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Lexical access in semantic variant PPA: Evidence for a postsemantic contribution to naming deficits

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Abstract

The most salient clinical symptom of semantic variant primary progressive aphasia (PPA) is a profound and pervasive anomia. These patients' naming impairments have been shown to reflect in large part a domain-general deterioration of conceptual knowledge that impacts both linguistic and non-linguistic processing. However, it is possible that post-semantic stages of lexical access may also contribute to naming deficits. To clarify the stages at which lexical access breaks down in semantic variant PPA, eleven French-speaking patients were asked to name objects, and were then queried for semantic, lexical-syntactic, and word form information pertaining to the items they could not name. Specifically, our goal was to determine whether patients can access intermediate representations known as lemmas, which mediate the arbitrary mapping between semantic representations and word forms (phonological and orthographic forms). The French language was chosen for this study because nouns in French are marked for grammatical gender, a prototypical type of lexical-syntactic information, represented at the level of the lemma. Access to word form information is also dependent on lemma access under some theoretical views. We found that six of the eleven patients showed partial access to either lexical-syntactic properties of unnamed items (grammatical gender), word form information (initial letter), or both. Access to these types of information suggests that a lemma has been retrieved, implying a breakdown at the post-semantic stage of word form retrieval. Our results suggest that although degraded conceptual knowledge is the main cause of naming deficits in semantic variant PPA, in some patients, a post-semantic component also contributes to the impairment.

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Keywords

semantic variant primary progressive aphasia; semantic dementia; lexical access; lemma; word form

1. Introduction

Lexical access refers to the process of retrieving a word from the mental lexicon and encoding it for speech production. Most researchers agree that lexical access involves a series of stages including at least: (1) conceptual preparation yielding a semantic representation of the word to be produced; (2) retrieval of an abstract entity known as a lemma that encodes word-level syntactic information (e.g., grammatical category, grammatical gender, argument structure); (3) retrieval of a word form (a phonological form in the case of speaking); and (4) transformation of this word form into a motor plan for the speech apparatus, involving processes such as syllabification and phonetic encoding (Dell, 1986; Dell, Schwartz, Martin, Saffran, & Gagnon, 1997; Dell, Schwartz, Nozari, Faseyitan, & Coslett, 2013; Levelt, Roelofs, & Meyer, 1999; Schwartz, Dell, Martin, Gahl, & Sobel, 2006). The first three of these stages are depicted in Figure 1A.

Theories of lexical access differ in many details, including the number of stages, the precise nature of representations at each stage (e.g., localist or distributed, componential or holistic), and how information flows between stages (e.g., strictly feed-forward, or interactive and bidirectional) (Caramazza, 1997; Dell, 1986; Levelt et al., 1999). However, one aspect of the model architecture is common to most approaches, and is critical to the present study. This is the assumption that there are intervening representations that mediate the arbitrary mapping between semantic representations and word forms (phonological and orthographic forms). These intermediate representations are referred to as lemmas (Kempen & Huijbers, 1983). The lemma concept has strong empirical support. Studies of spontaneous and experimentally induced speech errors have shown that word-level exchanges tend to respect grammatical category but are indifferent to word form, suggesting that these errors involve the manipulation of lemmas. In contrast, phoneme-level exchanges are sensitive to phonological but not syntactic factors, suggesting that they take place at a later stage of phonological encoding (Fromkin, 1971; Fay & Cutler, 1977; Garrett, 1975; Shattuck-Hufnagel, 1979). Reaction time studies have shown that semantic and phonological distractors impact picture naming with different time courses, again suggesting distinct stages (Schriefers, Meyer, & Levelt, 1990; Levelt et al., 1999). Patients have been described who can accurately report the grammatical gender of words even when they cannot retrieve the word form, suggesting access to lemma representations that encode lexical-syntactic information but are devoid of segmental content (Badecker, Miozzo, & Zanuttini, 1995; Caramazza, 1997; Henaff Gonon, Bruckert, & Michel, 1989). The "tip-of-the-tongue" phenomenon in healthy speakers can be interpreted similarly: the feeling of knowing a word reflects successful retrieval of the lemma, even though the word form cannot be retrieved (Brown, 1991; Vigliocco, Antonini, & Garrett, 1997). In languages that mark grammatical gender, this lexical-syntactic information can be reported with impressive accuracy in tip-of-the-tongue states (Miozzo &

Caramazza, 1997; Vigliocco et al., 1997). Taken together, there is a rich body of evidence that retrieval of lemmas can be dissociated from retrieval of word forms.

Semantic variant primary progressive aphasia (PPA), which we consider to be essentially equivalent to semantic dementia (Adlam et al., 2006), is a clinical syndrome characterized by progressive loss of conceptual knowledge or semantic memory due to degeneration of anterior and inferior temporal brain regions (Warrington, 1975; Schwartz, Marin, & Saffran, 1979; Snowden, Goulding, & Neary, 1989; Hodges, Patterson, Oxbury, & Funnell, 1992). Anomia is typically the earliest and most prominent symptom of semantic variant PPA. Word retrieval difficulty is modulated by factors including word frequency (Warrington, 1975; Hodges et al., 1992; Lambon Ralph, Graham, Ellis, & Hodges, 1998), object familiarity (Lambon Ralph et al., 1998), item specificity (Hodges, Graham, & Patterson, 1995), and item typicality (Woollams, Cooper-Pye, Hodges, & Patterson, 2008), and becomes increasingly severe over the course of the disease (Hodges et al., 1995).

At which stage(s) of the lexical access process does word retrieval go awry in semantic variant PPA? One stage that is clearly impacted in all individuals with semantic variant PPA is the first stage: conceptual preparation leading to a semantic representation. Several decades of research have shown that anomia in semantic variant PPA is just one manifestation of a domain-general deterioration of conceptual knowledge that affects all expressive and receptive modalities. Underlying impairments of conceptual knowledge have been demonstrated with non-linguistic semantic tasks such as semantic matching between pictures (Bozeat, Lambon Ralph, Patterson, Garrard, & Hodges, 2000), object use (Hodges, Bozeat, Lambon Ralph, Patterson, & Spatt, 2000), sound to picture matching (Bozeat et al., 2000), picture categorization (Rogers & Patterson, 2007), knowledge of object features (Adlam et al., 2006; Rogers et al., 2004) and delayed picture copy (Patterson & Erzinclio lu, 2009); see Hodges and Patterson (2007) for review. Furthermore, the progression and severity of naming deficits are strongly associated with the progression and severity of the deterioration of conceptual knowledge (Adlam et al., 2006; Hodges et al., 1995; Jefferies & Lambon Ralph, 2006; Lambon Ralph, McClelland, Patterson, Galton, & Hodges, 2001; Rogers et al., 2004; Reilly, Peelle, Antonucci, & Grossman, 2011).

A deficit at the stage of conceptual preparation leading to a semantic representation is depicted in Figure 1B. In this hypothetical example, one feature for 'dog' fails to be activated (woof), some features are only partially activated (guard, pet) and one feature that does not pertain to 'dog' is partially activated (meow). A degraded semantic representation may or may not lead to successful lemma retrieval, depending on the degree of degradation, and the integrity of the links between the semantic and lemma levels. In this example, lemma retrieval is not successful, as depicted by the lack of spreading activation to the lemma level. It is incontrovertible that deficient semantic representations will interfere with lexical access, if not derail the process entirely, thus making a major contribution to anomia in semantic variant PPA.

However, it is not clear whether semantic deficits are sufficient to completely explain anomia in semantic variant PPA. There are many patients in whom naming impairments seem disproportionate to the degree of semantic loss. For example, Graham, Patterson and

Hodges (1995) described a patient, FM, with "progressive and profound anomia" who had only a mild impairment of conceptual knowledge that remained stable over time. Graham et al. (1995) argued that FM's primary impairment was at a post-semantic stage of speech production, such that the semantic system could not communicate with the phonological output lexicon. Similarly, Mesulam and colleagues showed that in many instances of anomia in patients with semantic variant PPA (Mesulam et al., 2009) or neurodegeneration of the left anterior temporal lobe (Mesulam et al., 2013), patients were nevertheless able to provide accurate verbal definitions of unnamed objects. The ability to provide an accurate definition suggests a relatively intact semantic representation, implying that these instances of anomia may arise at a post-semantic stage of lexical access.

While these findings are suggestive, they do not clearly establish a contribution of postsemantic processes to naming impairments. An alternative explanation could be that partially degraded semantic representations are sufficient to perform tasks probing conceptual knowledge, yet insufficient to successfully drive lexical access. In a seminal study, Lambon Ralph and colleagues (2001) showed that patients like FM (Graham et al., 1995) lie on one end of a continuum, in terms of the extent to which naming deficits are commensurate with, or exceed, the degree of semantic impairment. They showed that the discrepancy between naming and semantic impairment is associated with the lateralization of anterior temporal atrophy, such that patients with left-lateralized atrophy have naming deficits that exceed their semantic deficits. Lambon Ralph et al. (2001) presented a computational model in which distributed semantic representations in the left and right anterior temporal lobes differ in the extent to which they are connected to left-lateralized phonological representations. This enabled the authors to account for the range of naming deficits in terms of disruption of semantic representations alone. Moreover, under the assumptions of their model, even modest semantic deficits were capable of causing profound anomia.

Lambon Ralph et al. (2001) acknowledged that although their account of naming deficits in terms of semantic damage alone has a strong advantage of parsimony, they could not rule out an alternative explanation involving an additional disruption to downstream processes, such as the lemma level, or the connections to the lemma level. The latter is depicted in Figure 1C, which shows an intact semantic representation, but damage to the mappings between semantic representations and lemmas, such that the correct lemma cannot be selected. In contrast to Figure 1B, the semantic representations themselves are intact. Because of the adequate semantic representation, a patient with damage to the links between semantic representations and lemmas would be expected to be able to provide a definition of a concept that cannot be named, and should be able to perform semantic matching tasks involving the concept. In principle it should be possible to distinguish empirically between 1B and 1C by assessing the integrity of conceptual knowledge (Graham et al., 1995; Mesulam et al., 2009, 2013). But in practice, it is hard to say how minimal the semantic impairment would need to be before one could conclude that the damage must be to the links rather than the representations themselves.

There is another possible post-semantic locus though that could contribute to anomia: the stage of word form retrieval, subsequent to access of the lemma. This is depicted in Figure

1D. Critically, a breakdown at this level can be empirically distinguished from a breakdown at earlier levels, because now the lemma has been accessed, so lexical-syntactic information such as grammatical gender that is associated with the lemma should be available (Badecker et al., 1995).

The goal of this study was to clarify at which stage(s) lexical access breaks down in semantic variant PPA, and in particular to determine whether patients ever access lemma representations of items they cannot name. The French language was chosen because nouns in French are marked for grammatical gender, a prototypical type of lemma-level lexicalsyntactic information. We asked eleven French-speaking individuals with semantic variant PPA to name objects, and then asked them to "guess" the grammatical gender of items they could not name. Because grammatical gender is semantically arbitrary in French, if a patient knows the grammatical gender of an item that they cannot name, this means they must have successfully activated and selected the appropriate lemma, which implies in turn that the lexical access breakdown happened at a post-semantic stage subsequent to lemma retrieval. In semantic variant PPA, this would effectively localize the breakdown to the stage of word form retrieval, because the fourth and final stage outlined above-transformation of a phonological form into a motor plan-can be excluded, since these patients make very few phonemic paraphasias or apraxic errors that would be characteristic of breakdown at this level (Warrington, 1975; Schwartz et al., 1979; Snowden et al., 1989; Hodges et al., 1992; Wilson et al., 2010).

We also queried two other types of information about unnamed items. First, we used a semantic matching task to assess conceptual knowledge of the item, so as to confirm that semantic representations were degraded but not completely destroyed. Second, we asked patients to guess the initial letter and the length of the orthographic form. Figure 1D depicts partial access to the word form, even though it cannot be retrieved in its entirety. In the "tipof-the-tongue" state, which is generally considered to be a breakdown of word form retrieval, limited word form information is often available: people are quite good at guessing the initial sound and the length of the word on the tip of the tongue (Brown, 1991; Brown & McNeill, 1966; Miozzo & Caramazza, 1997; Vigliocco et al., 1997). One possible explanation for this is that partial word form information at the lemma level may facilitate linking to the word form (Garrett, 1984; Vigliocco et al., 1997). In feed-forward models of lexical access (e.g. Levelt et al., 1999), partial knowledge of word form is strictly contingent on access to the lemma, and so would provide further evidence that the lemma was correctly selected. In interactive models (e.g. Dell, 1986; Lambon Ralph et al., 2001), because of the bi-directional spreading activation between semantic, lemma and word form levels, the interpretation of partial word form knowledge is more complicated, and will be discussed later.

2. Methods

2.1. Patients

Eleven French-speaking patients with semantic variant PPA and 18 healthy age-matched control participants took part in the study. The patients were recruited through the Centre de Référence "Démences Rares" (Reference Center for Rare Dementias) at the Pitié Salpêtrière

Hospital in Paris, France. The control participants were spouses, family members, or friends of the patients. The study was approved by the institutional review board at the Pitié Salpêtrière Hospital, and all participants gave written informed consent. De-identified data were analyzed at Vanderbilt University Medical Center.

Patients were diagnosed with semantic variant PPA according to recent guidelines (Gorno-Tempini et al., 2011). Clinical diagnosis was based on a multi-disciplinary evaluation including neurological examination, standard neuropsychological tests and a detailed language evaluation. A diagnosis of PPA required progressive deterioration of speech and/or language functions and that deficits be largely restricted to speech and/or language for at least two years. A diagnosis of semantic variant PPA in particular required two core features to be present: impaired confrontation naming and impaired single word comprehension. At least three of the four following features were also required: impaired object knowledge, surface dyslexia or dysgraphia, spared repetition, and spared speech production. Neuroimaging results were not used for diagnostic purposes, but only to rule out other causes of focal brain damage. However, neuroimaging revealed anterior temporal atrophy in all 11 patients. Additional inclusion criteria were (1) native speaker of French; (2) a score of at least 15 on the Mini-Mental State Examination (Folstein, Folstein, & McHugh, 1975); (3) left-lateralized atrophy of the anterior temporal lobe (note that patients meeting clinical criteria for semantic variant PPA but with right-lateralized atrophy were not included); and (4) naming no better than 65/80 on the confrontation naming test "Test de dénomination orale d'images: DO 80" (Deloche & Hannequin, 1997); this criterion was to ensure that there would be a sufficient number of unnamed items to investigate partial knowledge in these instances. This last criterion was applied retrospectively; an additional seven patients were run who were mildly impaired and whose naming scores exceeded 65/80, but these patients made too few errors to determine with any degree of confidence their degree of semantic, lexical-syntactic or word form knowledge for unnamed items.

Demographic, clinical, and neuropsychological characteristics of the patients and control participants are provided in Table 1. The controls did not differ from the patients in terms of age (p = 0.71), sex (p = 1) or years of education (p = 0.94). The patients had lower scores than controls on the MMSE (p = 0.0006). All patients and controls were right-handed.

2.2. Experimental design

Each patient was presented with a series of 63 items. Each item comprised up to six slides (Figure 2). The slides were successively presented by the examiner on a laptop computer. The first slide showed a colored picture of an object, which patients were asked to name. If they provided the expected target word, they were not presented with the other five slides, but moved directly to the next item. If they provided any response other than the expected target, they were presented with five follow-up slides as follows.

The first follow-up slide tested for knowledge of grammatical gender. It contained the picture again, with the words un (masculine indefinite determiner) and une (feminine indefinite determiner) printed below it. The patient was asked to point to which of these forms of the determiner went with the picture.

The second and third follow-up slides tested for non-verbal conceptual knowledge of the item. The picture of the item was shown in the center of the slide, surrounded by a circle. Four other pictures were shown in the four corners of the slide, one of which was related to the target, and three of which were not. The patient was asked to indicate which of the four pictures in the corner matched the target picture in the center. This is essentially identical to the structure of the Pyramids and Palm Trees—Pictures test (Howard & Patterson, 1992) and the Camel and Cactus Test (Bozeat et al., 2000).

The fourth follow-up slide tested for knowledge of the length of the orthographic word form. Below the picture were printed two series of dashes, one of which contained one dash for each letter of the target word, and the other of which was either three dashes shorter, or three dashes longer. The patient was asked to point to which series of dashes represented the length of the word.

The fifth and final follow-up slide tested for knowledge of the initial letter of the orthographic word form. Again, two series of dashes were presented below the picture, both of which were now the correct length. One side showed the correct initial letter, and the other side showed an incorrect initial letter. The patient was asked to point to which side showed the correct initial letter.

The procedure was the same for controls, except that controls completed all 6 slides for all items, even when the target words were produced on the first slide (as they almost invariably were).

2.3. Stimuli

The picture stimuli were colorized versions (Rossion & Pourtois, 2004) of the Snodgrass and Vanderwart (1980) pictures. Pictures were considered for inclusion if they had monomorphemic target names in French, and were thought likely to have high name agreement in French based on our intuitions and the French normative data provided by Rossion and Pourtois (2004). Of the pictures meeting these criteria, 63 were selected essentially randomly, and presented in the experiment. However of the 63 pictures presented, 11 proved to have name agreement less than 80% in the control participants. These items were excluded without further analysis, leaving 52 items on which all subsequent analyses were carried out.

The target words and their properties are shown in Table 2. There were 25 with masculine gender and 27 with feminine gender. Of the 52 items, 42 had name agreement of 100%, and the mean name agreement was $98.3 \pm 4.1\%$. The mean log frequency (per million words) was 2.65 ± 1.54 (New, Pallier, Brysbaert, & Ferrand, 2004).

The semantic matching trials were created using images of related or unrelated concepts obtained with Google image search. The word length foils were either three letters longer or three letters shorter than the length of the target word. Each foil initial letter was approximately matched to the target initial letter in terms of how many French words begin with that letter.

2.4. Data analysis

Naming responses were considered correct when the intended target or an acceptable alternative was produced. All acceptable alternatives which were accepted, which were few, are shown in Table 2. Only one patient with semantic variant PPA produced a single acceptable alternative (pointe 'nail' for clou 'nail'). Errors were classified as no response, semantic errors, or phonemic paraphasias.

For each task (conceptual knowledge, grammatical gender, and the two word form tasks), the performance of the group of 11 retained patients was compared to chance using a one sample t-test. Conceptual knowledge was defined as correct answers on both semantic matching slides. Since each slide involves 4 alternatives, chance performance on this task would be $1/4 \times 1/4 = 6.25\%$. On the grammatical gender task, chance performance was 50%, because grammatical gender is not predictable from meaning in French, with the exception of a few circumscribed semantic domains (Nelson, 2005). On the word form tasks, chance performance was also 50%. For each task, a chi-square test was used to determine whether there were genuine differences between patients, as opposed to random variability around the group mean.

Each individual patient's score on each task was compared to chance with a binomial test, to determine how many of the 11 patients had (partially) preserved access to the information in question. To account for multiple comparisons, a bootstrapping procedure was used for each task. The number of patients whose scores were better than chance (individual p < 0.05) was compared to the empirical distribution (based on 10,000 iterations) of 11 "patients" guessing on the exact number of trials that each patient actually performed (i.e. the number of unnamed or incorrectly named items).

Contingencies between different types of knowledge about unnamed or incorrectly named items were evaluated using Pearson correlations across the group of 11 patients, and by comparing accuracy was one aspect of knowledge (e.g. initial letter) when the response provided for another aspect (e.g. grammatical gender) was correct or incorrect.

3. Results

3.1. Naming

Naming accuracy in the 11 patients was $44.4 \pm 22.4\%$ (range 11.5% to 78.8%) (Figure 3, Table 3). This substantial range reflected genuine differences between patients and not just random variability around the group mean ($\chi^2 = 105.23$, p < 0.0001).

3.2. Grammatical gender

Grammatical gender judgment for unnamed or incorrectly named items was $57.9 \pm 14.1\%$ correct (range 34.8% to 76.9%) (Figure 3, Table 3). This was significantly better than chance at the group level (chance = 50%, t = 1.86, df = 10, p = 0.046), but the variability reflected genuine differences between patients ($\chi^2 = 18.67$, p = 0.045).

Four of the eleven patients (patients 2, 7, 10, 11) individually performed better than chance (bootstrapping p = 0.0003 for 4 or more out of 11 better than chance; see Table 3 for

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individual p values), suggesting that these patients accessed lemma representations for at least some unnamed items. Regarding the remaining seven patients, some of them were numerically better than chance, and therefore may have had partial access to grammatical gender which did not reach statistical significance given the numbers of unnamed items, whereas others were at chance or below, suggesting no access to grammatical gender.

Accuracy was also tabulated separately for masculine and feminine unnamed or incorrectly named items (Table 4). Two of the patients with above-chance knowledge of grammatical gender performed similarly well on masculine and feminine items (patients 2 and 10), one performed better on masculine items (patient 7), and one performed better on feminine items (patient 11). Response biases were also seen in some of the patients who did not perform better than chance: patients 1, 4, and 9 exhibited response biases towards masculine, while patients 5 and 8 were more likely to respond feminine. These data show that while response biases were often present in either direction in patients with or without preserved access to grammatical gender, the four patients with above-chance knowledge of gender clearly showed differential likelihoods of responding masculine or feminine depending on the actual grammatical gender of each item.

3.3. Conceptual knowledge

Accuracy on the conceptual knowledge task (i.e., correct answers on both semantic matching questions) for unnamed or incorrectly named items was $47.1 \pm 22.5\%$ (range 23.9% to 92.3%), which was significantly better than chance (chance = 6.25%, t = 6.00, df = 10, p = 0.0001) (Figure 3, Table 3). Variability on the conceptual knowledge task reflected genuine differences between patients ($\chi^2 = 47.22$, p < 0.0001). However, all 11 patients individually performed better than chance (bootstrapping p < 0.0001 for 11/11 better than chance; see Table 3 for individual p values), suggesting that conceptual knowledge was partially but not completely degraded. Conceptual knowledge of unnamed items was highly correlated with naming accuracy (r = 0.71, p = 0.014), consistent with the established finding that semantic impairments making a strong contribution to naming deficits in semantic variant PPA.

3.4. Word form

Initial letter judgment for unnamed or incorrectly named items was $64.1 \pm 16.9\%$ correct (range 41.3% to 87.5%) (Figure 3, Table 3). This was significantly better than chance at the group level (chance = 50%, t = 2.78, df = 10, p = 0.0098). The variability reflected genuine differences between patients ($\chi^2 = 31.71$, p = 0.0004).

Four of the eleven patients (patients 1, 2, 5, 7) individually performed better than chance (bootstrapping p = 0.0003 for 4 or more out of 11 better than chance; see Table 3 for individual p values), suggesting that these patients may have accessed lemma representations for some unnamed items. Some of the remaining seven may have had partial access to the initial letter that did not reach significance, whereas the others were at or below chance and probably had no access at all.

Of the four patients whose initial letter judgments were better than chance, two also performed better than chance for grammatical gender judgment (participants 2 and 7), while the other two were at chance for grammatical gender.

Length judgment for unnamed or incorrectly named items was $57.3 \pm 8.1\%$ correct (range 45.9% to 73.7%) (Figure 3, Table 3), which was significantly better than chance at the group level (chance = 50%, t = 2.98, df = 10, p = 0.0069). There was no evidence for genuine differences between patients ($\chi^2 = 6.78$, p = 0.75), and only one of the eleven patients (patient 3) was individually better than chance (bootstrapping p = 0.36, not significant). Although this patient also performed above chance (but not significantly so) for judgments of grammatical gender and initial letter, the evidence for lemma access is equivocal enough that it will be disregarded for this patient.

3.5. Contingencies between access to different kinds of information

Contingencies were then examined between access to different kinds of information about unnamed or incorrectly named items.

There was no correlation across patients between performance on the conceptual knowledge and grammatical gender judgment tasks (r = 0.10, p = 0.78). Grammatical gender judgment accuracy was numerically higher on items for which the conceptual knowledge questions were answered correctly ($4.9 \pm 13.6\%$ better), but this difference did not reach significance (t = 1.20, df = 10, p = 0.13).

There was a correlation between conceptual knowledge and initial letter judgment (r = 0.75, p = 0.0084), and a trend toward a correlation between conceptual knowledge and length judgment (r = 0.50, p = 0.12). Initial letter judgment accuracy was significantly better on items for which the conceptual knowledge questions were answered correctly ($12.0 \pm 19.7\%$ better, t = 2.02, df = 10, p = 0.036), but length judgment was not significantly better (3.3 $\pm 20.7\%$ better, t = 0.53, df = 10, p = 0.30).

Across patients, grammatical gender judgment was not correlated with either initial letter judgment (r = -0.22, p = 0.53) or length judgment (r = 0.39, p = 0.23). Judging the grammatical gender correctly did not significantly improve either judgment of the initial letter ($8.2 \pm 29.9\%$ better, t = 0.91, df = 10, p = 0.19) or the length ($4.3 \pm 18.3\%$ better, t = 0.78, df = 10, p = 0.23). Likewise, judging the initial letter correctly did not significantly improve judgment of grammatical gender ($10.0 \pm 39.9\%$ better, t = 0.83, df = 10, p = 0.21), and judging the length correctly did not significantly improve judgment of grammatical gender (4.1 + 18.1% better, t = 0.76, df = 10, p = 0.23).

3.6. Controls

The 18 healthy age-matched controls were essentially at ceiling on naming and the judgment of grammatical gender, initial letter and length (Table 3). The few errors reflected close semantic errors, and responses to follow-up questions that pertained to the lexical-syntactic and word form properties of the erroneous names produced (Table 2). Accuracy on the conceptual knowledge task was $92.0 \pm 4.9\%$ (range 82.7% to 100%), confirming that the items were generally appropriately constructed. The control data were not compared directly

to the patient data, since controls were queried on all items, whereas patients were queried only on items that were unnamed or incorrectly named.

4. Discussion

Our most important finding was that four of the eleven individuals with semantic variant PPA were above chance in reporting the grammatical gender of items that they could not name. According to well-developed theories of lexical access (Levelt et al., 1999; Dell et al., 1997), access to grammatical gender is mediated by activation and selection of the lemma. From the additional established fact that patients with semantic variant PPA rarely make phonemic paraphasias or apraxic speech sound errors that would be indicative of impairments at later stages of syllabification, phonetic encoding or articulation, we can infer that lexical access failed at least some of the time at the stage of word form retrieval (Figure 1D).

This conclusion holds in feed-forward as well as interactive models of lexical access. In Levelt et al.'s (1999) feed-forward model, each stage takes place in serial order. There is no access to grammatical gender until a lemma is selected, so knowledge of grammatical gender straightforwardly implies that a lemma has been selected. In Dell's (1986; Dell et al., 1997) interactive model, information flows bi-directionally between semantic, lemma and word form levels, but there is still a discrete step of lemma selection at which the most activated lemma is given a "jolt" of activation. Access to lexical-syntactic information can therefore only be explained as a consequence of one lemma being selected over all others. The model proposed by Lambon Ralph et al. (2001) is also interactive, but it cannot be assessed in terms of access to grammatical gender because it does not involve any intervening representations between the semantic and word form levels, and it makes no claims regarding how grammatical gender is represented.

Based on their performance on the grammatical gender judgment task, we can estimate how often these four patients with partially preserved access to grammatical gender accessed lemmas of unnamed items. The four patients reported grammatical gender correctly for 66%, 69%, 70%, and 77% of unnamed items. Because this was a two-alternative forced choice task, for each incorrect response, there was probably another item on which the patient also guessed but happened to be correct. So for example, for patient 11 who scored 70% on gender judgment, we know that on 30% of trials she gave the wrong answer, so she must not have known the gender. But this implies that there were another approximately 30% of trials where she also did not know the gender, but happened to guess correctly. So she probably knew the gender (and therefore accessed the lemma) about $100 - 30 \times 2 = 40\%$ of the time. Applying this same logic to each patient, the four patients appear to have accessed the lemma for between 32% and 54% of unnamed items. In other words, a non-trivial proportion of naming failures in these patients seem to reflect a failure at the level of word form retrieval, rather than directly reflecting semantic impairments.

Four of the eleven patients showed partial knowledge of the orthographic word forms of items they could not name; specifically, they were above chance in reporting the initial letter of the word. Two of these four also were above chance in reporting grammatical gender.

Although Levelt et al.'s (1999) feed-forward model pertains to phonological, not orthographic, retrieval, the strictly serial nature of processing in this model implies that retrieval of any word form information is subsequent to retrieval of the lemma. Hence according to this theory, these four patients must also have retrieved the lemma at least some of the time.

In Dell's (1986; Dell et al., 1997) interactive model, the most natural explanation for the availability of word form information is also that the lemma has been retrieved. The tip-ofthe-tongue state, in which partial phonological (and orthographic) information is often available, is generally interpreted as indicating lemma access with a failure of word form retrieval, just as it is in the Levelt model. However the interactive nature of Dell's model means that phonemes (and graphemes) are activated prior to selection of a lemma, making other explanations possible for partial knowledge of word form. For instance, suppose that due to degraded semantic representations, a small cohort of semantically related lemmas (e.g. dog, cat, wolf) were equally activated for the target dog. Due to interactive activation spreading, phonemes (and graphemes) of these words would be activated. If selection of a lemma failed due to no lemma being sufficiently active relative to the others, the phonemes could plausibly remain activated. Then, in a two-alternative forced-choice task where the patient was asked to choose between 'D' and any letter other than 'C' (for cat) or 'W' (for wolf), they may be able to choose 'D', even though the dog lemma was never selected. Partial activation through the system, even due to deficient semantic representations, has been similarly invoked to explain modest benefits from phonemic cues in semantic variant PPA (Jefferies, Patterson, & Lambon Ralph, 2008).

In sum, it is possible for an interactive model in which the only impairment is at the semantic level to account for partial knowledge of word forms. On the other hand, the most straightforward explanation even in an interactive model remains that the lemma was accessed. Therefore, we consider the partial word form knowledge demonstrated by four patients as suggestive but not conclusive evidence of a post-semantic impairment of word form retrieval. Note that a spreading activation account cannot similarly explain the above-chance knowledge of grammatical gender observed in four patients. This is because there are only two grammatical genders in French, so the only way for one to be more highly activated than the other is for a single lemma to be more highly activated than all other lemmas. Any cohort of mutually active semantically related lemmas would be likely to comprise both masculine and feminine nouns, which would not, on average, lead to activation of either grammatical gender above the other.

Even in the six patients for whom word form retrieval seemed to contribute to naming deficits, there were still many items where lexical-syntactic and word form information was unavailable, suggesting that lemmas were not accessed. Moreover, five patients showed little or no evidence for access to grammatical gender or word form form, suggesting that lemmas were never accessed. All of these lexical access failures therefore reflect either deterioration of conceptual knowledge, i.e. breakdown in the stage of conceptual preparation leading to a semantic representation (Figure 1B), or deficits in mapping semantic representations onto lemmas (Figure 1C). The strong correlation we observed between naming and performance on the semantic matching task suggests that the former—deterioration of conceptual

knowledge—is the predominant cause of naming deficits. This is consistent with much prior research, which has shown that the progression and severity of naming deficits are strongly associated with the progression and severity of the deterioration of conceptual knowledge (Adlam et al., 2006; Hodges et al., 1995; Jefferies & Lambon Ralph, 2006; Lambon Ralph et al., 2001; Rogers et al., 2004; Reilly et al., 2011). To argue convincingly for the alternative explanation of a deficit in mapping between semantic representations and lemmas, it would be necessary to demonstrate preserved semantic processing but no access to lemmadependent information. Only one of the patients we studied performed above 80% on the semantic matching task, and that patient showed statistically significant knowledge of grammatical gender and the initial letter of unnamed items, suggesting that he often accessed the lemmas of unnamed items. Although there were many instances in all patients where both semantic matching questions were answered correctly, but the grammatical gender and word form judgments were incorrect, these items can readily be explained in terms of a conceptual deficit alone, assuming that the semantic representations were intact enough to perform the matching task, but degraded enough to interfere with lemma selection (Lambon Ralph et al., 2001).

There were modest contingencies between accuracy on the conceptual knowledge task, and on the grammatical judgment and word form judgment tasks, which reached significance in just a few cases. Such contingencies would be predicted by any model, since the more degraded a conceptual representation is, the less likely that downstream representations can be accessed. Perhaps surprisingly, there were no correlations or contingencies between judgments of grammatical gender and orthographic word form, even though both of these types of information are thought to depend on lemma retrieval. This is also the case for healthy speakers in tip-of-the-tongue states (Caramazza & Miozzo, 1997). These authors argued that the lack of a positive relationship between these two types of knowledge is problematic for models of lexical access at which access to word forms is mediated by lemma nodes that encode lexical-syntactic information (e.g. Levelt et al., 1999). We concur with this view: we believe the model of Levelt et al. (1999) implies that grammatical gender should always be available when any word form information is accessible. Roelofs, Meyer, and Levelt (1998) argued that grammatical gender need not be accessed in such situations when it is not needed, but the problem is that it actually is needed, by virtue of being overtly queried (Caramazza & Miozzo, 1998). But we believe that the alternative model proposed by Caramazza and Miozzo (1997; see also Caramazza, 1997) actually also predicts a contingency between knowledge of grammatical gender and word form information, because although both syntactic and word form features are connected to the same lexical node, which would seem to allow their independent access, the tip-of-the-tongue state is claimed to reflect the relevant lexical node being "unselected but highly activated" (Caramazza & Miozzo, 1997, p. 332). In other words, the blocking mechanism is prior to the bifurcation into syntactic and word form networks, which seems to imply that the availability of syntactic and word form information should be impacted in parallel. Our findings support the model architecture proposed by Caramazza and Miozzo, in which there are distinct links between lemmas and lexical-syntactic and word form information, but suggest that word form access deficits may involve not the activation of the lemma, but rather the integrity of the links from the lemma to these two types of information.

As described in the introduction, several previous studies have suggested that post-semantic stages of lexical access contribute to anomia in semantic variant PPA (Graham et al., 1995; Mesulam et al., 2009, 2013). However, no studies to our knowledge have investigated the availability of lexical-syntactic information, which we have shown permits more specific inferences as to precisely where the mapping from semantic representations to spoken words breaks down. It is noteworthy that Lambon Ralph et al. (2001) showed that patients whose atrophy is more left-lateralized have a greater discrepancy between naming and semantic impairments than those with right-lateralized atrophy, because of the left-lateralized anterior temporal atrophy. It is likely that if we included patients with right-lateralized atrophy, we would see a smaller proportion of breakdowns at the levels of word form retrieval.

A number of other studies have shown that in semantic variant PPA, lexical syntactic information, including argument structure and the mass/count distinction, can be largely retained even when the semantic content of items is lost (Breedin & Saffran, 1999; Breedin, Saffran, & Coslett, 1994; Garrard, Carroll, Vinson, & Vigliocco, 2004; Schwartz et al., 1979; Saffran & Schwartz, 1994; Taler, Jarema, & Saumier, 2005). Unlike the present study which focuses on speech production, these studies involve the comprehension of spoken or written material. By essentially demonstrating access to the lemma (but not the semantic representation), they are showing that the links between word forms and lemmas are often more robust than semantic representations themselves or their links to lemmas. This suggests that the relative burdens on different levels of representation may differ between production and comprehension: conceptual knowledge deficits are a constant in either case, but the linguistic stages (lemmas, word forms) are more vulnerable in production than comprehension.

We are aware of only one previous study that has investigated grammatical gender in semantic variant PPA: Lambon Ralph et al., (2011) did not investigate access to the grammatical gender of items that could not be named, but rather asked whether patients could determine the grammatical gender of word forms that were presented to them, and whether this was impacted by the phonological typicality of the items. The authors found that gender errors were made for low-frequency atypical items, similar to the pattern that is seen in many other linguistic and non-linguistic domains in semantic variant PPA (Patterson et al., 2006).

5. Conclusion

In sum, we showed that anomia in semantic variant PPA does not always solely reflect deterioration of conceptual knowledge, but that in some patients there is also a contribution of the post-semantic stage of word form retrieval. The strongest evidence for word form retrieval playing a role was that four of the eleven patients we studied showed evidence for access to grammatical gender of items they could not name, indicating that lemma representations had been accessed, so the breakdown must have been subsequent to that. Two of these patients, and two additional patients, also showed evidence for partial knowledge of orthographic word forms, which is also most naturally explained as a

breakdown in word form retrieval subsequent to lemma access, although in this case, other accounts are tenable.

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Highlights

- Lexical access in semantic variant PPA was studied in eleven French-speaking patients
- Four patients showed partial knowledge of the grammatical genders of unnamed items
- Two of these patients and two others showed partial knowledge of phonological forms
- Access to these types of information suggests that lemmas have been retrieved
- This suggests a post-semantic contribution to anomia in six of the eleven patients



Figure 1.

Model of lexical access. (A) The architecture of the model is based on Dell et al. (1997). Blue shading and lines represent successful cascading activation of a feature-based semantic representation, a lemma and a word form, which would then be syllabified, encoded and mapped to a motor plan. (B) Impairment at the level of semantic representations (indicated by a red line). Note that one feature for 'dog' are not activated (woof), some features are only partially activated (guard, pet: light blue) and one feature that does not belong to 'dog' is partially activated (meow). A degraded semantic representation may or may not lead to successful lemma retrieval (depending on the degree of degradation, and the integrity of the links between the semantic and lemma levels). In this example, lemma retrieval is not successful. (C) Impairment at the level of lemma retrieval. In this example, the semantic representation is completely intact, but because of the degraded links between semantic representations and lemmas, no lemma is activated. (D) Impairment at the level of word form retrieval. The semantic representation is intact and a lemma has been selected, so lexical syntactic information (grammatical gender) is available. In this example, there is partial activation (light blue) of the word form (the first phoneme), which is not sufficient for the word to be produced.



Figure 2.

Structure of the items. The word in this example is papillon (masc.) 'butterfly'. The six slides investigate naming, grammatical gender judgment, conceptual knowledge (two slides), initial letter judgment and length judgment.



Figure 3.

Access to different aspects of lexical items. For each of the 11 patients whose naming accuracy was < 80%, the accuracies for naming, conceptual knowledge, gender, initial letter, and length tasks are shown. The chance levels for each task are indicated with gray dotted lines, and individual scores that significantly exceed chance (p < 0.05) are circled. The mean and standard error of the mean are indicated with black lines and error bars.

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Demographic and neuropsychological characteristics of the patients and controls

Patient	Age	Sex	Education (years)	MMSE (30)	Duration (years)	Mattis DRS	Naming (DO80)	BDAE SWC	BDAE Severity	PPT-W (52)	PPT-P (52)	Phonemic fluency	Semantic fluency
1	78	ц	17	28	3	119	65	66.0	5	45	43	15	7
2	62	Μ	17	29	б	136	59	71.0	4	44	44	18	12
3	64	ц	17	26	б	123	36	65.0	4	32	35	23	10
4	99	Μ	6	26	4	118	28	59.0	4	30	36	12	4
5	61	Μ	17	20	б		20	53.0	2	39	44	12	5
9	62	ц	12	25	9	124	24	59.0	ю	34	37	18	6
7	63	Μ	6	24	9	114	23	58.5	б	40	40	11	7
8	71	Μ	15	21	5	113	13	45.0	2	17	33	15	0
6	49	ц	6	18	4	118	15	28.0	ю	I	26	8	7
10	79	Μ	20	19	5	66	9	33.5	2	29	23	0	0
11	70	ц	12	23	8	108	9	43.5	ю	25	31	5	0
SvPPA mean	65.9 ± 8.4	6M/5F	14 ± 3.9	23.5 ± 3.7	4.5 ± 1.6	117.2 ± 9.9	26.8 ± 19.6	52.9 ± 13.8	3.2 ± 1	33.5 ± 8.8	35.6 ± 7.0	12.5 ± 6.5	5.5 ± 4.2
Control mean	67.1 ± 8.2	11M/7F	14.1 ± 3.8	28.9 ± 1.0									

MMSE = Mini Mental State Examination (Folstein et al., 1975); Mattis DRS = Mattis Dementia Rating Scale; DO 80: Test de dénomination orale d'images (Deloche & Hannequin, 1997); BDAE: Boston Diagnostic Aphasia Examination (Mazaux & Orgogozo, 1982); SWC = Single word comprehension; PPT-W and PPT-P: Pyramids and Palm Trees—Words and Pictures respectively (Howard & Patterson, 1992); SvPPA = Semantic variant primary progressive aphasia. Means and standard deviations are shown.

Agreement (%) Non-target responses	100	100	100	100	100	100	100	94 1 × pointe (m.) 'nail' (acceptable)	100	83 3 × porc (m.) 'pig' (acceptable)	100	94 $1 \times oie (f.)$ 'goose' (error)	83 3 × index (m.) 'index' (acceptable)	100	100	100	100	94 1 × moineau (m.) 'sparrow' (acceptable)	100	89 2 × gâteau (m.) 'cake' (error)	100	100	94 $1 \times crayon$ (m.) 'pencil' (error)	100	89 $1 \times violoncelle (m.) 'cello' (error); 1 \times guitare (f.). 'guitar' (error)$	83 3 × guêpe (f.) 'wasp' (error)	100
Foil letter	M	D	Н	Z	Ъ	Г	0	R	ц	А	Ъ	D	0	R	IJ	в	n	Υ	Ъ	R	D	L	IJ	Н	В	0	0
Initial letter	A	А	В	В	С	С	С	С	С	С	С	С	D	L	L	Z	0	0	0	Ъ	Р	Р	S	Т	Λ	А	A
Foil length	6	8	3	7	8	8	6	7	8	3	10	8	8	9	8	9	7	3	7	7	5	5	8	5	6	4	5
Length	6	S	9	4	S	S	9	4	S	9	7	S	S	ю	S	з	4	9	4	4	8	8	S	8	9	٢	8
Gender	ш	ш	ш	ш	ш	ш	ш	ш	ш	ш	ш	ш	ш	ш	ш	ш	ш	ш	ш	ш	ш	ш	ш	ш	ш	f	f
English	accordion	airplane	balloon	arm	cannon	dog	cigar	nail	clown	pig	necklace	swan	finger	bed	book	nose	eye	bird	bear	bread	butterfly	umbrella	pen	stool	violin	bee	needle
French	accordéon	avion	ballon	bras	canon	chien	cigare	clou	clown	cochon	collier	cygne	doigt	lit	livre	nez	oeil	oiseau	ours	pain	papillon	parapluie	stylo	tabouret	violon	abeille	aiguille

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Non-target responses			$1 \times \text{endive (f.) 'chicory' (error)}$																					
Agreement (%)	100	100	94	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
Foil letter	М	W	D	Я	Г	Μ	IJ	S	Т	T	K	в	Μ	J	Т	Ч	W	S	С	K	S	S	Z	В
Initial letter	А	A	А	В	В	В	С	С	С	С	С	ц	ц	Н	Н	J	Μ	0	Ч	S	Т	Т	>	^
Foil length	8	5	4	7	33	9	ю	9	9	6	4	8	ю	8	8	8	7	10	8	7	8	ю	8	6
Length	5	8	7	10	9	6	9	6	ю	9	7	5	9	5	S	S	4	7	S	4	S	9	5	9
Gender	f	f	f	f	f	Ŧ	f	f	Ŧ	f	f	Ŧ	f	f	f	f	f	f	f	f	f	f	f	f
English	anchor	spider	aspargus	swing	banana	bottle	carrot	shoe	key	bell	tie	flower	ant	ахе	harp	leg	motorcycle	ear	apple	saw	table	tomato	cow	suitcase
French	ancre	araignée	asperge	balançoire	banane	bouteille	carotte	chaussure	cle	cloche	cravate	fleur	fourmi	hache	harpe	jambe	moto	oreille	pomme	scie	table	tomate	vache	valise

Table 3

Lexical access measures

Patient	Namir	ıg	Semantic r	natching	Grammatica	l gender	Initial letter j	judgment	Length jud	lgment
	Accuracy	NR/S/P	Accuracy	d	Accuracy	d	Accuracy	d	Accuracy	d
_	41/52	7/4/0	4/11	0.0035 *	4/11	0.89	9/11	0.033 *	6/11	0.50
5	39/52	11/2/0	12/13	< 0.0001 *	10/13	0.046 *	11/13	0.011 *	8/13	0.29
3	33/52	18/1/0	11/19	< 0.0001 *	12/19	0.18	13/19	0.084	14/19	0.032^{*}
4	29/52	21/1/1	15/23	< 0.0001 *	8/23	0.95	15/23	0.11	12/23	0.50
6	28/52	24/0/0	18/24	< 0.0001 *	13/24	0.42	21/24	0.0001 *	16/24	0.076
6	19/52	33/0/0	13/33	< 0.0001 *	21/33	0.08	18/33	0.36	16/33	0.64
4	17/52	29/3/3	15/35	< 0.0001 *	23/35	0.045 *	26/35	0.0030 *	21/35	0.16
~	17/52	24/9/2	11/35	< 0.0001 *	21/35	0.16	15/35	0.84	18/35	0.50
•	15/52	28/9/0	10/37	< 0.0001 *	16/37	0.84	22/37	0.16	17/37	0.74
10	10/52	39/3/0	11/42	< 0.0001 *	29/42	0.0098 *	19/42	0.78	24/42	0.22
11	6/52	41/5/0	11/46	< 0.0001 *	32/46	0.0057 *	19/46	0.91	27/46	0.15
SvPPA mean	$44.4 \pm 22.4\%$		$47.1 \pm 22.5\%$		$57.9 \pm 14.1\%$		$64.1\pm16.9\%$		$57.3\pm8.1\%$	
Control mean	$98.9\pm1.9\%$		$92.0\pm4.9\%$		$99.5\pm1.4\%$		$99.9\pm0.5\%$		$97.9 \pm 5.9\%$	

Table 4

Accuracy by grammatical gender

Patient Masculine Accuracy Feminine Accuracy 1 3/4 1/7 2 3/4 7/9 3 7/9 5/10 4 5/9 3/14 5 3/9 10/15	
1 3/4 1/7 2 3/4 7/9 3 7/9 5/10 4 5/9 3/14 5 3/9 10/15	ccuracy
2 3/4 7/9 3 7/9 5/10 4 5/9 3/14 5 3/9 10/15	
3 7/9 5/10 4 5/9 3/14 5 3/9 10/15	
4 5/9 3/14 5 3/9 10/15	
5 3/9 10/15	
	5
6 11/15 10/18	8
7 15/19 8/16	
8 4/15 17/20)
9 14/15 2/22	
10 11/17 18/25	5
11 8/19 24/27	7