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What lies beneath: A comparison of reading aloud in Pure Alexia and Semantic Dementia

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ABSTRACT

Exaggerated effects of word length upon reading aloud performance define Pure Alexia, but have also been observed in Semantic Dementia. Some researchers have proposed a reading-specific account, whereby performance in these two disorders reflects the same cause: impaired orthographic processing. In contrast, according to the primary systems view of acquired reading disorders, Pure Alexia results from a basic visual processing deficit, whereas degraded semantic knowledge undermines reading performance in Semantic Dementia. To explore the source of reading deficits in these two disorders, we compared the reading performance of 10 Pure Alexic and 10 Semantic Dementia patients, matched in terms of overall severity of reading deficit. The results revealed comparable frequency effects on reading accuracy, but weaker effects of regularity in Pure Alexia than Semantic Dementia. Analysis of error types revealed a higher rate of letter-based errors and a lower rate of regularisation responses in Pure Alexia than Semantic Dementia. Error responses were most often words in Pure Alexia but most often nonwords in Semantic Dementia. Although all patients made some letter substitution errors, these were characterised by visual similarity in Pure Alexia and phonological similarity in Semantic Dementia. Overall, the data indicate that the reading deficits in Pure Alexia and Semantic Dementia arise from impairments of visual processing and knowledge of word meaning, respectively. The locus and mechanisms of these impairments are placed within the context of current connectionist models of reading.

Keywords: Reading Aloud; Pure Alexia; Letter-by-Letter Reading; Semantic Dementia; Surface Dyslexia.

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Efficient activation and integration of orthographic knowledge is essential in fluent reading. Any disruption to this process as a consequence of brain damage will result in some form of reading deficit, or acquired dyslexia. One such disorder is pure alexia (PA), which is seen after damage to or disconnection of the left ventral occipito-temporal cortex (vOTC). Behaviourally, the traditional definition of PA is as a highly selective reading deficit, without associated problems in spoken language (aphasia), spelling (dysgraphia) or object recognition (agnosia) (Déjerine, 1892). PA patients experience difficulties in accurate and rapid parallel activation of the letters in words, which undermines their reading. This is evident in a very marked effect of the number of letters in a word on patients' reading speed (Behrmann & Plaut, 2013a; Roberts et al., 2013), which stands in contrast to the minimal effects of word length seen in normal individuals' reading aloud (Henderson, 1982; Weekes, 1997). This exaggerated length effect in PA is interpreted as reflecting sequential letter identification, or letter-by-letter reading, and indeed some patients show this reading strategy overtly.

While the hallmark length effect that defines PA is well established and accepted, the cognitive cause of the reading deficit has been the matter of considerable debate. By one account, PA is a reading specific disorder, and reports of patients who have shown normal visual processing and recognition of objects have been used to support such a view (e.g.,(Kay & Hanley, 1991; Miozzo & Caramazza, 1998) and vice versa (e.g., (Yong, Warren, Warrington, & Crutch, 2013). Within this approach, a number of researchers have suggested that PA arises as a result of damage to an orthographic input lexicon (or its input connections) (e.g., (Marshall & Newcombe, 1973; Noble, Glosser, & Grossman, 2000; Warrington & Langdon, 1994; Warrington & Shallice, 1979; Warrington & Shallice, 1980), which contains entries for all known word forms, and has been associated with left vOTC (Cohen et al., 2002; Vinckier et al., 2007). As a result, these patients can no longer efficiently activate

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3 word forms, so the letter-by-letter reading strategy functions to boost activation of
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5 appropriate candidate lexical entries.
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8 Reading-specific accounts that focus on damage to orthographic *lexical*
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10 representations should predict an increased incidence of nonlexical reading responses which,
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12 in the case of irregular words, would take the form of regularisation errors (e.g., sew read as
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14 "sue"). While PA patients do show some evidence of enhanced effects of regularity on
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16 reading aloud (Behrmann, Nelson, & Sekuler, 1998; Rapcsak & Beeson, 2004), regularisation
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18 responses are relatively rare (Cumming, Patterson, Verfaellie, & Graham, 2006; Patterson &
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20 Kay, 1982). Hence a different form of a reading-specific account proposed that PA patients
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22 may in fact have difficulties with letter recognition, which would compromise input to both
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24 lexical and nonlexical processing (Arguin & Bub, 1993; Behrmann & Shallice, 1995; Bub,
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26 Black, & Howell, 1989; Hanley & Kay, 1996; Howard, 1991; Patterson & Kay, 1982; Perri,
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28 Bartolomeo, & Silveri, 1996; Reuter-Lorenz & Brunn, 1990; Rosazza, Appollonio, Isella, &
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30 Shallice, 2007). This account is consistent with the observation that PA patients often mis-
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32 identify the component letters of words (Cumming, et al., 2006).
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35 A contrasting perspective on PA is that it arises from a particular kind of visual deficit
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37 that undermines the input to the reading system (Behrmann, Plaut, & Nelson, 1998; Farah &
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39 Wallace, 1991). This view falls within the Primary Systems account of acquired dyslexia,
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41 whereby reading disorders arise due to disruption of more basic visual, phonological and
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43 semantic processing (Patterson & Lambon Ralph, 1999), which has been implemented in
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45 connectionist models of reading (Chang, Furber, & Welbourne, 2012a; Plaut & Behrmann,
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47 2011; Welbourne, Woollams, Crisp, & Lambon Ralph, 2011; Woollams, Lambon Ralph,
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49 Plaut, & Patterson, 2007). Neuroimaging studies reveal that vOTC receives high acuity
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51 foveal visual input (Hasson, Harel, Levy, & Malach, 2003; Hasson, Levy, Behrmann,
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53 Hendler, & Malach, 2002; Levy, Hasson, Avidan, Hendler, & Malach, 2001; Malach, Levy,
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& Hasson, 2002; Woodhead, Wise, Sereno, & Leech, 2011), which is particularly salient when dealing with complex and confusable visual stimuli like letter strings. In line with this view, pure alexia patients show reduced sensitivity to higher spatial frequency information (Roberts, et al., 2013), although this is not universal (Starrfelt, Nielsen, Habekost, & Andersen, 2013). Also in keeping with a visual deficit account, the exaggerated length effect is accompanied by increased sensitivity to the visual confusability of letters (Arguin, Fiset, & Bub, 2002; Fiset, Arguin, Bub, Humphreys, & Riddoch, 2005; Harris, Olson, & Humphreys, 2013; Johnson & Rayner, 2007). Interestingly, when higher spatial frequencies are artificially removed, normal individuals show increased effects both of word length and letter confusability (Fiset, Arguin, & Fiset, 2006; Tadros, Fiset, Gosselin, & Arguin, 2009). Yet letter strings are by no means the only stimuli that rely on such information, with this same brain region activated in face and object recognition (Behrmann & Plaut, 2013b; Malach, et al., 2002; Nestor, Behrmann, & Plaut, 2013; Price & Devlin, 2003, 2011; Vogel, Petersen, & Schlaggar, 2012; Woodhead, et al., 2011). By this account then, patients with damage to left vOTC should show impairments in processing any visual stimuli that require medium to high acuity foveal input for effective recognition.

When it has been assessed, the accuracy of non-linguistic visual processing in PA has varied across cases, with some patients apparently showing normal performance (e.g.,(Kay & Hanley, 1991; Miozzo & Caramazza, 1998), while others have shown significant impairments (e.g.,(Cumming, et al., 2006; Roberts, et al., 2013). In studies that have also considered reaction times, which is of course the measure by which their reading deficit is defined, clear evidence of visual processing impairments has emerged, particularly for complex stimuli. Behrmann et al. (1998a) reported five pure alexia patients to be slowed in naming pictures, but only those high in visual complexity. Similarly, a large case series of 21 PA patients revealed significantly impaired performance in matching checkerboard stimuli

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and unfamiliar logographic characters, most markedly for complex items in the presence of visually similar distracters (Roberts et al., 2013, see also (Mycroft, Behrmann, & Kay, 2009). Moreover, performance for this condition was strongly related to the severity of the reading deficit, as measured by the size of the length effect.

Despite mounting evidence for a visual deficit in PA, this is unlikely to be the only possible cause of abnormal word length effects, as these have also been reported in other neuropsychological conditions, such as semantic dementia (SD) (Cumming, et al., 2006; Gold et al., 2005; Patterson & Hodges, 1992). SD is a selective and progressive disorder of conceptual knowledge associated with atrophy and hypometabolism of the anterior temporal lobes (Adlam et al., 2006; Nestor, Fryer, & Hodges, 2006). Reading aloud in SD shows a near-universal pattern of surface dyslexia, where words with exceptional spelling sound correspondences, particularly those low in frequency, are read aloud according to more typical correspondences (regularised). Moreover, accuracy for these exception items is strongly related to the extent of the patients' receptive and expressive semantic deficits (Graham, Patterson, & Hodges, 2000; Patterson et al., 2006; Woollams, et al., 2007). The primary systems interpretation of these findings is that whole word semantic knowledge supports the pronunciation of exception word items (Patterson & Lambon Ralph, 1999; Patterson, et al., 2006).

Yet there have been a few reports of SD patients with accuracy of low-frequency exception word reading falling within the normal range despite an appreciable semantic deficit (Blazely, Coltheart, & Casey, 2005; Cipolotti & Warrington, 1995). This has led some researchers to propose that exception word reading in SD is undermined not by semantic deficits associated with ATL damage, but rather the posterior spread of atrophy into the left vOTC region (Coltheart, Tree, & Saunders, 2010). This account predicts that there should be clear similarities in the reading aloud performance of SD and PA patients. The

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observation of abnormally strong length effects in SD (Cumming, et al., 2006; Gold, et al., 2005), combined with reports of SD cases who have adopted an explicit letter-by-letter reading strategy (Noble, et al., 2000), have been considered evidence for this view. An alternative perspective, however, is that it is these length effects arise as a consequence of reduced support from whole word semantic knowledge that would usually bind the letters of a word together, offsetting costs associated with more letters.

In a direct comparison of the visual processing and reading performance of 3 PA patients with 3 SD patients (Cumming, et al., 2006), performance on non-verbal visual processing tasks for both familiar and unfamiliar objects was normal in SD, but impaired in PA. Letter matching was normal for SD at longer durations, whereas in PA it was universally impaired. Length effects were seen in both types of disorder, but these were significantly smaller for the SD than PA patients (although it should be kept in mind that accuracy was higher in SD than PA). Interestingly, error responses were usually words for the PA patients, but nonwords for the SD patients. This is consistent with work showing enhanced influences of whole word variables in PA (e.g.,(Roberts, Lambon Ralph, & Woollams, 2010). The notion of a bottom-up visual and a top-down semantic impairment both increasing length effects was reinforced by the finding that PA patients showed smaller length effects for words than nonwords, while SD patients showed equivalent effects. Taken together, these results speak to a visual origin of length effects in PA and a semantic cause in SD.

The goal of the present research was to illuminate the source of reading deficits in PA and SD by comparing patients matched on overall severity. Previous work has already compared the effects of length and lexicality in PA and SD (Cumming, et al., 2006), so here we explored the impacts of frequency and regularity using the Surface List (Patterson & Hodges, 1992) and considered not only overall accuracy but also the nature of the patients' reading errors. If the deficits in both PA and SD arise from damage to reading-specific

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orthographic processing, we would expect to see similar reading performance across the two groups. If, in contrast, the two reading deficits arise from underlying visual and semantic causes, respectively, then we would expect (a) weaker effects of regularity for PA than SD, (b) a higher proportion of nonword and regularisation responses in SD than PA, and (c) a higher proportion of incorrect word responses and letter-based errors in PA than SD.

Method:

Participants:

Pure Alexia: For this study we operationally characterised Pure Alexia in terms of a combination of damage to the left occipito-temporal cortex combined with slowed reading and an abnormally large word length effect. Ten PA patients with overt LBL reading of varying degrees participated. All were native speakers of English who had suffered from acute brain injury more than two years prior to the time of testing. These patients were recruited from local NHS speech and language therapy services on the basis of marked increases in word-reading latency as a function of letter length. On our reading list of 180 words (Roberts, et al., 2010), overt LBL responses were produced by every patient.

As can be seen in Table 1, all patients had damage in the occipito-temporal region, as judged by a neurologist, as a consequence of stroke or tumour resection. Scans for eight of the ten patients are provided in the Appendix. Scans for two other patients (PM and KW) were not available, hence the determination of damage was made on the basis of the neurologist's written report. Overall, neuropsychological background assessment indicated that the patients had preserved working memory (digit span (Wechsler, 1987)) and phonological processing, with only a one patient slightly impaired on the more demanding

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tests of phonological segmentation (EW). Deficits in visual processing on at least one subtest of the VOSP (Warrington & James, 1991) were apparent in all patients.

Performance on the Cambridge Picture Naming test (Bozeat, Lambon Ralph, Patterson, Garrard, & Hodges, 2000) revealed impaired performance in all bar one case (PM). Receptive semantic processing tests included the Cambridge Spoken Word to Picture Matching test (Bozeat, Lambon Ralph, et al., 2000) where a spoken word was matched to a target picture amongst nine semantically related alternatives; the Camel and Cactus Pictures test (Bozeat, Lambon Ralph, et al., 2000) , where a target picture was matched to a picture of an associated item in the context of three semantically similar items; and the 96 Synonyms test (Jefferies, Patterson, Jones, & Lambon Ralph, 2009), where a written target word was matched to a synonym in the context of two other related words of similar frequency and imageability (options are also read to the patient by the experimenter). Six patients (TS, KW, SC, EW, MS, & AT) showed mild but measureable impairments on at least one of these receptive semantic tests.

While the prevalence of deficits on these semantic tests could be interpreted as indicating deficits in conceptual knowledge, it is worth noting that all of the tests involved either pictures or written words. Poor performance on these tests is therefore consistent with optic aphasia, if conceptualised as a disconnection of semantics from visual input (Plaut & Shallice, 1993). Yet in light of the demonstrated visual impairments on the VOSP, it seems plausible that impaired performance on the semantic tests in this patient group may have arisen as a consequence of problems in visual processing. We hypothesise that reduced sensitivity to higher spatial frequencies could impair performance on (a) the more demanding subtests of the VOSP such as progressive silhouettes; (b) semantic tests that involve picture identification; and (c) semantic tests that also involve reading written words. Such an account would of course be consistent with the primary systems view and previous reports of

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object processing deficits in this population (e.g, (Behrmann, Nelson, et al., 1998; Mycroft, et al., 2009; Roberts, et al., 2013).

Data for spelling words of different lengths from the PALPA 39 subtest (Kay, Lesser, & Coltheart, 1992b) were available for only five cases. Although this test does not have published norms, according to http://www.neuro.mcw.edu/mcword/, the mean frequency of items is 108 per million, and the control range on the PALPA 40 is between 30 and 100% for items with a mean frequency 105 per million. Hence, although spelling performance was not perfect in all cases, it would seem there was good performance for shorter words of three or four letters, and performance for longer words was also good in most cases, with the only clearly impaired case being EW. Given that EW also showed deficits in tests of phonological and semantic processing, it is possible that aphasic deficits may have contributed to her impaired orthographic processing.

All patients showed elevated mean reading speeds on the 180-item list from Roberts et al. (2010) (RTs were derived using a voice recorder and manual analysis of reaction time data using WavePad software). All patients showed an appreciable influence of word length upon their reading speed, although the strength of the effect varied across different patients. This variability is also reflected in accuracy of Surface List reading, and demonstrates that any comparisons across patient types must take into account overall severity of the reading disorder.

Semantic Dementia: Ten SD patients with reading accuracy comparable to that of the PA patients on high-frequency regular words were selected from the cohort presented in Woollams et al. (2007). All patients had received a diagnosis of Semantic Dementia according to the (Neary et al., 1998) consensus criteria, which include atrophy of the anterior temporal lobe. Their selective semantic impairment is apparent in Table 2.

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MMSE Scores (Folstein, Folstein, & McHugh, 1975) were below the control range for all patients, as would be expected given that this test assesses some aspects of verbal ability. Working memory performance as assessed by digit span (Wechsler, 1987) was within the normal range in all but one case (DA1). Visuo-perceptual processing was reasonably intact, as indicated by scores within the normal range for all patients on the Rey Immediate Copy Test (Lezak, 1976). Where available, data from the VOSP showed preserved performance except for the Silhouettes subtest and in one case (MB1) on the Object Decision subtest, which is understandable given this draws on knowledge of object identity.

There was a marked impairment on tests tapping semantic memory. Performance was outside the control range for all patients on both the Cambridge Picture Naming and Spoken WPM tests (Bozeat, Lambon Ralph, et al., 2000; Hodges, Patterson, Oxbury, & Funnell, 1992), and on the Pyramids and Palm Trees Test (Howard & Patterson, 1992), reflecting the progressive anomia and declining comprehension that are key features of SD. Deficits in semantically-generated output are apparent on the Category Fluency Test (Hodges, Salmon, & Butters, 1992), in which patients are asked to generate as many examples as they can in one minute each for eight semantic categories, arguing against a visual contribution to the decreased performance seen on the semantic tests. Performance on the Surface List shows a consistent pattern of Surface Dyslexia, with all patients showing poor performance for low frequency exception words.

Stimuli:

The reading performance of all PA and SD patients was assessed using the Surface List (Patterson & Hodges, 1992, see Woollams et al., 2007 Appendix A). The Surface List consists of a factorial manipulation of frequency and regularity, with 42 items per cell.

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Within each level of frequency, the regular and exception items are matched on initial phoneme, and do not differ according to (Kučera & Francis, 1967) written frequency (HFR=811.43, HFE=798.83, $t(1,80)<1$; LFR=5.78, LFR=5.41, $t(1,78) <1$) or orthographic length (HFR=4.14, HFE=4.24, $t(1,82)<1$; LFR=4.83, LFR=4.81, $t(1,82) <1$).

Procedure:

For the PA patients, after an initial series of 12 practice items, patients viewed each item of the Surface List one at a time in the centre of a laptop screen. Items were displayed using e-prime software (Schneider, Eschman, & Zuccolotto, 2002) with an input of Arial 18 point that translated to the equivalent of 34 point once displayed on the screen (ascender/descender height = 0.9cm). Responses were digitally recorded for later coding. For the SD patients, practice and test items were presented one at a time on cards in Geneva 26 point font (ascender/descender height =0.7cm), and responses were coded in written form by the experimenter. Note that although presentation format differed over patient group, the two are near identical proportional fonts (e.g., pint vs pint), and while the font size was larger for the PA patients than the SD patients, this in fact works against our hypothesis of a more visual errors for PA than SD patients, as letter identification has been shown to be relatively independent of such variations in size (Pelli, Burns, Farell, & Moore-Page, 2006). For both groups, test items were presented in a fixed pseudo-random order that ensured a representative distribution of items from each condition over four blocks.

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Results:

Accuracy:

Reading accuracy for the PA and SD patients is presented in Figure 1. Data were analysed using a 2 (Patient: PA/SD) by 2 (Frequency: High/Low) by 2 (Regularity:

Regular/Exception) ANOVA, with repeated measures on the latter two factors. The results revealed no main effect of patient type (F(1,18)=0.74, p=.401), indicating that the severity matching had been successful. There were significant main effects of both frequency (F(1,18)=41.25, p<.0005) and regularity (F(1,18)=28.55, p<.0005), and their interaction (F(1,18)=12.49, p=.002). The two patient types showed comparable effects of frequency (F(1,18)=1.85, p=.191), but the impact of regularity was significantly stronger in SD than PA (F(1,18)=8.95, p=.008). The significant three way interaction (F(1,18)=6.27, p=.022) was driven by the SD patients' significantly worse performance specifically on the low frequency exception words (t(18)=2.49, p=.011, one-tailed). Repeated measures ANOVAs on the PA patients alone showed significant main effects of frequency (F(1,9)=19.10, p=.002), a marginal effect of regularity (F(1,9)=4.51, p=.063), and no interaction between them (F(1,9)=0.38, p=.551). A parallel analysis on the SD patients alone showed significant main effects of frequency(F(1,9)=22.79, p=.001), regularity(F(1,9)=25.05, p=.001), and an interaction between them (F(1,9)=29.72, p<.0005).

Error types:

All errors were transcribed in order to maximise orthographic similarity to the target. A variety of error types were observed amongst both PA and SD patients, and a summary of these is provided in Table 3. We classified each error into one of the following mutually exclusive categories (i) omissions (which were rare in both groups); (ii) Legitimate Alternative Reading of Components (LARC), in which the patient pronounced the word in line with spelling-sound correspondences of one or more other known words (e.g., *sew* > *"sue"*, as in *few* and *stew)*; (iii) visual errors, in which the response had at least 1 letter (out of 3 or 4) or 2 letters (out of 5 or 6) in common with target (e.g., *saw* > *"save"; cough* > *"coach"*); (iv) letter omissions, where all letters of the response were found in the target, but the response was one letter shorter than the target (e.g., *learn* > *"lean"*); (v) letter

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additions, where all letters of the response were found in the target, but the response was one letter longer than the target (e.g., *per* > *"pear"*); (vi) letter transpositions, where the response was the same length and contained all the letters of the target, but two adjacent letters had switched order (e.g., *trial* > *"trail"*); and (vii) letter substitutions, where the response was the same length as the target but one letter had been replaced (e.g., *food* > *"fool"*).

As can be seen in Table 3, omission errors were very rare in the PA patients, but as they were non-existent in the SD patients, this group difference was significant ($t(18)=1.97$, $p=.032$, one-tailed). As expected LARC errors were the most prevalent type of error for the SD patients and, while some LARC errors were made by the PA patients, these were significantly less common ($t(18)=3.21$, $p=.002$, one-tailed). Visual errors were marginally more common for the PA than SD patients ($t(18)=1.47$, $p=.079$, one-tailed). Neither letter omissions nor additions differed significantly between PA and SD patients ($t(18)=1.25$, $p=.115$, one-tailed; $t(18)=0.89$, $p=.194$, one-tailed, respectively). Letter transpositions, although rare overall, were significantly more common in PA than SD patients ($t(18)=2.16$, $p=.022$, one-tailed). The most prevalent error type for the PA patients was letter substitutions, and while such errors were also seen in the SD patients, they were significantly less common ($t(18)=2.42$, $p=.013$, one-tailed). No difference between PA and SD patients on other error types was apparent ($t(18)=0.35$, $p=.364$, one-tailed). To summarise, LARC errors were significantly more common for the SD than the PA patients, whereas at least some types of letter-based errors (visually related responses, transpositions and substitutions) were significantly more common in the PA than the SD patients. This pattern is displayed in Figure 2, and is consistent with reading performance disrupted by a semantic deficit in SD and by a visual deficit in PA.

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For all errors of commission, we also coded whether the responses corresponded to another known word, and these proportions are displayed in Table 4. There was a highly significant difference between the PA and SD patients on this measure ($t(18)=6.87$, $p<.000005$, one-tailed). As can be seen in Figure 3, the vast majority of errors of commission produced by the PA patients were words. The SD patients, on the other hand, were somewhat more likely to produce nonword than word errors. This striking difference is consistent with the idea that reading aloud in SD is characterised by a reduction of semantic activation, such that there is insufficient top-down information to prevent nonword responses. In contrast, the high proportion of word errors in the PA patients suggests that reading responses in the face of compromised bottom-up visual input are typically constrained by top-down information.

Letter substitutions:

The analysis of error types demonstrated that PA patients were significantly more likely than SD patients to substitute one of the component letters of a word. If these substitutions result from a visual processing deficit in PA, then we would also expect that the form of these errors will be driven more by visual similarity than in SD. To assess this hypothesis, we coded the letter presented and letter 'reported' (as reflected in the whole response) according to the letter confusability matrix in Patterson and Kay (1982), derived from the errors made by normal participants in identifying letters presented briefly in peripheral vision (Bouma, 1971). We selected this confusability matrix because: (i) it was based on lower-case letters, as used in our reading list; (ii) it was derived from peripheral vision, resulting in perception with reduced medium to high spatial frequency information, akin to deficits suggested in PA patients (Roberts, et al., 2013); and (iii) it has been used before with reference to letter substitutions in cases of PA (Patterson & Kay, 1982). The results for each group can be seen in Figure 4, where the values represent the proportion of all

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substitutions. The cells closest to the diagonal represent maximum visual similarity, and the substitutions of the PA patients fall closer to the diagonal than the SD patients, as hypothesised. In order to quantify this difference, we computed the Euclidean distance between the presented and reported letters within the matrix for each error in the following way: we created a matrix where each letter was assigned a number from 1 to 26 (e.g., a=2, o=3), and the absolute difference between the presented and reported letter yielded a distance for that confusion for a given patient (e.g., cat read as "cot" had a distance of 1). The average distance for PA patients across all letter substitution errors was 5.1, while that for SD patients was 7.0, which was significantly lower ($t(165)=2.38$, $p=.009$, one-tailed). This result is again consistent with a visual deficit undermining reading in PA.

The preceding analysis indicates a key role for visual similarity in the specific letter substitution errors of the PA patients. What might be the relevant relationship between stimulus and response words in SD reading errors? One possibility is that semantic impairment exerts its effects on reading aloud through mild perturbation of phonological/phonetic processing. To assess this hypothesis, we used (Bailey & Hahn, 2005) coding scheme to capture the sound similarity - in terms of number of shared features (place, manner, voice, sonorance) - corresponding to the phonemes involved in letter substitution errors. The results can be seen in Figure 5, where the values represent the proportion of all consonant-consonant substitutions. This reveals that the SD patients' letter substitutions were more likely to equate to phonemes sharing 2 or 3 features with the target phoneme, whereas for PA patients such substitutions typically shared either no, or just a single, phonetic feature. A comparison of the average number of shared phonetic features demonstrated greater phonemic similarity of substitutions amongst the SD (2.53) than PA patients (2.14) ($t(165)=1.69$, $p=.038$, one-tailed).

Discussion:

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This study investigated the extent to which the reading deficits seen in PA and SD arise from similar or different causes. The fact that increased word length effects have been seen in reading performance in both these disorders has led some researchers to propose that they share a common cause in terms of disruption to reading-specific orthographic processing (e.g.,(Coltheart, et al., 2010; Noble, et al., 2000). In contrast, the primary systems view attributes all characteristics of these two reading disorders, including length effects, to a deficit in general visual processing in PA and to a deficit in central semantic processing in SD (Patterson & Lambon Ralph, 1999; Roberts, et al., 2013; Woollams, et al., 2007). These two accounts therefore diverge in the extent to which they predict resemblances between reading performance in the two disorders. Here, we explored this issue by directly comparing the impact of frequency and regularity on reading accuracy, and the nature of error types, in 10 cases of PA and 10 cases of SD who were matched on their accuracy in reading single words aloud.

In terms of reading accuracy, the PA and SD patients were similar in that they showed comparable effects of frequency, which concurs with results previously reported in the literature (e.g.,(Behrmann, Plaut, et al., 1998; Graham, et al., 2000). While this result could be consistent with a shared locus of impairment in orthographic processing, it could also arise from different sources. In PA, the perception of high frequency words may be less disrupted due to feedback from intact higher-order linguistic/semantic representations (Roberts, et al., 2010), whereas in SD, the production of low frequency words may be more disrupted because semantic representations of these items are most vulnerable to damage (Lambon Ralph, Graham, Ellis, & Hodges, 1998; Rogers et al., 2004; Woollams, Cooper-Pye, Hodges, & Patterson, 2008). This notion that the influence of top-down activation is increased in PA but reduced in SD is consistent with the striking finding reported here and previously (Cumming,

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et al., 2006) that PA patients are much more likely to produce errors that are nevertheless known words, while SD patients are in fact more likely to produce errors that are nonwords.

The impact of regularity on reading accuracy was significantly weaker in PA than SD, and the incidence of LARC errors was also significantly lower. Consistent with previous work, there was a marginally significant effect of regularity on PA reading accuracy (Behrmann, Nelson, et al., 1998; Rapcsak & Beeson, 2004), but LARC errors were the least common error type for the PA patients (Cumming, et al., 2006; Patterson & Kay, 1982). This contrasts with the very strong impact of regularity on reading accuracy for the SD patients, and the fact that LARC errors were the most common error type in SD, as has been previously seen in larger samples (Graham, et al., 2000; Woollams, et al., 2007). The prevalence of LARC errors in SD speaks to intact processing along a direct pathway between orthography and phonology in the face of compromised whole-word knowledge due to damage to the semantic system.

Consideration of the nature of reading errors also highlighted a higher incidence of certain letter based errors in PA than SD – specifically those where the stimulus and response shared most of their letters (visual errors, see also Rapcsak & Beeson, 2004), where letters in the response re-ordered those in the stimulus (transpositions: see also (Pflugshaupt et al., 2011), and where a single letter in the stimulus was replaced by another in the response (substitutions, see Patterson & Kay, 1982). Indeed, it was letter substitutions that were the most common type of error for the PA patients, but some substitution errors were also produced by the SD patients. To understand the source of the substitution errors in the two patient types, we first considered the extent to which the presented and reported letters were visually similar, as measured by their degree of confusability by normal participants when letters are presented in peripheral vision (Bouma, 1971; Patterson & Kay, 1982), a technique which may simulate the lower spatial frequency information available to PA patients with

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unlimited duration central presentation (Roberts, et al., 2013). The visual similarity of the presented and reported letters was significantly higher in PA than SD, consistent with a visual processing impairment as the cause of the reading deficit in PA.

We then further explored the source of letter substitution errors in SD by considering the extent to which they were driven by phonological similarity, as measured by overlap in terms of the phonetic features of the presented and reported consonant phonemes (Bailey & Hahn, 2005). The motivation behind this analysis was the possibility that semantic damage could exert its effects on reading aloud through disruption of phonological processing. This notion is supported by a body of literature demonstrating poorer repetition by SD patients of short sequences of words whose meanings they no longer know, when compared to words with meanings that are still known (Knott, Patterson, & Hodges, 1997, 2000; Patterson, Graham, & Hodges, 1994). This poorer performance is characterised by phoneme migration errors (e.g., mint, rug will be reproduced as rint, mug), suggesting that semantic activation helps to bind together phonological elements. Consistent with this view, the phonological similarity of the letter substitutions of SD patients was significantly higher than for PA patients.

The phonological similarity of letter substitution errors in SD does suggest that semantic impairment exerts effects on reading aloud through disruption of phonological processing, but there are multiple mechanisms by which this could occur. SD patients' poor performance in repetition of lists of words with degraded meaning has been viewed as reflecting dramatically reduced semantic activation of phonology, consistent with the prevalence of omission errors in SD patients' picture naming (Woollams, et al., 2008) and the ineffectiveness of phonological cueing for their anomia (Graham, Patterson, & Hodges, 1995; Jefferies, Patterson, & Lambon Ralph, 2008). It is possible that degraded knowledge not only reduces phonological activation but also adds noise to it, consistent with the occurrence of

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errors of commission in SD picture naming (Woollams, et al., 2008). This noisy activation would be inherited by phonological representations during reading, and indeed this is the approach taken by Woollams et al. (2007) in their simulations of reading aloud in SD within the connectionist triangle model of (Plaut, McClelland, Seidenberg, & Patterson, 1996). To the extent that phonological representations are organised according to phonetic features (e.g.,(Harm & Seidenberg, 2004), then this noisy activation would result in the substitution of similar phonemes during reading aloud, as observed in the present study.

Overall then, a consideration of the reading aloud performance in PA and SD patients matched for accuracy of reading aloud has shown that the two groups perform very differently. The prevalence of visual errors and the visual similarity of letter substitutions in PA indicate a general visual processing deficit, whereas the prevalence of LARC errors and the phonetic similarity of phoneme substitutions in SD are consistent with a semantic impairment, in line with a primary systems account of reading disorders. This account of PA and SD reading is represented schematically in Figure 6 within the connectionist triangle framework. The assumption of a general visual processing deficit in PA is supported not only by the present data, but also previous work showing visual processing deficits to varying degrees in these patients (Behrmann, Nelson, et al., 1998; Behrmann & Plaut, 2013a; Behrmann & Shallice, 1995; Farah & McClelland, 1991; Friedman & Alexander, 1984; Mycroft, et al., 2009; Roberts, et al., 2013; Starrfelt & Behrmann, 2011; Starrfelt, Habekost, & Gerlach, 2010; Starrfelt, Habekost, & Leff, 2009), and recent neuroimaging work implicating the vOTC in the processing of high spatial frequency foveal visual information (Hasson, et al., 2003; Hasson, et al., 2002; Levy, et al., 2001; Malach, et al., 2002; Vogel, et al., 2012; Woodhead, et al., 2011). The assumption of disruption specifically to semantics is similarly supported by patient neuroimaging data: SD patients have structural and functional abnormality of the ATL but not vOTC (Acosta-Cabronero et al., 2011; Nestor, et al., 2006;

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Woollams, Lambon Ralph, Plaut, & Patterson, 2010), and the extent of ATL damage has been directly linked to level of success on non-reading semantic tasks (Adlam, et al., 2006; Mion et al., 2010).

Within the primary systems account, the visual deficit in PA undermines input to orthographic processing, producing the patients' visual errors, letter transpositions and visually similar letter substitutions. This can, however, be offset to some extent by top-down activation from intact semantic and phonological information feeding back to orthography, producing the effects of frequency (and possibly regularity) observed here, combined with the prevalence of real-word error responses. In contrast, the semantic impairment in SD reduces and disrupts activation of phonology during reading, increasing the incidence of nonword error responses. Effects of frequency arise because semantic representations of low frequency words are less robust to damage, while regularity effects arise as reading of words with atypical spelling-sound mappings come to rely more upon semantic activation of phonology over the course of learning (Plaut, et al., 1996). The intact mappings directly between orthography and phonology produce LARC errors in the case of words with atypical mappings, particularly those low in frequency. In some cases the direct activation of phonology can be disrupted by the noise from degraded semantic activations, and the result is the substitution of a phonetically similar phoneme.

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Our account requires further exploration within implemented connectionist computational models of reading aloud. Some of these models incorporate phonological representations in the form of phonetic features (e.g.,(Harm & Seidenberg, 2004), allowing exploration of SD patients' errors. More recently, connectionist models have been extended to accept raw visual input (Chang, et al., 2012a; Chang, Furber, & Welbourne, 2012b) and could therefore potentially simulate PA patients' reading behaviour. This investigation has provided target data for such simulations, and has demonstrated that despite surface

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similarities in the reading impairments of PA and SD patients, a deeper consideration indicates that these arise due to distinct impairments of visual processing vs. semantic representation.

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Table 1. *Demographic and background neuropsychological data for the ten pure alexic patients included in the current study, ordered from least to most impaired according to high frequency regular word reading accuracy.*

	Max.	PM	JW	JM	TS	KW	SC	JWF	MS	AT	EW
Demographics											
Age	-	64	59	67	57	44	81	54	70	73	74
Years of education	-	10	11	10	10	10	11	10	10	10	10
Lesion information											
Neuroimaging summary	-	Occipito-temporal	Occipito-temporal	Occipito-temporal	Occipito-temporal	Occipito-temporal	Occipito-temporal	Occipito-temporal	Occipito-temporal	Occipito-parietal	Occipito-temporo-parietal
Aetiology	-	PCA stroke	PCA stroke	PCA tumour resection	PCA tumour resection	MCA stroke	PCA stroke	Post aneurism PCA infarct	PCA stroke	PCA stroke	MCA stroke
Working memory											
Digit span (scaled score)	18	NT	9	15	8	14	7	10	14	10	7
Visual processing											
Right visual field impairment*	-	Upper quadrant	Hemianopia	Upper quadrant	Hemianopia	Hemianopia	Hemianopia	Hemianopia	Hemianopia	Upper quadrant	Hemianopia
VOSP											
Incomplete letters	20	NT	19	20	19	20	18	17	16	16	19

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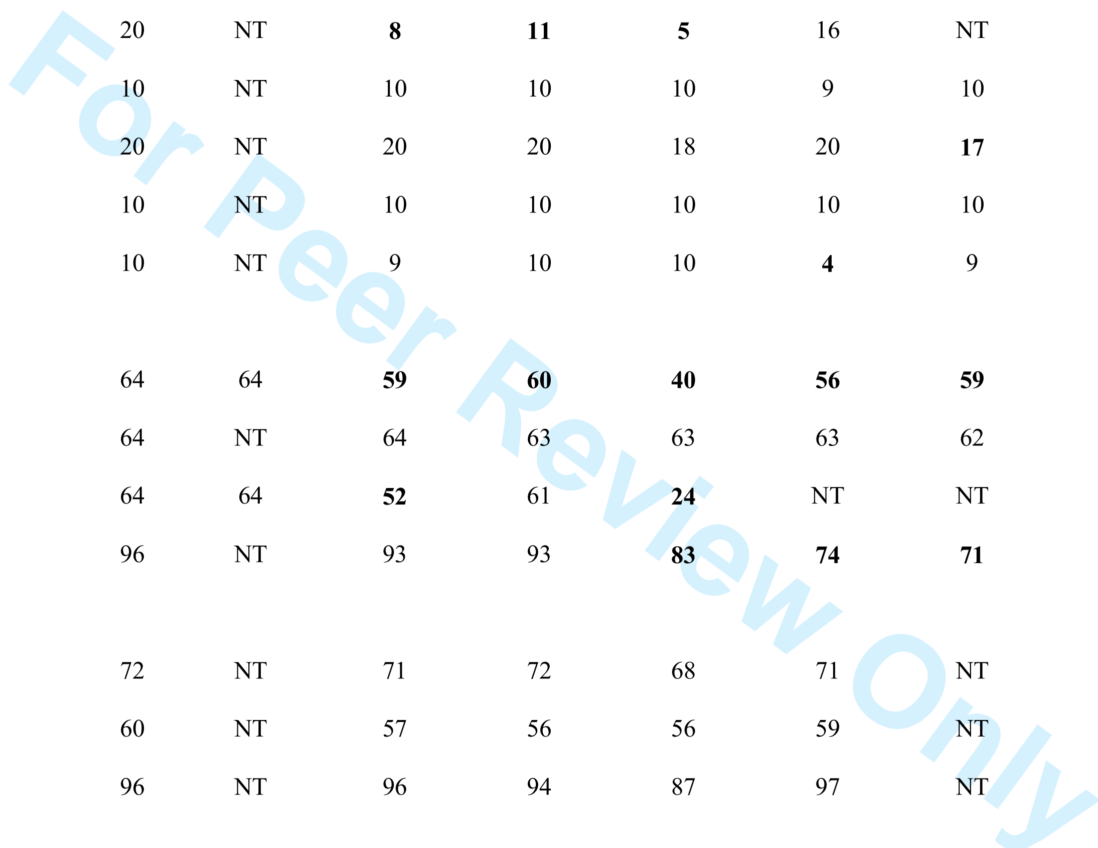

Silhouettes	30	NT	25	18	22	19	**3**	24	19	**13**	**12**
Object decision	20	NT	17	17	18	20	14	19	16	17	17
Progressive silhouettes	20	NT	**8**	**11**	**5**	16	NT	NT	**9**	**9**	**12**
Dot counting	10	NT	10	10	10	9	10	10	9	10	10
Position discrimination	20	NT	20	20	18	20	**17**	**16**	19	20	20
Number location	10	NT	10	10	10	10	10	8	10	9	10
Cube analysis	10	NT	9	10	10	**4**	9	10	7	10	7
Semantic processing											
Naming+	64	64	**59**	**60**	**40**	**56**	**59**	**54**	**45**	**54**	**45**
Spoken Word to Picture matching+	64	NT	64	63	63	63	62	NT	62	63	**57**
Camel and Cactus (pictures) +	64	64	**52**	61	**24**	NT	NT	61	**47**	NT	**45**
96 Synonyms (%)~	96	NT	93	93	**83**	**74**	**71**	94	**81**	NT	**76**
Phonological processing											
PALPA 2: Phonological judgement	72	NT	71	72	68	71	NT	72	71	NT	65
PALPA 15: Rhyme judgement	60	NT	57	56	56	59	NT	58	53	NT	56
Phonological segmentation#	96	NT	96	94	87	97	NT	96	91	NT	**69**
Spelling											
PALPA 39 Written											
Short	100	NT	92	100	100	NT	NT	NT	100	NT	75

Long	100	NT	50	75	100	NT	NT	NT	75	NT	**17**
Reading Aloud											
180-item list:	-										
Mean RT (ms)	-	1013	7530	5432	5158	5903	7910	6484	12667	15683	7010
Mean Accuracy (%)	-	100	91	96	95	94	83	53	75	57	58
Length effect (ms per letter)	-	170	1299	911	1060	651	1843	1369	1650	523	2248
Length effect (% per letter)^	-	0	0.75	-1.25	-1.25	0	-3.75	1.5	-8.75	-4	-3.25
Surface List:											
High Frequency Regular	42	41	41	41	**40**	**39**	**36**	**34**	**32**	**30**	**29**
Low Frequency Regular	42	40	38	**37**	39	**36**	**26**	39	**24**	**22**	**15**
High Frequency Exception	42	39	40	**39**	**37**	41	**31**	**37**	**30**	**29**	**25**
Low Frequency Exception	42	37	**28**	**33**	**34**	**32**	**16**	**34**	**20**	**27**	**26**

Bold denotes abnormal performance represented by scores falling beyond two standard deviations below control performance where normative data available; ;For Digit Span, abnormal scores are two standard deviations below age appropriate means (Ivnik et al., 1992); PCA = Posterior Cerebral Artery; NT - Not tested; NA = Not available. * = Assessed using LERNREHA from Kasten, Strasburger, & Sabel (1997); VOSP: Visual Object and Space Perception battery (Warrington & James, 1991); PALPA: Psycholinguistic Assessment of Language Processing in Aphasia (Kay, Lesser, & Coltheart, 1992a); [+] Tests from (Bozeat, Gregory, Lambon Ralph, & Hodges, 2000); [~] Test from Jefferies et al. (2009); [#] Tests from (Patterson & Marcel, 1992); ^ represents decrease in accuracy for each additional letter in string..

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Table 2. *Demographic and background neuropsychological data for the ten semantic dementia patients included in the current study, ordered from least to most impaired according to high frequency regular word reading accuracy.*

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	Max.	GC6	LS3	MB1	DC1	DA1	AM4	NS2	MA6	FM8	AT6
Demographics											
Age	-	60	62	65	77	75	65	69	73	57	68
Years of education	-	12	13	11	8	16	16	9	13	10	19
Cognitive Status											
MMSE	-	NT	**24**	**22**	**18**	**9**	**8**	**25**	**5**	**22**	**15**
Raven's coloured	-	NT	NT	**17**	33	NT	30	36	NT	25	34
Working memory											
Digit span (scaled score)	18	5	7	4	7	**3**	6	6	NT	4	9
Visual processing											
Rey Immediate Copy	36	34	29	26	32	34	35	36	NT	32	36
VOSP											
Incomplete letters	20	20	19	19	18	17	NT	19	NT	NT	18
Silhouettes	30	**5**	NT	**9**	**1**	NT	NT	NT	NT	NT	NT
Object decision	20	14	NT	**13**	17	18	NT	NT	NT	NT	NT
Progressive silhouettes	20	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT
Dot counting	10	10	10	9	10	9	NT	10	NT	NT	10
Position discrimination	20	20	20	20	20	19	NT	20	NT	NT	20

Number location	10	8	10	7	10	10	NT	9	NT	NT	8
Cube analysis	10	10	9	8	10	8	NT	10	NT	NT	10
Semantic processing											
Naming[+]	64	**13**	**34**	**44**	**20**	**12**	**0**	**8**	**10**	**0**	**5**
Spoken Word to Picture matching[+]	64	**35**	**60**	**58**	**44**	**50**	**17**	**42**	**43**	**59**	**29**
Pyramids and Palm Trees (pictures)	52	NT	**30**	**39**	**40**	**39**	**35**	**39**	**26**	**46**	**38**
Pyramids and Palm Trees (words)	52	NT	NT	NT	**30**	**41**	**30**	**33**	**26**	NT	**27**
Category (8 categories)	-	NT	NT	**25**	**13**	**4**	**1**	**19**	**0**	**0**	NT
Reading Aloud											
Surface List:											
High Frequency Regular	42	41	41	**40**	**39**	**39**	**36**	**36**	**33**	**32**	**29**
Low Frequency Regular	42	40	**35**	41	39	**37**	**34**	**15**	**25**	**29**	**29**
High Frequency Exception	42	**38**	40	40	**33**	**35**	**33**	**31**	**37**	**21**	**21**
Low Frequency Exception	42	**20**	**26**	**32**	**20**	**28**	**21**	**7**	**26**	**15**	**10**

Bold denotes abnormal performance represented by scores falling beyond two standard deviations below performance of a group of between 100 and 24 (depending on the test) control participants comparable in terms of age and education; For Digit Span, abnormal scores are two standard deviations below age appropriate means (Ivnik, et al., 1992); For the Raven's, abnormal performance is that below the 50%th centile for older controls in norms ; NT - Not tested; VOSP: Visual Object and Space Perception battery (Warrington & James, 1991); PALPA: Psycholinguistic Assessment of Language Processing in Aphasia (Kay, et al., 1992b); [+] Tests from (Bozeat, Lambon Ralph, et al., 2000).

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Table 3. Proportion of different error types for the 10 PA and 10 SD cases. Standard deviations are provided in parentheses.

		HFR*	LFR*	HFE*	LFE*	Total~
Omission Errors	PA	0 (0)	0.017 (0.017)	0 (0)	0.038 (0.017)	0.021 (0.034)[1]
	SD	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)[1]
LARC Errors	PA	0.017 (0.017)	0.096 (0.052)	0.248 (0.092)	0.268 (0.042)	0.198 (0.111)[1]
	SD	0.31 (0.098)	0.142 (0.056)	0.36 (0.107)	0.547 (0.054)	0.434 (0.203)[1]
Visual Errors	PA	0.213 (0.066)	0.365 (0.081)	0.191 (0.051)	0.288 (0.048)	0.279 (0.152)[#]
	SD	0.139 (0.074)	0.193 (0.07)	0.289 (0.081)	0.17 (0.033)	0.187 (0.128)[#]
Letter Omissions	PA	0.052 (0.034)	0.161 (0.057)	0.185 (0.074)	0.097 (0.018)	0.122 (0.067)
	SD	0.028 (0.021)	0.137 (0.069)	0.16 (0.068)	0.074 (0.018)	0.086 (0.065)
Letter Additions	PA	0.035 (0.019)	0.066 (0.035)	0.008 (0.008)	0 (0)	0.021 (0.021)
	SD	0.089 (0.05)	0.006 (0.006)	0.022 (0.015)	0.014 (0.007)	0.029 (0.019)
Letter Transpositions	PA	0.112 (0.054)	0.013 (0.009)	0 (0)	0.004 (0.004)	0.024 (0.022)[1]
	SD	0.061 (0.036)	0 (0)	0 (0)	0 (0)	0.007 (0.012)[1]
Letter Substitutions	PA	0.332 (0.098)	0.258 (0.076)	0.34 (0.092)	0.166 (0.044)	0.242 (0.07)[1]
	SD	0.177 (0.075)	0.446 (0.075)	0.125 (0.04)	0.117 (0.016)	0.175 (0.051)[1]
Other Errors	PA	0.24 (0.129)	0.024 (0.01)	0.029 (0.015)	0.139 (0.034)	0.093 (0.069)
	SD	0.197 (0.1)	0.077 (0.032)	0.044 (0.021)	0.078 (0.015)	0.083 (0.054)

Note: *Proportions = error type/errors per condition. ~Proportion = error type/total errors. [1] Significant group difference at p<.05, one-tailed; [#] Marginally significant group difference at p<..08, one-tailed.

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Table 4. Proportion of errors of commission that were phonologically identical to another known word for the 10 PA and 10 SD cases. Standard deviations are provided in parentheses.

	HFR*	LFR*	HFE*	LFE*	Total~
PA	0.823 (0.1)	0.903 (0.04)	0.826 (0.062)	0.649 (0.057)	0.777 (0.084)^
SD	0.665 (0.1)	0.556 (0.063)	0.43 (0.077)	0.411 (0.039)	0.46 (0.111)^

Note: *Proportions = word errors/commission errors per condition. ~Proportion = word errors/total commission errors. ^ Significant group difference at p<.000005, one-tailed.

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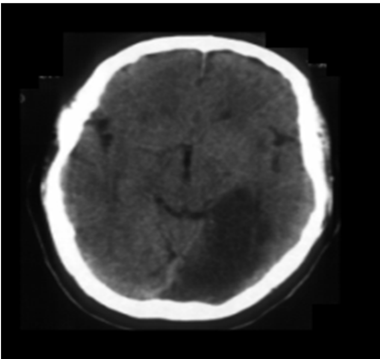
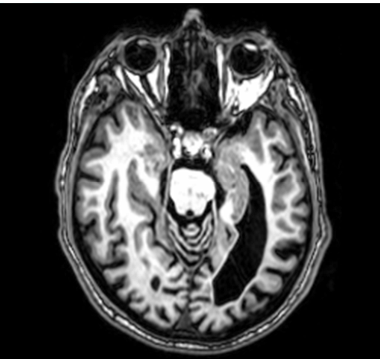
APPENDIX

Structural scans for eight patients in the present study where these were available. Patients are ordered from mildest to most severe ordered from least to most impaired according to high frequency regular word reading accuracy.

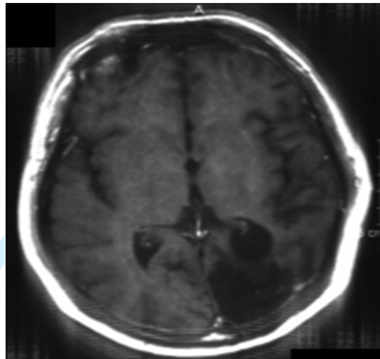
Patient JW



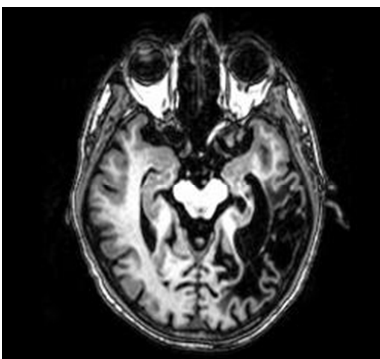
Patient JM



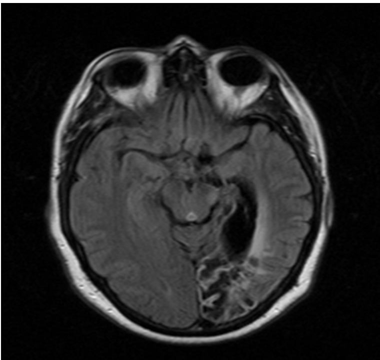
Patient TS



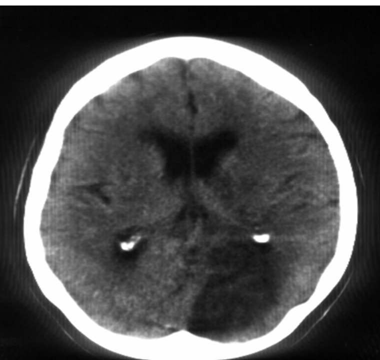
Patient SC



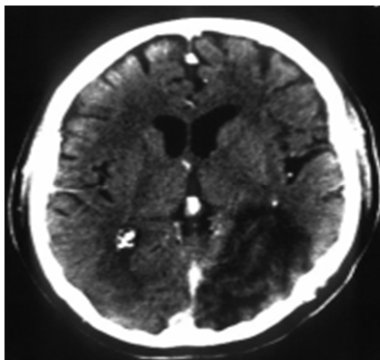
Patient JWF



Patient MS



Patient AT



Patient EW

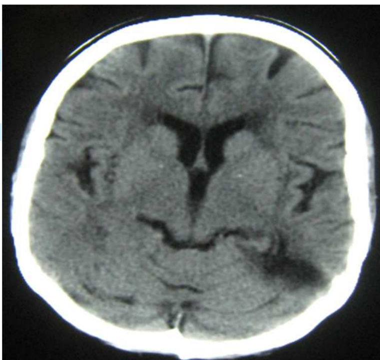


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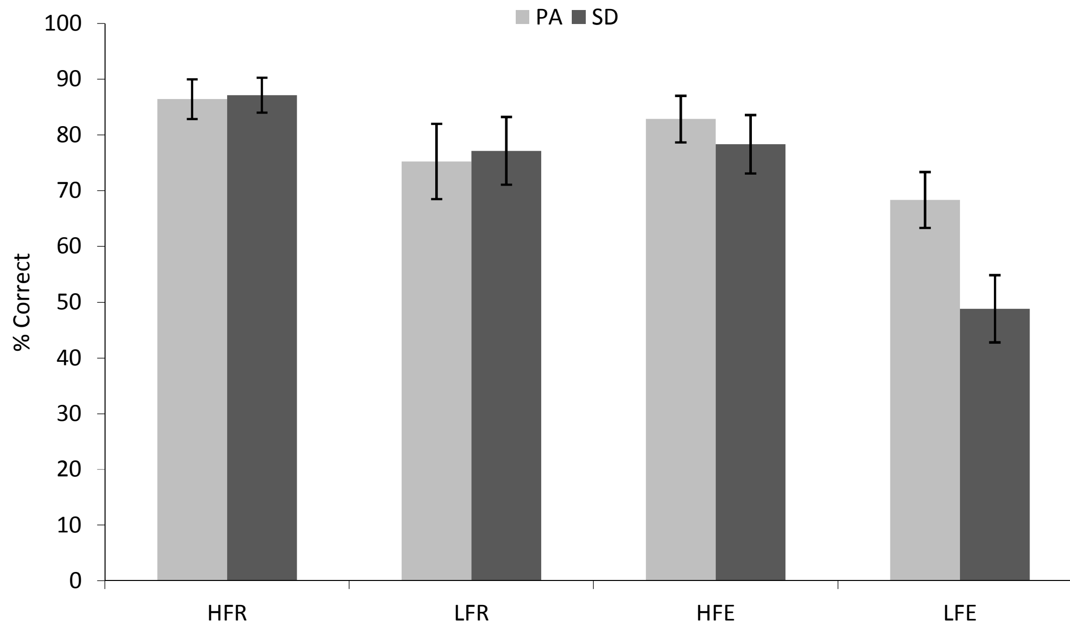
Figure 1. Reading aloud accuracy for 10 pure alexic and 10 semantic dementia patients according to frequency and regularity. Error bars represent +/- standard error.



HFR= High Frequency Regular; LFR = Low Frequency Regular; HFE = High Frequency Exception; LFE – Low Frequency Exception

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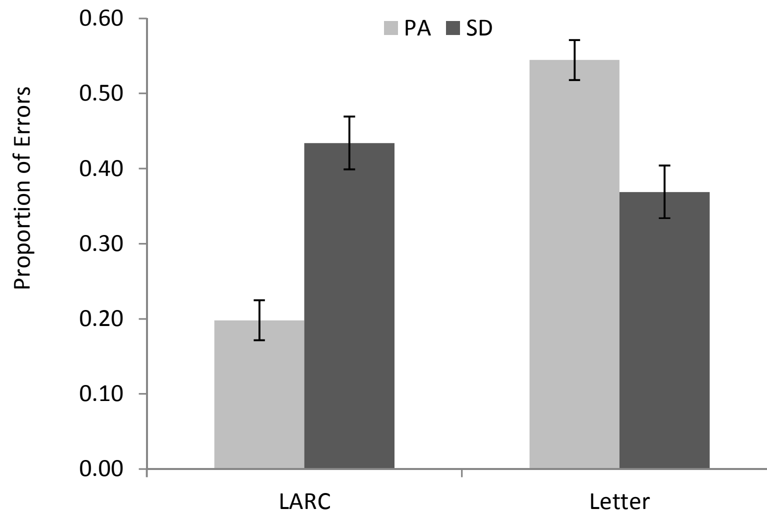

Figure 2. Proportion of LARC and Letter (Visual + Transposition + Substitution) errors for the 10 PA and 10 SD patients. Error bars represent +/- standard error.

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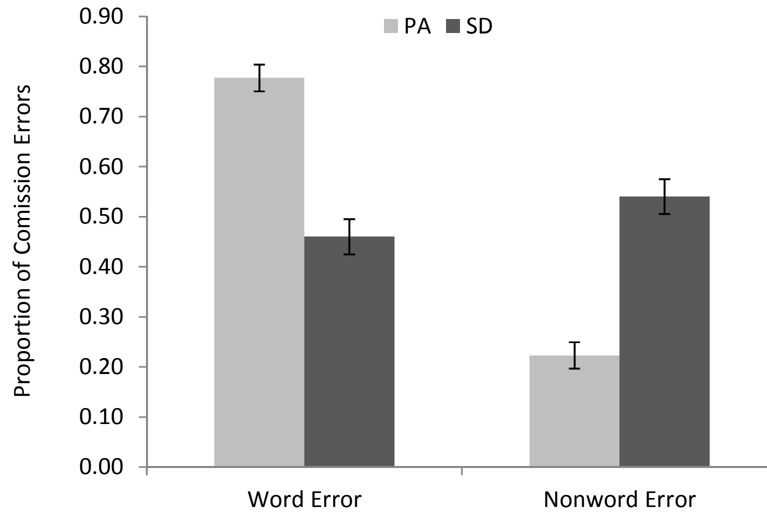

Figure 3. Proportion of word and nonword errors for the 10 PA and 10 SD patients. Error bars represent +/- standard error.

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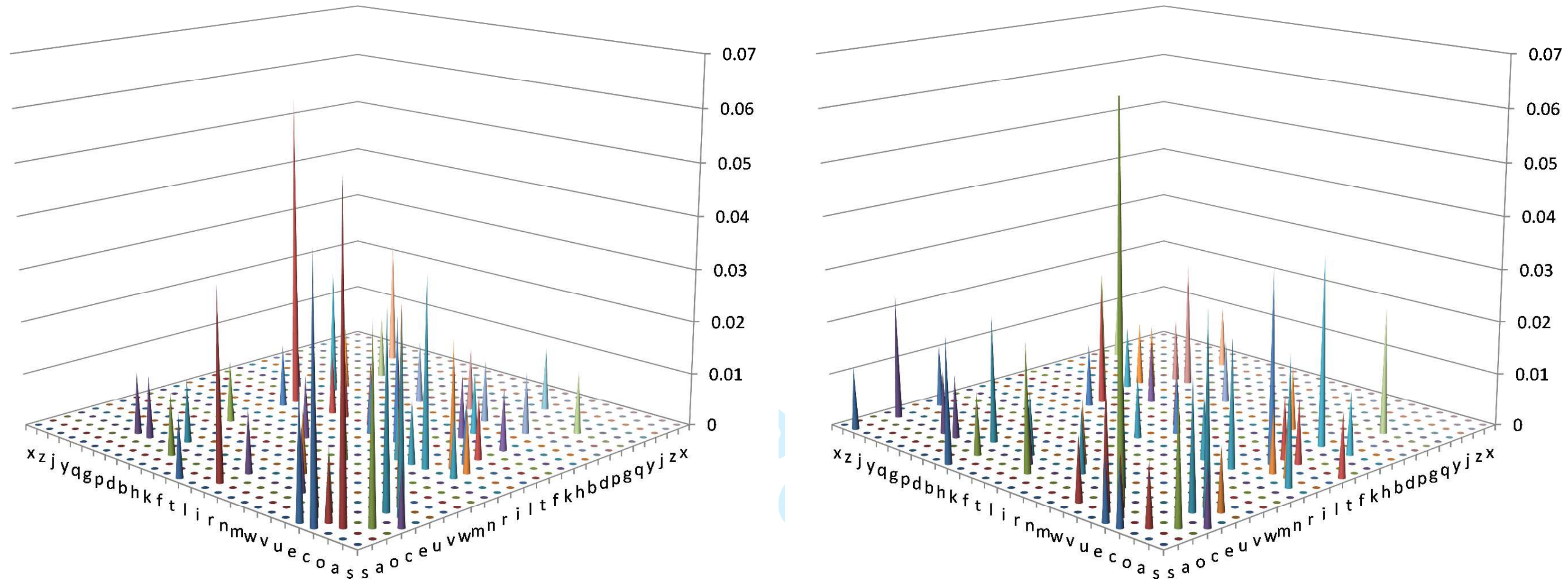

Figure 4. Visual similarity of letter substition errors for the 10 PA (left) and 10 SD (right) patients. Values representation proportion of all substitution errors.

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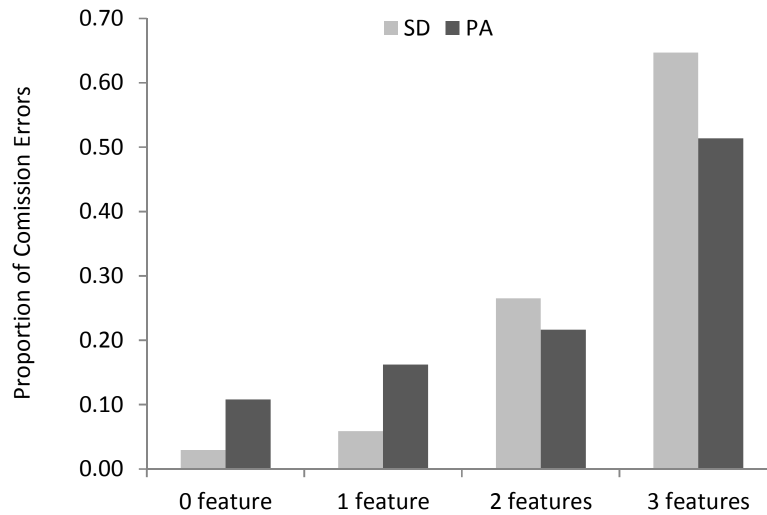

Figure 5. Proportion of consonant substitution errors according to number of phonetic features (place, manner, voice, sonorance) shared between presented and reported phonemes for the 10 PA and 10 SD patients.

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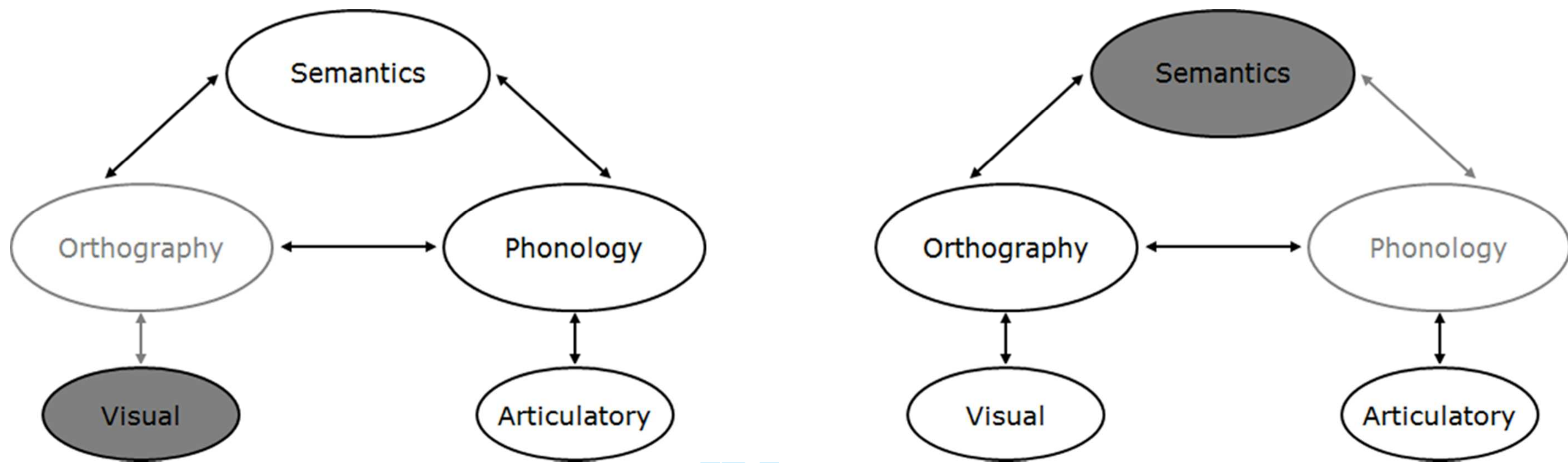

Figure 6. Schematic representation of the loci of deficits undermining reading in PA (left) versus SD (right) within a triangle model of reading. Filled ovals represent damaged components, grey ovals represent subsequently disrupted processing.

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