order to assess separate effects of neighborhood

density and frequency, including possible interactions. However, the much larger frequency effect

across all groups in this Set 2 compared to those in Set 1 (frequency and AoA) supports that word length

has a substantial influence on frequency effects, despite our efforts to control for this variable within

each set.

The data in Set 2 revealed disproportional effects of neighborhood density across the groups.

The analyses for the control group yielded medium- to large-sized effects of frequency across accuracy

and RT, but there was decidedly no effect of neighborhood density (non-significant with effect sizes

close to zero). On the contrary, effects of neighborhood density were observed in individuals with

nfvPPA and lvPPA, with a positive effect of high neighborhood density compared to low neighborhood

density. The effect of neighborhood density on lexical decision accuracy in individuals with nfvPPA and

lvPPA was also significantly stronger than in the control group. This result was in line with the prediction

that aspects of word-form, such as neighborhood density, are affected in individuals with nfvPPA and

lvPPA because their atrophy overlaps with brain regions linked to word-form. Individuals with nfvPPA

displayed a stronger effect of neighborhood density than those with lvPPA, and the nfvPPA group was the only one to encounter an interaction effect in which neighborhood density specifically affected accuracy in low-frequency words compared to high-frequency words. Such an interaction effect between frequency and neighborhood density is consistent with results by Balota et al. (2004) and Sears et al. (1995). Also predicted by this study's hypothesis, individuals with svPPA did not show an effect of neighborhood density on accuracy nor did accuracy performance differ from the control group on this variable. While individuals with svPPA did show a neighborhood density main effect on RT, pairwise comparisons did not demonstrate an independent neighborhood density effect within either only high-frequency or only low-frequency words.

In sum, the results reflect a brain-language relationship on lexical-semantic processing in PPA resulting in different proportional effects of frequency, AoA, and neighborhood density consistent with the organization of the mental lexicon. Individuals with nfvPPA and lvPPA, who are characterized as having no semantic impairment, did not experience an effect of AoA—a psycholinguistic variable with semantic locus—in lexical decision accuracy. Instead, individuals with nfvPPA or lvPPA experienced an effect of neighborhood density—a psycholinguistic variable operating at the lexeme level—in line with their brain atrophy affecting regions typically associated with lexical analysis and word form processing. Individuals with svPPA, who have semantic impairment as its hallmark, showed the opposite pattern with no effect of neighborhood density and a solid effect of AoA on accuracy performance. These results argue in favor of words being organized in the brain according to a mental lexicon structure including a conceptual (semantic) and lexeme (word-form) level as proposed by Bock and Levelt (1994). Thus, the deterioration of language at word-level in individuals with PPA seems to be driven by impairment at a particular level of the mental lexicon as a result of atrophy to relevant brain regions for that level (e.g., for word-form or semantics). Future studies should investigate whether these psycholinguistic variables

interact with any conceptual information in lexical-semantic processing and, if so, how this relates to the

organization of the mental lexicon.

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Table 1. Participant characteristics

	Controls	nfvPPA	lvPPA	svPPA
Number	25	13	14	14
Gender (female)	18	10	8	11
Handedness	R = 24, L = 1, A = 0	R = 10, L = 2, A = 1	R = 11, L = 2, A = 1	R = 12, L = 2, A = 0
Age	69.6 (7.6)	67.3 (8.2)	65.1 (5.3)	72.1 (4.4)
Education (years)	17.7 (1.3)	15.8 (1.6)	15.7 (2.0)	16.9 (1.9)
MMSE	29.2 (.9)	22.8 (6.3)	21.9 (4.7)	21.5 (6.4)
CDR	0.0 (.1)	2.1 (2.1)	3.4 (1.3)	5.4 (2.5)

Note. mean (SD); nfvPPA = non-fluent primary progressive aphasia (PPA), lvPPA = logopenic PPA, svPPA = semantic PPA, L = left-handed, R = right-handed, A = ambidextrous, MMSE = Mini-Mental State Examination, CDR = Clinical Dementia Rating

Table 2. Mean performance in accuracy (%) and response time (log)

		Overall Set 1	High freq-early AoA	High freq-late AoA	Low freq-early AoA	Low freq-late AoA	Overall Set 2	High freq-high ND	High freq-low ND	Low freq-high ND	Low freq-low ND
Controls	Acc	99.2 (2.4)	100 (.0)	99.4 (2.2)	99.4 (2.2)	98.1 (3.5)	98.8 (3.4)	100 (.0)	99.7 (1.6)	97.7 (4.5)	97.7 (4.5)
nfvPPA		97.0 (5.4)	100 (.0)	98.2 (3.5)	94.9 (8.0)	95.0 (5.4)	96.8 (5.3)	98.7 (3.2)	98.2 (3.5)	98.2 (3.5)	92.2 (7.4)
lvPPA		96.8 (6.8)	99.4 (2.1)	96.4 (9.6)	95.9 (7.1)	95.3 (6.3)	96.3 (7.2)	99.4 (2.1)	98.2 (4.9)	96.5 (5.4)	91.2 (11)
svPPA		89.4 (18)	98.9 (2.9)	93.5 (13.6)	9.6 (11.2)	74.5 (26.4)	87.2 (19.9)	98.2 (6.7)	98.3 (3.4)	8.3 (2.1)	72.1 (25.6)
Controls	RT	6.5 (.1)	6.5 (.2)	6.5 (.1)	6.5 (.1)	6.6 (.1)	6.5 (.1)	6.5 (.1)	6.5 (.1)	6.6 (.1)	6.6 (.1)
nfvPPA		7.0 (.4)	7.0 (.4)	7.0 (.4)	6.9 (.3)	7.3 (.3)	7.1 (.5)	7.0 (.5)	6.9 (.4)	7.2 (.4)	7.4 (.5)
lvPPA		6.8 (.3)	6.7 (.3)	6.8 (.2)	6.8 (.2)	6.8 (.3)	6.8 (.2)	6.8 (.2)	6.8 (.2)	6.8 (.2)	6.9 (.3)
svPPA		6.8 (.2)	6.8 (.2)	6.9 (.2)	6.9 (.1)	7.1 (.0)	6.8 (.2)	6.8 (.3)	6.7 (.2)	6.7 (.2)	6.9 (.2)

Note. mean (SD); Acc = accuracy, RT = response time (log), nfvPPA = non-fluent primary progressive aphasia (PPA), lvPPA = logopenic PPA, svPPA = semantic

PPA, freq = frequency, AoA = age of acquisition, ND = neighborhood density

Table 3. Main effects and interactions of frequency with age of acquisition and neighborhood density

within each diagnostic group

		Accuracy				RT			
Group	Set 1	df (1, x)	F	p	d	df (1, x)	F	p	d
Control	Freq	100	4.819	.030	.47	75	38.537	<.001	.42
	AoA	100	4.819	.030	.47	75	17.967	<.001	.29
	Freq x AoA	100	.535	.466		75	1.156	.286	
nfvPPA	Freq	52	11.671	.001	.89	39	9.299	.004	.22
	AoA	52	.539	.466	.20	39	4.892	.033	.16
	Freq x AoA	52	.637	.428		39	1.722	.197	
lvPPA	Freq	56	2.238	.140	.40	42	2.422	<.001	.35
	AoA	56	1.378	.245	.31	42	3.212	.080	.14
	Freq x AoA	56	.577	.451		42	1.624	.210	
svPPA	Freq	56	22.721	<.001	1.29	42	56.847	<.001	.69
	AoA	56	14.014	<.001	1.01	42	37.011	<.001	.56
	Freq x AoA	56	3.503	.066		42	1.528	.223	
	Set 2								
Control	Freq	100	12.744	.001	.74	75	101.944	<.001	.66
	ND	100	.073	.788	.07	75	.78	.380	.06
	Freq x ND	100	.073	.788		75	1.35	.249	
nfvPPA	Freq	52	7.803	.007	.78	39	28.051	<.001	.35
	ND	52	7.803	.007	.78	39	1.157	.289	.07
	Freq x ND	52	5.419	.024		39	.858	.360	
lvPPA	Freq	56	1.311	.002	.86	42	53.512	<.001	.68
	ND	56	4.419	.040	.57	42	2.454	.125	.15
	Freq x ND	56	1.734	.193		42	1.981	.167	

svPPA	Freq	56	54.276	<.001	1.99	42	42.553	<.001	.82
	ND	56	1.847	.180	.37	42	5.8	.020	.31
	Freq x ND	56	1.912	.172		42	2.013	.163	

Note. Freq = frequency, AoA = age of acquisition, ND = neighborhood density, df = degrees of freedom, x = denominator df, d = effect size reported in Cohen's d

Table 4. Group comparisons of effects in each PPA group versus controls

		Accuracy			RT		
Group comparison	Set 1	df (1, x)	F	p	df (1, x)	F	p
Controls vs. nfvPPA	Freq	114	8.907	.003	114	.227	.635
	AoA	114	.005	.943	114	.214	.644
Controls vs. lvPPA	Freq	117	1.162	.283	117	2.722	.102
	AoA	117	.465	.497	117	.034	.854
Controls vs. svPPA	Freq	117	27.401	< .001	117	15.000	< .001
	AoA	117	16.208	< .001	117	12.419	< .001
	Set 2						
Controls vs. nfvPPA	Freq	152	.820	.367	114	2.040	.156
	ND	152	6.264	.013	114	.631	.429
Controls vs. lvPPA	Freq	117	3.608	.060	117	7.457	.007
	ND	117	4.258	.041	117	1.394	.240
Controls vs. svPPA	Freq	117	61.085	< .001	117	12.898	.019
	ND	117	2.348	.128	117	5.700	.019

Note. Freq = frequency, AoA = age of acquisition, ND = neighborhood density, df = degrees of freedom, x = denominator df, d = effect size reported in Cohen's d

Figure 1. Frequency vs. age of acquisition in individuals with semantic primary progressive aphasia
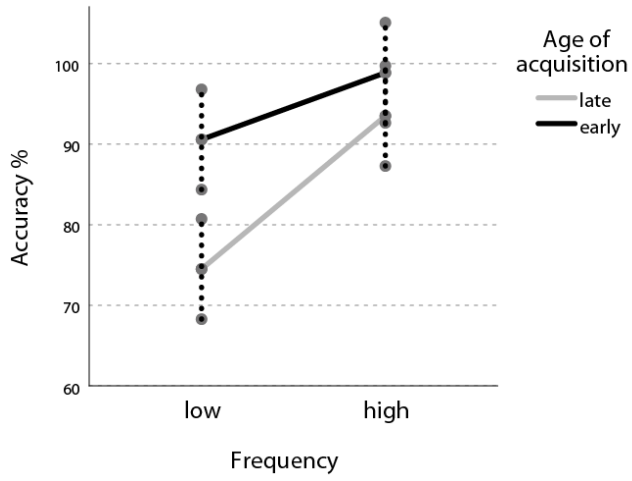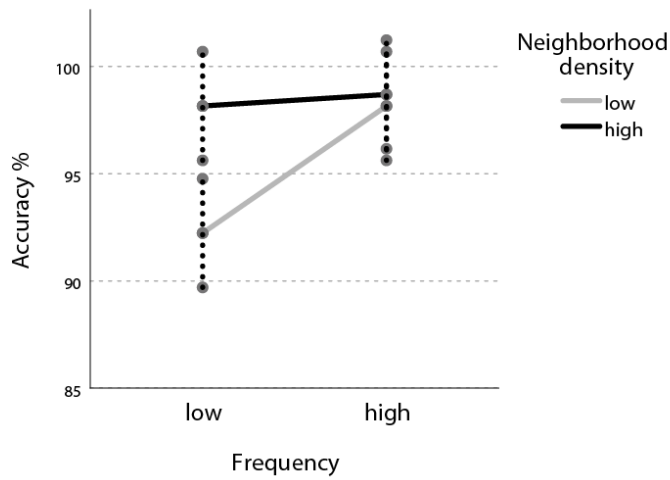

Figure 2. Frequency vs. neighborhood density in individuals with non-fluent primary progressive aphasia

Appendix

Stimulus materials

Category (Set 1)

High freq-late AoA	High freq-early AoA	Low freq-late AoA	Low freq-early AoA
taxi	wheel	racket	sofa
priest	cheese	bleach	chalk
valley	knife	wrench	cereal
sweat	square	blush	cola
lawyer	snow	razor	stove
prison	dress	siren	straw
flesh	sugar	staple	stripe
radar	plant	wedge	bubble
crowd	truck	lasso	melon
drug	circle	herb	crayon
mayor	movie	cube	carrot
thief	table	violin	spoon

Category (Set 2)

High freq-high ND	Low freq-low ND	High freq-low ND	Low freq-high ND
rose	crow	edge	mane
line	mule	copy	pail
wire	wasp	club	bead
gate	plum	desk	pear
rain	snot	spot	cone
meat	germ	town	rake

seat	pond	gift	lace
lake	claw	wolf	pine
mail	sofa	soda	bean
hall	cola	snow	seed
date	yolk	girl	rack
race	moth	yard	hose

Note. Freq = frequency, AoA = age of acquisition, ND = neighborhood density