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Abstract

The semantic variant of primary progressive aphasia (sv-PPA) is a degenerative condition which causes surface dyslexia/dysgraphia, resulting in reading/writing errors of irregular words with non-transparent grapheme-to-phoneme correspondences (e.g., ‘plaid’) as opposed to regular words (e.g., ‘cat’). According to connectionist models, most authors have attributed this deficit to semantic impairments, but this assumption is at odds with symbolic models, such as the DRC account, stating that the reading/writing of irregulars relies on the mental lexicon. Our study investigated whether sv-PPA affects the lexicon in addition to the semantic system, and whether semantic or lexical deficits cause surface dyslexia/dysgraphia, while challenging the two major models of written language.

We explored a cohort of 12 sv-PPA patients and 25 matched healthy controls using a reading and writing task, a semantic task (category decision: living vs. non-living), and a lexical task (lexical decision: word vs. no-neighbor non-word). Correlation analyses were conducted to assess the relationship between reading/writing scores of irregulars and semantic vs. lexical performance. Furthermore, item-by-item analyses explored the consistency of reading/writing errors with item-specific semantic and lexical errors.

Results showed that sv-PPA patients are impaired at reading and writing irregular words, and that they have impaired performance in both the semantic and the lexical task. Reading/writing scores with irregulars correlated significantly with performance in the lexical but not the semantic task. Item-by-item analyses revealed that failure in the lexical task on a given irregular word is a good predictor of reading/writing errors with that item (positive predictive value: 77.5%), which was not the case for the semantic task (positive predictive value: 42.5%).

Our findings show that sv-PPA is not restricted to semantic damage but that it also comprises damage to the mental lexicon, which appears to be the major factor for surface dyslexia/ dysgraphia. Our data support symbolic models whereas they challenge connectionist accounts.

Keywords: semantic variant of primary progressive aphasia; surface dyslexia and dysgraphia; semantics; lexicon

1. Introduction

The semantic variant of primary progressive aphasia (sv-PPA) is a degenerative condition affecting the anterior temporal lobes and causing relatively selective damage to semantic representations (Gorno-Tempini et al., 2004; 2011). In the language domain, this condition leads to anomia, deficits in single-word comprehension, and, frequently, to surface dyslexia/ dysgraphia. The latter impairment is reflected by reading/writing errors with irregular words (also called exception words) for which the phoneme-grapheme correspondence is non-transparent (e.g., 'plaid' incorrectly read as "/pleɪd/" and written as "plad"), as opposed to regulars for which this correspondence is transparent (e.g., 'cat'). Written language has been much less explored in sv-PPA than oral language but surface dyslexia and dysgraphia have already been integrated in the most recent diagnosis criteria (Gorno-Tempini et al., 2011), and they have causatively been attributed to impaired semantics (Patterson and Hodges, 1992; Graham et al., 2000; Woollams et al., 2007; Caine et al., 2009; Brambati et al., 2009; S.M. Wilson et al., 2009; M.A. Wilson et al., 2012; Binney et al., 2016). More specifically, it has been shown that reading errors with irregulars in sv-PPA patients correlate with their scores in the Pyramid and Palm Trees Test requiring semantic associations (Binney et al., 2016), and with their scores on picture naming tasks requiring lexical-semantic aptitudes (Brambati et al., 2009). Likewise, some authors have shown that reading errors with irregulars are correlated with cortical thickness measures of the anterior temporal lobe implementing semantics (Brambati et al., 2009; Binney et al., 2016), and functional MRI in healthy adults has revealed that this region is activated during the reading of irregular words (M.A. Wilson et al., 2012;

Hoffman et al., 2015; Provost et al., 2016). However, several studies have shed substantial doubt on this semantic-centered view by reporting patients who had massive semantic deficits without any surface dyslexia (Schwartz et al., 1979; Cipolotti and Warrington, 1995; Lambon Ralph et al., 1995; Blazely et al., 2005; M.A. Wilson and Martínez-Cuitiño, 2012). Recently, Playfoot et al. (2018) assessed two sv-PPA patients with different language tasks and did not find correlations between semantic impairment and difficulties in reading of irregular words. Moreover, an investigation of sv-PPA cases has suggested that surface dyslexia in sv-PPA might not be related to semantic deficits but to lexical impairment (Boukadi et al., 2016).

In line with this controversy, the two most influential models of reading, namely connectionist and symbolic accounts, postulate two completely different mechanisms for dyslexia/ dysgraphia. The prototype of connectionist accounts is the triangular Parallel Distributed Processing (PDP) model (Plaut et al. 1996), in which semantic, phonological/sound and orthographical patterns are directly interconnected via ‘hidden layers/units’, without any explicit implementation of lexical representations. The model claims that the processing of irregular words, especially of low-frequency irregulars, necessarily depends on a reading/ writing route involving semantics, while regular words can also be processed via a direct route from orthographical to sound patterns. This route is also crucial for novel or non-words which are exclusively processed via this direct pathway. Conversely, symbolic reading models and more particularly the Dual Route Cascaded (DRC) model (Coltheart et al., 2001) state that, in addition to semantic, phonological/sound and orthographical patterns, there is an intermediate and explicit mental lexicon, which contains whole word forms. According to DRC models, this lexical level is critical to the processing of irregular words independently from semantics, mapping word entries in the orthographic lexicon directly onto word entries in the phonological lexicon, during reading, and vice versa during writing.

In sv-PPA the supposedly causative association of semantic failure and surface dyslexia/ dysgraphia is in line with PDP models. However, this causality is at odds with the DRC account predicting that sv-PPA patients also demonstrate critical damage to the orthographic or phonological component of the mental lexicon, which would be the causative factor for reading/writing errors with irregulars (Coltheart et al., 2010). In this controversial context, testing the reading/writing of irregular words in a cohort of sv-PPA patients along with contrastive tasks tapping item-specific semantic and lexical representations would allow for challenging the two models. Likewise, it would provide answers regarding the language components related to surface dyslexia/dysgraphia in sv-PPA by exploring the relationship between reading/writing of irregular words and lexical vs. semantic performances, on both a global correlative and an item-by-item basis.

Regarding tasks specifically tapping lexical representations, lexical decision paradigms (word vs. non-word) are claimed to be a reliable method as attested by computational simulations including computational models with sv-PPA-like lesions (Coltheart et al., 2010). Some connectionist network modellers, however, have suggested that lexical decision relies on the activation of semantic word knowledge (e.g., Woollams et al., 2007; Dilkina et al., 2010). It appears that the critical parameter which makes lexical decision about a real word a genuine lexical task is the nature of the non-words used in the task, namely their word-unlike characteristics (see e.g., Binder et al., 2003). More specifically, some models assuming both lexical and semantic word codes suggest that, in lexical decision tasks, lexical representations are activated by words and by word-like non-words (e.g., McClelland and Rumelhart, 1981). Such quasi-equal lexical activation levels would force the intervention of the semantic system allowing for deciding that a meaningful item is a word (YES answer in lexical decision) and that an item having no meaning is a non-word (NO answer in lexical decision). The parameter of ‘word-likeness’ is reflected by the orthographical/phonological neighborhood size: no-neighbor non-words are ‘word-unlike’ whereas multi-neighbor non-words are ‘word-like’ (Andrews, 1992; Coltheart et al., 2010). Thus, only lexical decision tasks mixing real words and no-neighbor non-words would allow for specifically tapping the lexical level. This claim is also corroborated by a seminal work of James (1975) who found faster lexical decision responses with semantically concrete than abstract words when mixing words with word-like (multi-neighbor) non-words. Such semantic effects totally disappeared when the non-words were unfamiliar letter strings (no-neighbor non-words). Similarly, Evans et al. (2012) found that semantic priming effects in lexical decision tasks increase in magnitude when the added non-words become progressively more word-like, as measured by their orthographical and phonological neighbor size.

In the present study, we therefore explored a cohort of sv-PPA patients using, in addition to reading and writing tasks, a lexical decision paradigm with stimuli comprising non-words without any orthographical or phonological neighbor to provide a reliable lexical marker. Conversely, to directly assess semantic representations, and to diversify the tasks for the patients, we used category decision (living vs. non-living) to provide a semantic marker. Importantly, the tasks included the same irregular word stimuli to allow for direct comparisons/correlations, and for item-by-item analyses of the consistency of reading/writing errors with item-specific category and lexical decision errors. This approach contrasts with previous studies on sv-PPA, which rarely assessed both reading and writing and/or did not use both lexical and semantic markers comprising the same stimuli for item-specific analyses with the exception of some rare studies exploring mainly single cases. With such a stringent approach, we aimed to determine whether sv-PPA patients demonstrate both semantic and lexical damage as predicted by DRC models, whether lexical or/and semantic deficits are related to surface dyslexia/dysgraphia, and whether sv-PPA cohort-based data can provide novel support for either connectionist or symbolic models.

2. Methods

2.1. Participants

Twelve sv-PPA patients were included in the study at the National Reference Center for "PPA and rare dementias" of the Pitié Salpêtrière Hospital, Paris, France. Clinical diagnosis was based on a multi-disciplinary evaluation including neurological examination, standard neuropsychological tests and a detailed language evaluation. All patients satisfied the current consensus criteria for sv-PPA (Gorno-Tempini et al., 2011): they demonstrated isolated or highly predominant language disorders and had progressive single-word comprehension deficits and anomia. They did not have sentence repetition deficits, agrammatism or motor speech disorders. The diagnosis of sv-PPA was also imaging-supported given that all patients had atrophy on MRI affecting the anterior temporal lobes, with left hemispheric lateralization. Patients did not present any neurological/psychiatric disease other than sv-PPA and they did not have non-degenerative lesions on routine MRI such as cerebrovascular disorders. Twenty-five healthy controls, matched with the patients for age and number of years of education were also included in the study (both Fs < 1). Healthy controls were tested with the Mini Mental State Examination (MMSE; Folstein et al., 1975) to ensure the normality of their cognitive abilities (mean score 28.9/30 $\pm$ 1.1; normal $\geq$ 27). They did not have any neurological disease or medical problem that could interfere with cognitive functioning. All participants were native French speakers. Demographic data are summarized in Table 1.

All data were generated during a routine clinical work-up and were retrospectively extracted for the purpose of this study. Therefore, according to French legislation, explicit consent was waived. However, regulations concerning electronic filing were followed, and patients and their relatives were informed that anonymized data might be used in research investigations. The study received approval from the Ethics Committee of the Pitié Salpêtrière Hospital.

Table 1 Demographic data of healthy controls and sv-PPA patients

	controls (mean ± SD)	**sv-PPA** (mean ± SD)
Number of subjects	25	12
Sex (women, men)	13W/12M	8W/4M
Age (years)	65.8 ± 8.6	66.4 ± 7.2
Handedness (R/L)	25R/0L	12R/0L
Years of education	13.4 ± 3.4	12.9 ± 4.3
Symptom duration (years)	///////	3.5 ± 2.1

SD = standard deviation

2.2. General cognitive/language assessment

The general cognitive assessment included among various standard tests the MMSE and the Frontal Assessment Battery (FAB; Dubois et al., 2000). The language assessment consisted of a picture naming test (D080; Deloche and Hannequin, 1997) and the Boston Diagnostic Aphasia Evaluation (BDAE; Mazaux & Orgogozo, 1982). The BDAE included an evaluation of aphasia severity taking into account spontaneous speech and the description of the 'cookie theft picture', a sentence repetition task, and a single-word comprehension task requiring pointing to pictures upon auditory word presentation. We also applied a verbal fluency test comprising letter and category fluency (Cardebat et al., 1990) and a semantic matching test in its verbal and picture version (Pyramids and Palm Trees Test; Howard and Patterson, 1992). Cognitive/language scores are summarized in Table 2.

	sv-PPA **(mean ± SD)**	**Normal threshold**
MMSE (/30)	23.7 ± 3.5	≥ 27
FAB (/18)	14.7 ± 2.9	≥ 16
BDAE – aphasia severity scale	3.1 ± 0.8	> 4
BDAE – single-word comprehension	59.3 ± 4.1	≥ 68
BDAE – sentence repetition	15.1 ± 3.4	≥ 14
Category fluency ('fruits' / 2 minutes)	9.9 ± 5.0	≥ 15
Letter fluency ('P' / 2 minutes)	13.8 ± 8.5	≥ 15
DO80 (/80)	39.5 ± 15.8	≥ 75
PPTT verbal (/50)	33.9 ± 9.7	≥ 45
PPTT pictures (/50)	34.7 ± 9.3	≥ 45

Table 2 Cognitive/language scores of sv-PPA patients

SD = standard deviation. MMSE = Mini Mental State Examination. FAB = Frontal Assessment Battery. BDAE = Boston Diagnostic Aphasia Examination. DO80 = Picture naming task. PPTT = Pyramids and Palm Trees Test. Normal thresholds are calculated as a function of normative values according to the age, sex and educational level of our patient population.

2.3. Experimental Tasks

2.3.1. Reading and Writing tasks

The materials of the reading task included 30 irregular words for both reading and writing according to the irregularity criteria of Beauvois and Derouesné (Brain, 1981) (nouns corresponding to living and non-living entities). There were no homophones among the stimuli. They were contrasted with 30 regular words (nouns corresponding to living and non-living entities), which can also be processed via a direct route from orthographical to phonological patterns, and with 30 non-words the processing of which necessarily depends on this direct sublexical route. Participants were asked to read aloud the stimuli printed in black on white paper sheets (*Times New Roman* font, size 48).

For the writing task, the materials consisted of 15 irregular and 15 regular words (nouns corresponding to living and non-living entities), and of 15 non-words. The participants were asked to write-to-dictation the stimuli, which were auditorily presented by a native French speaker.

Within and between both tasks irregular and regular words were matched for frequency, number of letters and bigram and trigram frequencies (all Fs < 1), and non-words were matched for number of letters with the irregular and regular words (both Fs < 1) (LEXIQUE 2 database, New et al., 2004).

Non-words did not have any orthographical or phonological neighbor and they were orthographically and phonotactically legal.

2.3.2. Lexical decision task

This task was designed as a marker for lexical representations. It contained a written/visual and an auditory version to assess two distinct access routes to abstract representations within the mental lexicon (orthographical and phonological codes), which were predicted to be correlated. The two versions of the task were used to explore access to the distinct components of the mental lexicon given that reading involves the orthographic input component followed by the phonological output component, whereas writing involves the phonological input component followed by the orthographic output component. In this vein, our two versions of the lexical decision task probed for the integrity/breakdown of these four different lexical components.

Both versions contained 45 irregular words, 45 regular words and 100 non-words. The stimulus materials were the same for both versions and the irregular and regular items were identical to those used in the reading task, on the one hand, and in the writing task, on the other hand. Irregular and regular words were matched for frequency, number of letters and bigram and trigram frequencies (all $Fs < 1$). Non-words were matched with regular and irregular words for the number of letters (all $Fs < 1$). Importantly, non-words were matched for bigram frequencies with both regular words ($t = 1.15$, $p = 0.254$) and irregular words ($t = -1.307$, $p = 0.194$). Likewise, non-words were matched for trigram frequencies with both regular words ($t = 1.3567$, $p = 0.179$) and irregular words ($t = -1.75$, $p = 0.083$). Non-words did not have any orthographical or phonological neighbor. They were orthographically and phonotactically legal.

The stimuli were presented on a computer using *E-prime* software. In the written/visual version each trial began with a fixation cross (800 ms), followed by the stimulus word written in black (5000 ms). Between each trial there was a blank screen during 700 ms. In the auditory version each stimulus trial consisted in the presentation of a fixation cross (800 ms) followed by an auditory target stimulus delivered through headphones. All words had been recorded by a female native French speaker and digitized for binaural headphone presentation using *COOL EDIT* software. In both versions the participants were asked to decide as accurately and as fast as possible whether the word target exists in French or not, by pressing the "YES" or the "NO" button on a computer keyboard. Participants answered by pressing "YES" or "NO" with the index finger and the middle finger of their dominant hand, respectively. Before being tested on each version of the task participants were familiarized with the procedure by five training trials.

2.3.3. Category decision task

The task assessed whether a given written word refers, or not, to a living entity, and was conceived as a marker for semantic representations. In contrast to the lexical decision task we only used a written version because it is usually assumed that there are no distinct phonological or orthographical codes of semantic representations. This binary task of semantic capacities was used because the procedure, and the involved response mechanisms, are similar to the lexical decision task (word vs. non-word) given that YES/NO answers are also required for (living vs. non-living) decisions. The task takes also into account aspects of interactive models positing that the access to semantic features can be activated by orthographical/phonological features (e.g., Joanisse & Seidenberg, 1999), even if hidden layers, which might reflect an equivalent of lexical representations, are degraded. More specifically, we included 32 words reflecting ‘living’ categories (e.g., “cat”) and 64 words reflecting ‘non-living’ categories (e.g., “mat”), using 45 irregular words and 51 regular words. The 45 irregular items, and the 45 regular items out of the 51, were exactly the same as those used in the lexical decision task, and as those used in the reading and writing tasks. Among the irregular words 20 corresponded to ‘living’ items and 25 corresponded to ‘non-living’ items. ‘Living’ and ‘non-living’ items were matched for frequency and number of letters (both $Fs < 1$). To ensure that our stimuli do not contain semantically ambiguous items regarding the living/non-living contrast we previously conducted a pilot study with 20 young healthy adults who classified with high accuracy the living and non-living items (allover 98% of correct responses).

The stimuli were presented on a computer using *E-prime* software. Each trial began with a fixation cross (800 ms), followed by the stimulus word written in black (5000 ms). Between each trial there was a blank screen during 700 ms. Participants were asked to decide as accurately and as fast as possible whether the word target represents a 'living' entity or not, by pressing the "YES" or the "NO" button on a computer keyboard. Participants answered by pressing "YES" or "NO" with the index finger and the middle finger of their dominant hand, respectively. Before being tested on the task participants were familiarized with the procedure by five training trials.

The order of the experimental tasks was randomized. They were administered at 60-90 minute intervals to minimize potential cross-task biases given that they included the same irregular and regular word stimuli. To further minimize such biases the tests of the general cognitive and language assessment were administered during these intervals.

2.4. Statistical analyses

We first computed *d'* and c-values for the auditory and visual versions of the lexical decision task and for the category decision task in patients to assess the sensitivity of these tasks and possible response biases. Then, we used a *mixed-effects model* to look for differences between performances of sv-PPA patients and healthy controls, and to compare the different stimulus conditions within the experimental tasks. *Linear mixed models* were used to identify differences between reaction times (RT) on correct answers for sv-PPA patients and healthy controls in the auditory and visual versions of the lexical decision task and in the category decision task. We then conducted Pearson's correlations assessing the relationship between performance in the lexical decision and the category decision task, to strengthen the claim that the two tasks tap distinct representations, namely lexical and semantic information. We also assessed the relationship between word frequency and RT in the lexical decision task to support that lexical access was occurring in this task. Correlation analyses were also used to explore the relationship between the reading/writing performances on irregular words and performance on these irregulars in the lexical decision task (lexical marker) and the category decision task (semantic marker). All these correlation analyses were conducted in patients and in healthy controls. Bonferroni correction for multiple comparisons was applied. In a second step we analyzed, on an item-by-item basis (consistency analyses), whether lexical decision errors and/or category decision errors on a given irregular word reliably predict errors on that item in the writing and the reading task. Finally, we conducted a multiple regression assessing the prediction of reading/writing errors with irregular words based on category decision and visual lexical decision measures with the aim to identify which of those two latter measures has the best power to explain reading/writing errors on irregulars.

3. Results

3.1. Sensitivity and response bias

Mean *d'* for the auditory and visual lexical decision tasks and for the category decision task were, respectively, 2.72, 2.55 and 1.13. All *d'* values were significantly different from '0' (all $p < 0.001$) indicating that patients were answering above the chance level. Mean *c-values* were 0.23 and 0.02 for the auditory and visual lexical decision tasks, respectively, showing a small bias towards 'YES' answers ('word exists') which was not significant. For the category decision task patients also showed a non-significant bias towards 'YES' answers (mean *c-value* = 0.07).

3.2. Analyses of the experimental tasks

All analyses were conducted with 'group' (sv-PPA, controls) and 'stimulus type' as fixed effects and 'subjects' and 'items' as random effects. Results of the reading and the writing task are illustrated in Figure 1. Results of the two versions of the lexical decision task and the results of the category decision task are illustrated in Figure 2. Mean values and standard deviations for patients and healthy controls, and for all tasks are illustrated in the Supplementary Tables 1-5.

3.2.1. Reading task: The stimulus types were 'irregular words', 'regular words' and 'non-words'. A significant main effect of 'group' was found, with patients showing poorer performances than controls ($p < 0.001$). There was also a 'stimulus type' effect ($p < 0.001$) and a significant interaction between 'group' and 'stimulus type' ($p < 0.001$). Pairwise comparisons with Sidak adjustment for multiple comparisons showed that this interaction was related to the fact that patients had poorer performance with irregular words than with non-words ($p = 0.001$) and regular words ($p < 0.001$) whereas controls demonstrated the inverse pattern for non-words ($p = 0.029$). Performance with regular words was better than with non-words for controls ($p = 0.001$) whereas there was no difference between regular and irregular words. The comparison between controls and patients showed that irregular words yielded poorer performance in patients than in controls ($p < 0.001$) whereas performance with regular words and non-words was similar in patients and controls. Detailed statistical results are shown in Table 3.

Table 3 Mixed-effects model for the reading task (df = degrees of freedom)

Source	Numerator df	Denominator df	F-value	p-value
Intercept	1	100.210	2566.660	<0.001
Group	1	35.000	30.86	<0.001
Stimulus type	2	88.762	8.723	<0.001
Interaction	2	3202.000	77.548	<0.001

3.2.2. Writing task: We used the same stimulus types as in the reading task. A significant main effect of 'group' was found, with patients showing poorer performances than controls ($p < 0.001$). There was also a 'stimulus type' effect ($p < 0.001$) and a significant interaction between 'group' and 'stimulus type' ($p < 0.001$). Pairwise comparisons with Sidak adjustment for multiple comparisons showed that this interaction was related to the fact that patients had poorer performance with irregular words than with non-words, and performance with regular words was better than with irregular words and non-words (regular vs. irregular words: $p < 0.001$ regular words vs. non-words: $p = 0.016$). There was no difference between stimulus type for controls. The comparison between controls and patients showed that irregular words and non-words yielded poorer performance in patients than in controls (irregular words: $p < 0.001$; non-words: $p = 0.017$) whereas performance with regular words was similar in patients and controls. Detailed statistical results are shown in Table 4.

Table 4 Mixed-effects model for the writing task (df = degrees of freedom)

Source	Numerator df	Denominator df	F-value	p-value
Intercept	1	55.996	2104.967	<0.001
Group	1	35.000	82.972	<0.001
Stimulus type	2	44.648	25.704	<0.001
Interaction	2	1582.000	108.861	<0.001

3.2.3. Lexical decision task: The independent variables were “group” and “stimulus type” (regular words, irregular words). For the written/visual version, a significant main effect of ‘group’ was found, with patients showing poorer performances than controls ($p < 0.001$). There was no stimulus type effect and no group x stimulus type interaction. Using reaction times (RT) as the dependant variable, there was a main effect of ‘group’, with patients showing slower RT than controls ($p < 0.001$). There was no stimulus type effect and no group x stimulus type interaction. For the auditory version, there was also a main effect of ‘group’, with patients showing poorer performance than controls ($p < 0.001$). There was no stimulus type effect and no group x stimulus type interaction. Using RT as the dependant variable, there was a main effect of ‘group’, with patients showing slower RT than controls ($p < 0.001$). There was no stimulus type effect and no group x stimulus type interaction. Detailed statistical results are shown in Table 5a and 5b.

Table 5a Mixed-effects model for performances in the visual version of the lexical decision task (df = degrees of freedom)

Source	**Numerator df**	**Denominator df**	**F-value**	**p-value**
Intercept	1	47.769	7590.323	<0.001
Group	1	35.800	35.479	<0.001
Stimulus type	2	204.196	1.453	0.236
Interaction	2	6802	0.668	0.513

Table 5b Mixed-effects model for performances on the auditory version of the lexical decision task (df = degrees of freedom)

Source	**Numerator df**	**Denominator df**	**F-value**	**p-value**
Intercept	1	56.993	10680.742	<0.001
Group	1	35.594	52.413	<0.001

Stimulus type	2	205.820	0.486	0.616
Interaction	2	6802	10.698	<0.001

3.2.4. Category decision task: The independent variables were "group" (sv-PPA, controls), category ('living', 'non-living') and "stimulus type" (regular words, irregular words). A significant main effect of 'group' was found, with patients showing poorer performances than controls ($p < 0.001$). There was no category effect, no stimulus type effect and no interaction between the variables. Using RT as the dependent variable, there was a main effect of 'group', with patients showing slower RT than controls. There was no category effect, no stimulus type effect and no interaction between the variables. Detailed statistical results are shown in Table 6.

Table 6 Mixed-effects model for performances in the category decision task (df = degrees of freedom)

Source	Numerator df	Denominator df	F-value	p-value
Intercept	1	63.699	1438.975	<0.001
Group	1	36.501	42.078	<0.001
Stimulus type	1	97.951	0.112	0.739
Category	1	97.951	0.141	0.708
Group*StimulusType*Category	2	197.480	2.163	0.118
Group*StimulusType	1	3417.000	0.865	0.352
Group*Category	1	3417.000	0.928	0.335

3.3. Pearson's correlation analyses

Correlation analyses were performed by extracting the mean performance (all items aggregated) for each participant for each of the tasks. The analyses were first conducted in patients which provide sufficient performance variability i) to explore whether the lexical markers (lexical decision scores) and the semantic markers (category decision scores) tap distinct language representations, i.e. lexical vs. semantic codes, and ii) to evaluate whether lexical and/or semantic markers are related to reading/writing failures with irregular words. Correlation results are summarized in Table 7. In addition, we also conducted correlation analyses in healthy controls even if their performance variability and near ceiling-effects might make such correlations less informative and meaningful (see Table 8).

Regarding the first issue, performance of patients and of healthy controls in the auditory and written/visual lexical decision task were correlated, indicating that both tasks tap related, yet distinct representations within the mental lexicon containing orthographic and phonological codes. By contrast, performance in the category decision task did not correlate with those in the written/visual or the auditory version of the lexical decision task, with the exception of written/visual lexical decision in controls. In patients and controls there was a negative correlation between word frequency and response reaction times (RT) in the visual and in the auditory version of the lexical decision task i) for all word items, ii) for irregular items, and iii) for regular items (with the exception of auditory lexical decision in controls), supporting that lexical access was occurring in the task.

Regarding the second issue, reading performance of patients with irregular words was significantly correlated with scores in the written/visual and in the auditory version of the lexical decision task. By contrast, there was no correlation between reading scores and scores in the category decision task. Likewise, writing performance with irregulars was correlated with scores in the written/visual version and in the auditory version of the lexical decision task. Conversely, no correlation was found between the scores on irregulars and the scores in the category decision task. In controls there were no significant correlations probably due to ceiling effects, with the exception of writing performance with irregular words and performance in the visual lexical decision task. In addition, we conducted correlation analyses with two standard test of semantics: the Pyramids and Palm Trees Test and the single-word comprehension test of the BDAE. Scores of the verbal version but not of the picture version of the PPTT were correlated with reading and writing performance on irregular words. Scores of the Pyramids and Palm Trees Test did not correlate with values of the category decision task. Scores on single-word comprehension correlated significantly with the scores of the experimental category decision task indicating that our task genuinely assesses semantic capacities constituting the main criterion for sv-PPA diagnosis (Gorno-Tempini et al., 2011). As for the category decision task, scores of the single-word comprehension test were not correlated with reading and writing performance on irregular words.

Table 7 Pearson's correlation results between the different measures for sv-PPA patients

Correlated measures	R	p-value
Auditory lexical decision / Visual lexical decision	0.86	0.0003
Category decision / Visual lexical decision	0.29	0.35
Category decision / Auditory lexical decision	0.28	0.38
Word frequency (total) / Visual lexical decision RT	-0.31	0.003
Word frequency (regulars) / Visual lexical decision RT	-0.38	0.009
Word frequency (irregulars) / Visual lexical decision RT	-.052	<0.001
Word frequency (total) / Auditory lexical decision RT	-0.3	0.005
Word frequency (regulars) / Auditory lexical decision RT	-0.36	0.015
Word frequency (irregulars) / Auditory lexical decision RT	-0.34	0.0023
Reading (irregulars) / Visual lexical decision	0.82	0.001
Reading (irregulars) / Auditory lexical decision	0.69	0.009
Reading (irregulars) / Category decision	0.38	0.39

Writing (irregulars) / Visual lexical decision	0.74	0.006
Writing (irregulars) / Auditory lexical decision	0.75	0.005
Writing (irregulars) / Category decision	0.27	0.45
Reading (irregulars) / Verbal PPTT	0.59	0.043
Writing (irregulars) / Verbal PPTT	0.58	0.046
Reading (irregulars) / Picture PPTT	0.41	0.18
Writing (irregulars) / Picture PPTT	0.18	0.57
Reading (irregulars) / Single-word comprehension	0.126	0.694
Writing (irregulars) / Single-word comprehension	- 0.007	0.982
Category decision / Verbal PPTT	-0.168	0.602
Category decision / Visual PPTT	-0.532	0.075
Category decision / Single-word comprehension	0.63	0.028

RT = Reaction times. PPTT = Pyramids and Palm Trees Test

Table 8 Pearson's correlation results between the different measures for the healthy controls

Correlated measures	**R**	**p-value**
Auditory lexical decision / Visual lexical decision	0.4033	0.045
Category decision / Visual lexical decision	0.49	0.012
Category decision / Auditory lexical decision	0.261	0.207
Word frequency (total) / Visual lexical decision RT	-0.4	0.0001
Word frequency (regulars) / Visual lexical decision RT	-0.545	0.0001
Word frequency (irregulars) / Visual lexical decision RT	-0.442	0.0024
Word frequency (total) / Auditory lexical decision RT	-0.3622	0.001
Word frequency (regulars) / Auditory lexical decision RT	-0.171	0.262
Word frequency (irregulars) / Auditory lexical decision RT	-0.415	0.005
Reading (irregulars) / Visual lexical decision	0.1	0.634
Reading (irregulars) / Auditory lexical decision	0.279	0.175

Reading (irregulars) / Category decision	0.222	0.285
Writing (irregulars) / Visual lexical decision	0.434	0.03
Writing (irregulars) / Auditory lexical decision	-0.289	0.161
Writing (irregulars) / Category decision	0.037	0.86

3.4. Item-by-item consistency analyses

In the patient group, we analyzed the consistency of errors for each of the irregular words between the reading and writing tasks, and the two versions of the lexical decision task and between the reading and writing tasks and the category decision task. This procedure allowed for determining the predictive value of the lexical task (lexical decision) and the semantic task (category decision) for reading/writing errors on irregular words. More specifically, we calculated 1) the number of item-specific co-occurring reading/writing errors and lexical decision errors (written/visual version) on irregular words divided by the total number of errors on irregulars in the written/visual version of the lexical decision task, 2) the number of item-specific co-occurring reading/writing errors and lexical decision errors (auditory version) on irregular words divided by the total number of errors on irregulars in the auditory version of the lexical decision task, 3) the number of item-specific co-occurring reading/writing errors and category decision errors divided by the total number of errors on irregulars in the category decision task.

The results showed that the item-specific consistency is high between the reading/writing tasks and the two versions of the lexical decision task (Positive Predictive Values written/visual version: 77.6%; auditory version: 77.4%). By contrast, the consistency is lower between the reading/writing tasks and the category decision task (Positive Predictive Value: 42.4%). Thus, lexical errors for a given irregular item are highly predictive of reading/writing errors with that item whereas semantic errors for a given irregular item are less predictive of reading/writing errors with that item.

3.5. Multiple regression model

A multiple regression was conducted using the number of reading/writing errors with irregulars as the dependent variable and category decision and visual lexical decision performances as explanatory variables. Auditory lexical decision was not included in the model as an explanatory variable since there is a high correlation between this measure and visual lexical decision, which would violate the multicollinearity assumption that requires that no strong correlation exists between explanatory variables in order to perform a multiple regression. Our multiple regression model statistically significantly predicted reading/writing errors with irregulars ($F(2, 9) = 6.974$, $p = 0.01$, adjusted $R^2 = 0.521$). In particular, only the visual lexical decision variable, but not the category decision variable, added statistically significantly to the prediction ($p = 0.005$). Regression coefficients and standard errors are shown in Table 9.

Table 9 Summary of multiple regression analysis

Variables	B	SE_B	β
Intercept	117.661	24.693	
Category decision	-0.170	0.117	-0.315
Visual lexical decision	-0.902	0.243	-0.803*

* $p < 0.005$. B = unstandardized regression coefficient. SE_B = Standard error of the coefficient. β = standardized coefficient

4. Discussion

We explored a cohort of sv-PPA patients to investigate whether surface dyslexia/dysgraphia is related to damage to the semantic system as proposed by authors adhering to connectionist models or whether, in accordance with symbolic accounts, it is linked to impairments of the orthographic or phonological component of the mental lexicon. Concomitantly we investigated two directly related issues: whether sv-PPA patients demonstrate lexical damage in addition to semantic breakdown, and whether cohort-based sv-PPA findings can provide novel evidence supporting either symbolic or connectionist models. Our findings, based on reading/writing scores with irregular words, on lexical and semantic markers, and on the application of correlations, item-by-item consistency analyses, and a multiple regression model show i) that sv-PPA affects the mental lexicon, ii) that the lexical but not the semantic impairment correlates with markers of surface dyslexia/dysgraphia, iii) that lexical failure on a given irregular item reliably predicts reading/writing errors on that item, and iv) that lexical decision markers but not semantic category decision markers predict reading/writing errors with irregulars.

More specifically, our results showed that in sv-PPA reading and writing performance with irregular words was significantly lower than performance with regular words and non-words, thus providing the signature of surface dyslexia/dysgraphia. Results from both the auditory and the written/visual version of the no-neighbor non-word controlled lexical decision task revealed poor performance in sv-PPA, indicating lexical impairment. Importantly, trigram/ bigram frequencies were matched between irregular (and regular) words and non-words to avoid that lexical decisions might be made upon orthographical/sound features, as often stipulated by connectionist modelers, and to show that they rather depend on genuine lexical representations. There was also a negative correlation between word frequency and reaction times in both versions of the task for i) all items (regulars and irregulars combined), ii) for regulars, and iii) for irregulars. These results further corroborate that lexical access was occurring, and they justify the use of no-neighbor non-words which enabled participants to access word-specific knowledge rather than word meaning. Such lexical deficits concomitantly occurred with semantic breakdown as shown by massive impairment in the category decision task. The correlation analyses showed that reading/writing performance with irregulars was significantly related to lexical decision scores whereas there was no correlation with semantic-based category decision results. The link between surface dyslexia/ dysgraphia and lexical impairment was substantiated by the item-by-item analyses revealing a high item-specific consistency between reading/writing errors and lexical decision errors. These analyses demonstrated a high positive predictive value (77.5%) indicating that lexical errors on an irregular item co-occur with reading/writing failure on that item. By contrast, semantic errors were poorer item-specific predictors of reading/writing errors (42.5%). Finally, the multiple regression analysis showed that the lexical decision marker, but not the category decision marker, significantly predicts reading/writing errors with irregular words, thus reinforcing and extending our item-by-item analyses. Regarding correlations in our healthy control group with lexical or semantic markers it is probable that the lack of significant results is simply related to the low performance variability in the healthy population yielding near-ceiling effects. However, this lack of correlations in healthy adults does not weaken our data or conclusions. Sv-PPA was explored because it represents a powerful model of semantic/lexical disorders and of reading/writing impairments with irregular words, thus allowing for elucidating the issue whether disorders with irregular words are predicted by semantic or lexical impairment, or both factors. Furthermore, sv-PPA patients demonstrate an exploitable variability of performance levels, thus allowing for meaningful correlation analyses which show that only lexical markers correlate significantly with performance on irregular words. However, future studies could explore the link between irregulars and semantic vs. lexical capacities in healthy participants by using more continuous markers/measures of reading/writing which might provide the necessary data variability as for example millisecond-measures of reading times for irregulars.

Our findings are in line with previous studies showing the existence of surface dyslexia in sv-PPA (e.g., Patterson and Hodges, 1992; Caine et al., 2009, Brambati et al., 2009; M.A. Wilson et al., 2012), demonstrating poor performance on lexical decision in sv-PPA (Graham et al., 2000; Rogers et al., 2004; Benedet et al., 2006; Patterson et al., 2006; Jeffries et al., 2010), and suggesting lexical disorders in this PPA variant (Mesulam et al., 2013; 2014; Wilson et al., 2014; 2017; Boukadi et al., 2016). Our data extend and enrich previous evidence, and challenge several findings suggesting that surface dyslexia is specifically related to semantic breakdown (e.g., Macoir and Bernier, 2002; Brambati et al., 2009; Wilson et al., 2012). First, unlike most investigations focusing primarily on surface dyslexia in sv-PPA, our study extends the processing failure on irregular words to the writing modality. Although some rare studies did find surface dysgraphia in sv-PPA (Graham et al., 2000; Macoir and Bernier., 2002; Caine et al., 2009; Shim et al., 2012), they did not provide direct comparisons between reading and writing with experimental materials using the same word stimuli. The only exception for such a direct comparison is the study of Henry et al. (2012) who included 6 sv-PPA patients within a cohort of 15 PPA patients, yet without providing statistical analyses of reading/writing data for the sv-PPA subgroup. Second, our results enrich and specify findings from previous lexical decision tasks, and proposals that sv-PPA entails lexical impairment, given that investigations applying lexical decision paradigms in sv-PPA used word and non-word stimuli which could hardly demonstrate that low performance was related to lexical rather than semantic failure. In this context, the exclusive use of no-neighbor non-words in the present lexical decision design allowed for specifically assessing lexical representations (Binder et al., 2003; Coltheart, 2010), thus confirming the existence of genuine lexical impairment in sv-PPA. Furthermore, negative correlation between word frequency and reaction times in both versions of the lexical decision task for regulars and irregulars corroborate that lexical access occurs. The claim about lexical impairment is also consistent with our correlation analyses indicating that the lexical decision task and the category decision task tap distinct representations, i.e. lexical (orthographic or phonological) vs. semantic information. More specifically, they showed significant correlation values between the auditory and the written/visual version of the lexical decision task whereas no correlation was found between lexical decision and category decision scores. This lexical/semantic distinction also holds for the item-by-item analyses showing that the co-occurrence of errors in the written/visual and auditory version of the lexical decision task was high (85%) whereas it was low for the lexical decision and the semantic-based category decision task (35%). Third, our main finding challenges previous accounts assuming the causal role of exclusively semantic deficits in surface dyslexia, as our results have revealed a direct relationship between reading/writing errors on irregular words and lexical markers, via both correlation and item-by-item consistency analyses.

These outcomes, however, do not allow for inferring that semantics does not play a role in surface dyslexia/dysgraphia given that scores on the verbal version of the Pyramids and Palm Trees Test slightly correlated with performance on irregular words in the reading and writing task. This is consistent with findings of Binney et al., (2016) who also showed correlations between reading of irregulars and the verbal but not the picture version of the Pyramids and Palm Trees Test. Furthermore, in our study the item-specific consistency of reading/writing errors with semantic failure is not negligible, reflecting about 40% of concomitant semantic and reading/writing errors with irregulars. Nevertheless, this percentage is substantially lower than the item-by-item consistency between surface dyslexia/dysgraphia and lexical breakdown. Our results regarding item-by-item consistency are also in line with previous studies exploring such consistency in single cases (Graham et al., 1994; Funnell, 1996; Macoir and Bernoer., 2002; Blazely et al., 2005) or in small series of sv-PPA patients (McKay et al., 2007). However, our cohort-based data add the information that item consistency is higher when analyzing lexical markers in addition to semantic markers. Blazely et al. (2005) reported that their patient had semantic impairments, as shown by performances on picture naming, single-word comprehension and word-picture matching tasks, along with surface dyslexia. This patient also showed impairments in a lexical decision task. However, while performances in the three semantic tasks correlated with each other, performances in the lexical decision task did not correlate significantly with performances in the semantic tasks. These results suggest, as ours do, that impairment in lexical decision is driven also by impairments other than semantic ones. However, in this study the authors did not explore item-by-item consistency between reading errors with irregulars and any other task, which did not allow for making inferences regarding the semantic vs. lexical mechanism underlying surface dyslexia in semantic dementia patients. Our cohort-based data add the information that item consistency in reading/writing of irregulars is higher when analyzing lexical markers (lexical decision task) then when analyzing semantic markers.

One might wonder whether the category decision task, using the same irregular items as the lexical decision task, allows for assessing semantic knowledge on lexically rejected words (NO-answers in lexical decision). Strictly serial models state that the access to semantic representations critically depends on the fact that a given item has been activated in the mental lexicon. Interactive models however (e.g., Rumelhart & McClelland, 1986; Joanisse & Seidenberg, 1999) propose that degraded lexical representations allow for the activation of semantic information presumably via the involvement of an associative pathway directly connecting sound/letter patterns to semantic representations, eventually via 'hidden layers'. Without presuming the existence of such a direct associative pathway, our data indicate that degraded lexical representations in sv-PPA, leading to NO-answers in lexical decision, can allow for accessing correct semantic category representations for a given item. They more specifically highlight that similar proportions of lexically rejected and lexically non-rejected items result in correct living/non-living categorizations (69% and 71%, respectively in the written version; 68% and 73%, respectively in the auditory version).

4.1. Reconciliation with connectionist-inspired literature on dyslexia/dysgraphia in sv-PPA?

How can our findings be reconciled with previous studies attributing surface dyslexia to semantic breakdown and, anatomically, to damage to brain regions involved in semantic processing? Regarding behavioral results on sv-PPA, most authors implicitly accepted connectionist accounts without contrasting them against symbolic models and their predictions. Apparently in line with such connectionist approaches, the available sv-PPA cohort studies have reported significant correlations between reading/writing of irregular words and standard tests of semantics such as the Pyramids and Palm Trees Test or picture naming tasks (e.g., Brambati et al., 2009; Shim et al., 2012; Binney et al., 2016). Our results are compatible with such accounts stating that surface dyslexia/dysgraphia is related to semantic capacities as reflected by our item consistency analyses showing that 40% of semantic errors with a given item co-occur with reading/writing errors on that irregular item. However, item consistency was higher for lexical errors. The previous semantic-centered findings might in part be biased by the use of 'routine' tests which depend on multiple non-semantic factors involving lexical aspects, as well as attention and executive factors which are minimized in our binary category decision task. In line with authors using such routine tests we replicated that scores on the verbal version, but not on the picture version, of the Pyramids and Palm Trees Test are slightly correlated with reading/writing with irregular words. One should note that this test is assumed to assess semantic performance but that its verbal version also depends on lexical access to the test items, requiring the complex processing of three words to find the association between two of them, while our task is a more direct semantic task that requires only the processing of one word at a time.

The most important point is, however, that no investigation on sv-PPA has provided direct comparisons between surface dyslexia and lexical vs. semantic markers, and no study has used item-specific consistency analyses for both lexical and semantic processing domains at a sv-PPA cohort level. Based on this stringent methodology we show that semantic failure plays a role, predicting surface dyslexia in almost half of the items, but we crucially provide novel evidence that lexical impairment is a better predictor and a more important contributor to surface dyslexia/dysgraphia. The latter finding is consistent with several case studies which have reported that semantic breakdown in the explored sv-PPA patients was not associated with reading errors on irregular words (Schwartz et al., 1979; Cipolotti and Warrington, 1995; Lambon Ralph et al., 1995; Blazely et al., 2005; Wilson and Martínez-Cuitiño, 2012). Such results dissociating surface dyslexia and semantics have recently been strengthened by a study on two sv-PPA cases showing a double dissociation with respect to reading performance on irregular words and lexical decision with pseudohomophones, such as the non-word 'brane' derived from the real word 'brain' (Boukadi et al., 2016). According to connectionist models, both lexical decision on such word-like non-words and reading of irregulars depend on the semantic system and therefore no dissociations between the two tasks are predicted. However, there was such a dissociation, and the authors thus propose that their data are compatible with DRC models containing lexical representations, allowing for double damage dissociations within the lexical system itself, which comprises interconnected orthographical and phonological components. In summary, we do not state that surface dyslexia/dysgraphia is unrelated to semantic competency but our data temper this relationship. They indicate that the relationship was probably over-weighted culminating in the widely assumed view that specifically semantic failure causes surface dyslexia/dysgraphia without exploring whether lexical disorders might be the major causative factor.

Regarding the anatomical correlates of surface dyslexia, imaging studies on sv-PPA have primarily implicated semantic-related regions of the temporal cortex, namely left anterior areas (e.g., Brambati et al., 2009; Wilson et al., 2012). However, in sv-PPA atrophy is mainly located in such anterior areas whereas more posterior temporal regions, implementing lexical representations (e.g., Kotz et al., 2002; Graves et al., 2008; 2010), demonstrate lower atrophy variability. This pattern of atrophy in sv-PPA might constitute a bias in finding anatomo-functional correlations between surface dyslexia and brain regions other than anterior temporal regions, leading to non-significant correlation results with posterior temporal areas. Despite this possible bias, and in line with our data highlighting the crucial role of the lexicon, a recent cortical thickness study with one of the largest sv-PPA cohorts (N=33) has shown that more posterior temporal cortices are significantly correlated with surface dyslexia scores (Binney et al., 2016). In the same vein, Binder et al. (2016) have shown surface dyslexia without semantic impairment in stroke patients and their data of voxel-based lesion-symptom mapping suggested “that the posterior middle temporal gyrus may compute an intermediate representation linking semantics with phonology”. This so-called intermediate level represents presumably the mental lexicon which has been demonstrated to be implemented by such posterior temporal cortices (e.g., Kotz et al., 2002; Graves et al. 2008). Nevertheless, the current antomo-functional uncertainty regarding surface dyslexia/agraphia encourages future imaging investigations using rigorously controlled stimulus materials for correlations in large cohorts of PPA patients and for functional MRI investigations in large populations of healthy adults.

Finally, a fundamental issue is whether our data are compatible with connectionist models of reading/writing such as the influential triangle PDP model (e.g., Plaut et al. 1996). The model claims that semantic impairment causes surface dyslexia/dysgraphia, and that the mental lexicon does not play any role because, in their view, it does not exist. Our data are at odds with this line of models by indicating that lexical impairment is critically related to surface dyslexia and dysgraphia. Connectionist modelers could, however, claim that lexical decision tasks, including controlled experimental designs containing no-neighbor non-words, tap semantics, just as category decision tasks do. From this point of view, one should predict significant correlations between the scores from both tasks (lexical decision and category decision), significant correlations between reading/writing of irregular words and both tasks, and item-specific consistency of reading/writing errors with error scores in both tasks. None of these predictions is validated by our data. By contrast, our results are in line with symbolic models such as DRC accounts proposing the existence of a mental lexicon and its major role in reading/writing deficits with irregular words (Coltheart et al., 2010). However, to adopt an equilibrated position, it should be mentioned that several connectionist models implement the notion of 'hidden layers' serving error back-propagation to adjust hidden layer units mediating between semantic, sound and orthographic features. Nevertheless, it has been argued that such hidden units might function as internal representations (Pinker and Prince, 1988), representing in reality the equivalent of aspects of the mental lexicon, and which might computationally model some mechanisms linked to genuine lexical representations. Finally, it could be mentioned that various studies have investigated the existence of the mental lexicon showing its morphological, phonological and syntactic properties while demonstrating that these properties, and operations acting on them such as verb inflection, can not be fully simulated by connectionist hidden layer models (see e.g., Pinker and Ullman, 2002).

5. Conclusion

Our findings refine the knowledge about language deficits in sv-PPA indicating that it is not only characterized by semantic but also by lexical impairment, and demonstrating that the lexical impairment is a crucial factor for surface dyslexia and dysgraphia. Our results also provide novel patient-cohort-based support for symbolic models of reading/writing processes such as DRC accounts whereas they are less compatible with connectionist models. Additional research is now required to specify the precise roles of semantic and lexical competencies for reading/writing in healthy subjects and patients, to enrich models of written language, and to clarify the linguistic targets of rehabilitation strategies.

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References

Andrews, S. (1992). Frequency and neighborhood effects on lexical access: Lexical similarity or orthographic redundancy? *Journal of Experimental Psychology: Learning, Memory, and Cognition*, 18, 234-254.

Beauvois, M.A., Dérouesné, J. (1981). Lexical or orthographic agraphia. *Brain*, 104, 21-49.

Benedet, M., Patterson, K., Gomez-Pastor, I., de la Rocha, M.L.G. (2006). 'Non-semantic' aspects of language in semantic dementia: As normal as they're said to be? *Neurocase*, 12:15-26.

Binder, J.R., McKiernan, K.A., Parsons, M.E., Westbury, C.F., Possing, E.T., Kaufman, J.N., Buchanan, L. (2003). Neural correlates of lexical access during visual word recognition. *J Cogn Neurosci*, 15(3), 372-93.

Binder, J.R., Pillay, S.B., Humphries, C.J., Gross, W.L., Graves, W.W., Book, D.S. (2016). Surface errors without semantic impairment in acquired dyslexia: a voxel-based lesion-symptom mapping study. *Brain*, 139, 1517-1526.

Binney, R.J., Henry, M.L., Babiak, M., Pressman, P.S., Santos-Santos, M.A., Narvid, J., Mandelli, M.L., Strain, P.J., Miller, B.L., Rankin, K.P., Rosen, H.J., Gorno-Tempini, M.L. (2016). Reading words and other people: A comparison of exception word, familiar face and affect processing in the left and right temporal variants of primary progressive aphasia. *Cortex*, 82, 147-63.

Blazely, A.M., Coltheart, M., Casey, B.J. (2005). Semantic impairment with and without surface dyslexia: Implications for models of reading. *Cogn Neuropsychol*, 22(6), 695-717.

Boukadi, M., Potvin, K., Macoir, J., Jr Laforce, R., Poulin, S., Brambati, S.M., Wilson, M.A. (2016). Lexical decision with pseudohomophones and reading in the semantic variant of primary progressive aphasia: A double dissociation. *Neuropsychologia*, 86, 45-56.

Brambati, S.M., Ogar, J., Neuhaus, J., Miller, B.L., Gorno-Tempini, M.L. (2009). Reading disorders in primary progressive aphasia: A behavioral and neuroimaging study. *Neuropsychologia*, 47, 1893-1900.

Caine, D., Breen, N., Patterson, K. (2009). Emergence and progression of 'nonsemantic' deficits in semantic dementia. *Cortex*, 45(4), 483-494.

Cardebat, D., Doyon, B., Puel, M., Goulet, P., Joanette, Y. (1990). Evocation lexicale formelle et sémantique chez des sujets normaux. Performances et dynamiques de la production en fonction du sexe, de l'âge et du niveau d'étude. *Acta Neurologica Belgica*, 90, 207-17.

Cipolotti, L., Warrington, E.K. (1995). Semantic memory and reading abilities: a case report. *J Int Neuropsychol Soc*, 1(1), 104-110.

Coltheart, M., Rastle, K., Perry, C., Langdon, R., Ziegler, J. (2001). DRC: A dual route cascaded model of visual word recognition and reading aloud. *Psychological Review*, 108, 204-256.

Coltheart, M., Saunders, S.J., Tree, J.J. (2010). Computational modelling of the effects of semantic dementia on visual word recognition. *Cogn Neuropsychol*, 27(2), 101-14.

Deloche, G., Hannequin, D. (1997). *Test de dénomination orale d'images : DO 80*. Paris: Éditions du Centre de Psychologie Appliquée.

Dilkina, K., McClelland, J.L., Plaut, D.C. (2010). Are there mental lexicons? The role of semantics in lexical decision. *Brain Res*, 13, 66-81.

Dubois, B., Slachevsky, A., Litvan, I., Pillon, B. (2000). The FAB, a frontal assessment Battery at bedside. *Neurology*, 55, 1621-1626.

Evans, G.A., Lambon Ralph, M.A., Woollams, A.M. (2012). What's in a word? A parametric study of semantic influences on visual word recognition. *Psychon Bull Rev*, 19(2), 325-31.

Folstein, M., Folstein, S., McHugh, P.R. (1975). Mini-Mental State: a practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, 12, 189-198.

Funnell E. (1996). Response biases in oral reading: an account of the co-occurrence of surface dyslexia and semantic dementia. *Q J Exp Psychol A, 49(2)*, :417-46.

Gorno-Tempini, M.L., Dronkers, N., Ranklin, K.P., Ogar, J., Phengrasami, L., Rosen, H.J., et al. (2004). Cognition and Anatomy in three variants of Primary Progressive Aphasia. *Annals of Neurology*, 55, 335-46.

Gorno-Tempini, M.L., Hillis, A.E., Weintraub, S., Kertesz, A., Mendez, M., Cappa, S.F., et al. (2011). Classification of Primary Progressive Aphasia and its variants. *Neurology*, 76*,* 1006-14.

Graham KS, Hodges JR, Patterson K. (1994). The relationship between comprehension and oral reading in progressive fluent aphasia. *Neuropsychologia., 32(3)*, 299-316.

Graham, N.L., Patterson, K., Hodges, J.R. (2000). The impact of semantic memory impairment on spelling: Evidence from semantic dementia. *Neuropsychologia*, 38, 143-163.

Graves, W.W., Grabowski, T.J., Mehta, S., Gupta, P. (2008). Left posterior superior temporal gyrus participates specifically in accessing lexical phonology. *Journal of Cognitive Neuroscience*, *20*, 1698-1710.

Graves, W.W., Desai, R., Humphries, C., Seidenberg, S.S., Binder, J.R. (2010). Neural systems for reading aloud: A multiparametric approach. *Cerebral Cortex*, 20*,* 1799-1815.

Henry ML, Beeson PM, Alexander GE, Rapcsak SZ. (2012). Written language impairments in primary progressive aphasia: a reflection of damage to central semantic and phonological processes. *J Cogn Neurosci, 24(2)*, 261-75.

Hoffman, P., Lambon Ralph, M.A., Woollams, A.M. (2015). Triangulation of the neurocomputational architecture underpinning reading aloud. *Proceedings of the National Academy of Sciences U.S.A.*, 112(28), E3719-28.

Howard, D., Patterson, K. (1992). Pyramids and palm trees: a test of semantic access from pictures and words. *Bury St Edmunds: Thames Valley Test Company*.

James, C.T. (1975). The role of semantic information in lexical decisions. *Journal of Experimental Psychology: Human Perception and Performance*, 104*,* 130-136.

Jefferies, E., Rogers, T.T., Hopper, S., Ralph, MA. (2010). "Pre-semantic" cognition revisited: critical differences between semantic aphasia and semantic dementia. *Neuropsychologia*, 48(1), 248-61.

Joanisse, M.F., Seidenberg, M.S. (1999). Impairments in verb morphology following brain injury: A connectionist model. *Proceedings of the National Academy of Sciences U.S.A.*, 96, 7592–7597.

Kotz, S.A., Cappa, S.F., von Cramon, D.Y., Friederici, A.D. (2002). Modulation of the lexical-semantic network by auditory semantic priming: an event-related functional MRI study. *NeuroImage*, 17(4), 1761-72.

Lambon Ralph, M.A., Ellis, A.W., Franklin, S. (1995). Semantic loss without surface dyslexia. *Neurocase*, 1(4), 363-369.

Macoir, J., Bernier, J. (2002). Is surface dysgraphia tied to semantic impairment ? Evidence from a case of semantic dementia. *Brain and Cognition*, 48(2-3), 452-7.

Mazaux, J.M., Orgogozo, J.M. (1982). *Boston Diagnostic Aphasia Examination. Adaptation française*. Paris: Éditions du Centre de Psychologie Appliquée.

McKay A, Castles A, Davis C, Savage G. (2007). The impact of progressive semantic loss on reading aloud. *Cogn Neuropsychol. 24(2)*, 162-86.

McClelland, J.L., Rumelhart, D.E. (1981). An interactive activation model of context effects in letter perception: Part 1. An account of basic findings. *Psychological Review,* 88*,* 375-407.

Mesulam, M.M., Wieneke, C., Hurley, R., Rademaker, A., Thompson, C.K., Weintraub, S., al. (2013). Words and objects at the tip of the left temporal lobe in primary progressive aphasia. *Brain,* 136, 601-18.

Mesulam, M., Rogalski, E., Wieneke, C., Hurley, R., Geula, C., Bigio, E., et al. (2014). Primary Progressive Aphasia and evolving neurology of the language network. *Nature Reviews Neurology*, 10, 554-69.

New, B., Pallier, C., Ferrand, L., Matos, R. (2004). Une base de données lexicales du français contemporain sur internet: LEXIQUE 2. *Année Psychologique*, 101, 447-62.

Patterson, K., Hodges, J.R. (1992). Deterioration ofword meaning: Implications for reading. *Neuropsychologia*, 30(12), 1025-1040.

Patterson, K., Lambon Ralph, M.A., Jefferies, E., Woollams, A., Jones, R., Hodges, J.R., Rogers, T.T. (2006). "Presemantic" cognition in semantic dementia: Six deficits in search of an explanation. *Journal of Cognitive Neuroscience*, 18, 169-183.

Pinker S., Prince A. (1988). On language and connectionism: analysis of a parallel distributed processing model of language acquisition. *Cognition*, 28(1-2), 73-193.

Pinker S., Ullman MT. (2002). The past and future of the past tense. *Trends Cogn Sci*, 6(11), 456-463.

Plaut, D.C., McClelland, J.L., Seidenberg, M.S., Patterson, K. (1996). Understanding normal and impaired word reading: Computational principles in quasi-regular domains. *Psychol.Rev*, 103(1), 56-115.

Playfoot, D., Billington, J., Tree, J.J. (2018). Reading and visual word recognition ability in semantic dementia is not predicted by semantic performance. *Neuropsychologia,* 111, 292-306.

Provost, J.-S., Brambati, S.M., Chapleau, M., Wilson, A.M. (2016). The effect of aging on the brain network for exception word reading. *Cortex,* 84, 90-100.

Rogers, T.T., Lambon Ralph, M.A., Hodges, J.R., Patterson, K. (2004). Natural selection: The impact of semantic impairment on lexical and object decision. *Cognitive Neuropsychology*, 21, 331-352.

Rumelhart, D., McClelland, J. (1986). On learning the past tenses of English verbs: Implicit rules or parallel distributed processing? In J. McClelland, D. Rumelhart, & the PDP Research Group (Eds.), Parallel distributed processing: E (pp. 216–271). Cambridge: MIT Press.

Schwartz M.F., Marin, O.S., Saffran E.M. (1979). Dissociations of language function in dementia: A case study. *Brain and Language*, 7, 277-306.

Shim, H., Hurley, R.S., Rogalski, E., Mesulam, M.M. (2012). Anatomic, clinical, and neuropsychological correlates of spelling errors in primary progressive aphasia. *Neuropsychologia*, *50*(8), 1929-1935.

Wilson, M.A., Joubert, S., Ferré, P., Belleville, S., Ansaldo, A.I., Joanette, Y., et al. (2012). The role of the left anterior temporal lobe in exception word reading: Reconciling patient and neuroimaging findings. *NeuroImage*, 60(4), 2000-2007.

Wilson, M.A. and Martínez-Cuitiño, M. (2012). Semantic dementia without surface dyslexia in Spanish: unimpaired reading with impaired semantics. *Behav Neurol*. 25(3), 273-84.

Wilson, S.M., Brambati, S.M., Henry, R.G., Handwerker, D.A., Agosta, F., Miller, B.L., Wilkins, D.P., Ogar, J.M., Gorno-Tempini, M.L. (2009). The neural basis of surface dyslexia in semantic dementia. *Brain*, 132(1), 71-86.

Wilson, S.M., DeMarco, A.T., Henry, M.L., Gesierich, B., Babiak, M., Mandelli, M.L., et al. (2014). What role does the anterior temporal lobe play in sentence-level processing? Neural correlates of syntactic processing in semantic PPA. *Journal of Cognitive Neuroscience*, 26, 970-85.

Wilson, S.M., Dehollain, C., Ferrieux, S., Christensen, L.E.H., Teichmann, M. (2017). Lexical access in semantic variant PPA: Evidence for a post-semantic contribution to naming deficits. *Neuropsychologia*, 106, 90-99.

Woollams, A.M., Lambon Ralph, M.A., Plaut, D.C., Patterson, K. (2007). SD-squared: On the association between semantic dementia and surface dyslexia. *Psychological Review*, 114(2), 316-339.

Figure legends

Figure 1 Performance of sv-PPA patients and healthy controls in the reading and writing tasks.

Figure 2 Performance of sv-PPA patients and healthy controls in the lexical decision task (written/visual version, auditory version) and in the category decision task.