The oral spelling profile of Posterior Cortical Atrophy and the nature of the graphemic representation.

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Abstract

Spelling is a complex cognitive task where central and peripheral components are involved in engaging resources from many different cognitive processes. The present paper aims to both characterize the oral spelling deficit in a population of patients affected by a neurodegenerative condition and to clarify the nature of the graphemic representation within the currently available spelling models. Indeed, the nature of graphemic representation as a linear or multi-componential structure is still debated. Different hypotheses have been raised about its nature in the orthographic lexicon, with one positing that graphemes are complex objects whereby quantity and identity are separately represented in orthographic representations and can thus be selectively impaired. Posterior cortical atrophy (PCA) is a neurodegenerative condition that mainly affects visuoperceptual and visuospatial functions. Spelling impairments are considered part of the disease. Nonetheless the spelling deficit has received little attention so far and often it has been interpreted in relation to peripheral impairments such as writing difficulties associated with visuoperceptual and visuospatial deficits. In the present study we provide a detailed characterization of the oral spelling profile in PCA. The data suggest that multiple deficits underpin oral spelling problems in PCA, with elements of surface and phonological dysgraphia but also suggesting the involvement of the graphemic buffer. A large phenotypic individual variability is reported. Moreover, the larger proportion and the specific nature of errors involving geminate (i.e., double) as compared to non-geminate (i.e., non-double) letters suggest that a further central impairment might be associated with the abstract graphemic representation of letter numerosity. The present study contributes to the clinical characterization of PCA and to the current debate in the cognitive literature on spelling models; findings, despite not definitive, support the hypothesis that graphemic representations are multidimensional mental objects that separately encode information about grapheme identity and quantity.

Key words: Posterior Cortical Atrophy; oral spelling; geminate words; graphemic representation.

1. Introduction

Spelling is a complex cognitive task which has been relatively neglected in the last decades in comparison with other research areas, such as reading. Available cognitive models of spelling show a good level of agreement about the basic processes involved and they generally postulate a dual-route elaboration of the input stimulus (e.g., Ellis, 1982). Neuropsychological evidence suggests two relatively distinct mechanisms (for reviews see Barry, 1994; Tainturier & Rapp, 2001): a phonology-to-orthography conversion pathway (sublexical or phonological route) and a direct access pathway to orthographic learned word forms (lexical route). The sublexical route relies on phoneme –grapheme conversion rules in order to convert auditory phoneme strings into written or orally spelled lexical representations. This system can be relied on to spell nonwords and low frequency words. The lexical system is involved during rapid and online access to representations of high frequency and irregularly spelled words (e.g., *yacht*), which are stored in the orthographic lexicon in the form of visual word images. Selective damage to one of the two systems is possible and may give rise to specific spelling problems (see Ward, 2003 for a review). An important structure of the spelling system is the graphemic buffer, where the lexical and sublexical pathways converge (Houghton & Zorzi, 2003; Glasspool & Houghton, 2005). The graphemic buffer is a working memory system which temporarily stores orthographic representation of words before the output motor systems (hand writing or oral spelling) are activated for response production. Peripheral processes are referred to the output motor systems and are specific to the output mode (i.e., oral or written). In accordance to such cognitive models, there is a general consensus about the distinction between central and peripheral dysgraphias: following Ellis (1982) terminology central dysgraphias arise from a linguistic problem affecting the spelling system, while peripheral dysgraphias reflect a modality-specific disorder selectively affecting one of the output motor systems and thus involving writing, oral spelling or typing.

Single-route models of spelling (e.g., Brown & Loosemore, 1994; Olson & Caramazza, 1994; Bullinaria, 1997) are currently unable to account for the full range of empirical data (Houghton & Zorzi, 2003). Despite the fact that different spelling models have been proposed [symbolic (e.g., (Barry, 1994), more interactive (Rapp, Epstein, & Tainturier, 2002), connectionist (Houghton & Zorzi, 2003)], dual-route models are generally accepted in the international literature. Nonetheless, a debated issue concerns the nature of the graphemic representations at the level of the graphemic buffer. In particular, for a long time it has been accepted that it consists of a linear system of abstract letter identities (Wing & Baddeley, 1980; Caramazza, Miceli, Villa, & Romani, 1987). However, more recently it has been proposed that graphemic representations are multidimensional mental objects or structures that separately encode information about not only grapheme identity, order and consonant-vowel status, but also about grapheme quantity (Caramazza & Miceli, 1990). The 'quantity' proposal arises primarily from the observation of patients with brain damage who exhibit specific problems (Caramazza & Miceli, 1990; Venneri & Cubelli, 1993; McCloskey, Badecker, Goodman-schulman, & Aliminosa, 1994) or, by contrast, selectively spared performance (Tainturier & Caramazza, 1996) in spelling geminate words (i.e.; which contain geminate or double letters; e.g., puzzle). Venneri and colleagues (Venneri, Cubelli, & Caffarra, 1994) reported the case of a patient who made perseverative errors in spelling geminate words (e.g. the Italian word INTE*LL*E*TT*O [intellect] spelled as INTELLLETTTTTTO). The case of a patient showing a selective deficit in processing double letters with a strong tendency in deleting one consonant in geminate clusters has been reported (Miceli, Benvegnù, Capasso, & Caramazza, 1995). Specific error patterns for geminate words involving the shifting, duplication or exchange of the geminate feature (e.g., SORE*LL*A [sister] spelled as SORRELA, SORRELLA or SOLLERA, respectively) have also been described (Caramazza & Miceli, 1990) and empirically strengthen the theoretical proposal of a partially independent processing for letter identity and letter quantity. The origin of these types of errors has been interpreted differently. Some researchers have attributed such errors to a post-graphemic level of processing (e.g. Venneri et al., 1994). Others have proposed that such errors originate from impairment in visual and kinestetic feedback mechanisms (Ellis, Young, & Flude, 1987). To our knowledge, the topic has not received recent attention and the nature of the processing which defines the doubling of a letter has not been clarified. In fact, according to Caramazza et al. (1990), whereas all non-geminate letters of a word are connected to distinct units on the identity tier, geminate letters are connected to only one such unit; the fact that this particular letter identity appears twice contiguously in the word is specified at another level of the representation. It remains an open question as to what sort of information is processed by the quantity tier and how it is specified.

Individuals with posterior cortical atrophy (PCA) may offer a valuable perspective on spelling models. PCA is a progressive neurodegenerative syndrome mainly characterized by progressive visuospatial and visuoperceptual dysfunction in a profile of preserved memory, insight, and judgment (Benson, Davis, & Snyder, 1988). In addition, individuals with PCA often manifest alexia, dysgraphia, acalculia, apraxia and some or all of the features of Balint's syndrome such as simultanagnosia, oculomotor apraxia, optic ataxia and environmental agnosia (Mendez, Ghajarania, & Perryman, 2002; Renner et al., 2004; Tang-Wai et al., 2004; Charles & Hillis, 2005; McMonagle, Deering, Berliner, & Kertesz, 2006; Lehmann et al., 2011). Individuals with PCA have problems in processing quantity information and in mathematical knowledge. Indeed, dyscalculia was named as one of the prominent symptoms in the original study of PCA (Benson et al., 1988) and was evident in 86% of patients in a recent case series study (Lehmann et al., 2011). However, quantity deficits in such patients are not restricted to calculation tasks, with performance also impaired in tasks requiring access to an internal representation of numbers such as mental number bisection, approximation, estimation and semantic facts (Delazer, Benke, Trieb, Schocke, & Ischebeck, 2006). This raises the possibility that quantity processing deficits may also have an impact on the spelling performance. According to Caramazza & Miceli's hypothesis (1990) of a multicomponent structure and possible dissociation for the graphemic representation between letter identity and letter quantity, individuals with PCA might be predicted to show a particular difficulty in spelling geminate words. If the letter identity elaboration is spared, but the quantity information is impaired, the deletion of one of the geminate letters might be predicted.

To the best of our knowledge, the relationship between spelling and quantity processing has not been examined previously, and only single case reports have investigated the details of the spelling deficit in PCA (Hecaen & Marcie, 1974; Ardila & Rosselli, 1993; Ross et al., 1996; Alfredo Ardila, Rosselli, Arvizu, & Kuljis, 1997; O'Dowd & Zubicaray, 2003). The nature of the spelling deficit in PCA has often been considered as peripheral and linked to visual difficulties (Graham, 2000). In fact, the illegibility of hand writing and the random placement of letters on a page have received much of the attention and have been considered as the manifestation of the 'spatial' disorder (Hecaen & Marcie, 1974; Ardila & Rosselli, 1993). However, a few single cases described in the literature indicate that the spelling deficit might also contain elements of a central impairment. For example, one patient out of three described by Ross et al (1996) showed symptoms of peripheral dysgraphia, whereby performance was worse for written than oral spelling and it was unaffected by the regularity of the word. Two further patients described in the same study demonstrated, however, symptoms of both central and peripheral deficits (Ross et al., 1996) with a prevalence of non-phonologically plausible errors, mainly letter deletions and substitutions. By contrast, a further case study reported symptoms of surface dysgraphia, a different central impairment characterized by the prevalent use of grapheme-phoneme conversion strategy, preserved spelling of regular words and regularization of irregular words (Ardila et al., 1997). More recently O'Dowd & Zubicary (2003) described a PCA patient, LM, whose spelling deficit was characterized by letter substitutions, insertions, deletions and transpositions. Her performance was sensitive to word length while insensitive to word-nonword category, word frequency, regularity, imagery, grammatical class, and ambiguity. The authors suggested a primary graphemic buffer disorder, which may be associated with deterioration of the verbal working memory (O'Dowd & Zubicaray, 2003). In summary, so far the reported single case studies have not been conclusive in terms of characterizing the nature of the spelling profile in PCA and identifying the most common locus (or loci) of impairment.

The first aim of the present study is to characterize the oral spelling profile of PCA and to identify the involved mechanism(s) in the context of the available spelling models. The lexical and phonological systems or the graphemic buffer may be selectively impaired or multiple locus of impairment might shape spelling performance. In order to exclude the confounding associated with visuospatial deficit and praxis problem and thus being able to study the central components involved in the spelling processes in individuals with PCA, we only tested patients' spelling abilities orally. The second aim is to further explore the nature of the 'quantity' feature of the representation of graphemic units. In particular, the well described loss of the impaired numerical knowledge and cognitive estimates processing in PCA might provide a novel perspective on the multidimensional structure of graphemic representation.

2. Method

2.1. Experiment 1

Experiment 1 sought to investigate how spelling errors of individuals with PCA are distributed between phonologically plausible and implausible typologies.

2.1.1. Participants

Experiment 1 involved 60 patients who met current criteria for a diagnosis of PCA owing to probable AD (Mendez et al., 2002; Tang-Wai et al., 2004). This diagnosis was made based on clinical and neuroimaging data. Demographics and clinical data on all participants are summarised in Table 1. All patients were enrolled in a longitudinal study of PCA. Total tau and Aβ42 CSF biomarker data were available for 6/60 patients; all had raised levels of tau and low Aβ42 (Tau/Aβ42 ratio > 0.52, Duits et al., 2014), a CSF profile previously described in association with pathologically proven AD.

Table 1. Demographic data and mean (SD) neuropsychological scores for the 60 individuals with PCA enrolled in Experiment 1.

	Max score	**PCA patients (N=60)**	**N (%) below 5%ile**	**Normative Mean (SD)**
Gender M:F		25:35	NA	NA
Age (years)		62.6 (7.7)	NA	NA
Education (years)		13.3 (2.4)	NA	NA
Disease duration (years)*		4.6 (2.5)	NA	NA
Background neuropsychology				
MMSE	30	19.5 (5.8)	NAv	NAv
Short Recognition Memory Test for words	25	20.2 (3.1)	38 (63.3)	23.5 (2.1)
Concrete Synonyms	25	20.3 (4.3)	25 (41.7%)	20.8 (3.0)
Naming (verbal)	20	14.2 (5.3)	40 (66.7%)	18.9 (1.5)
Cognitive estimates (error score)	30	11.7 (7.9)	15 (25.0%)	3.6 (1.9)
Calculation (GDA)	26	11.0 (4.7)	46 (76.7%)	20.7 (3.1)
Spelling (GDST - Set B)	20	10.1 (6.6)	19 (31.7%)	19.5 (6.5)
Gesture production test	15	11.5 (4.2)	-	15.0 (0.0)
Digit Span Forward (max)	12	5.8 (1.3)	39 (65.0%)	Range: 5-9
Digit Span Backward (max)	12	2.8 (1.1)	43 (71.7%)	NAv
Early visual processing				
Visual acuity (CORVIST): Snellen **	6/9	6/9	NA	NAv
Figure-ground discrimination (VOSP)	20	16.2 (3.2)	53 (88.3%)	19.9 (0.3)
Shape discrimination - Efron squares	20	13.6 (4.3)	54 (90.0%)***	20 (0.0)
Hue discrimination (CORVIST)	4	2.8 (1.7)	NA	NAv
Visuoperceptual processing				
Object decision (VOSP)	20	10.7 (4.8)	44 (73.3%)	17.7 (1.9)
Unusual and usual views: unusual	20	5.0 (5.1)	39 (65.0%)	17.1 (3.0)
Unusual and usual views: usual	20	13.1 (6.5)	34 (56.7%)	19.7 (0.5)
Visuospatial processing				
Fragmented letters (VOSP)	20	5.5 (6.1)	52 (86.7%)	18.8 (1.4)
Number location (VOSP)	10	2.5 (3.0)	57 (95.0%)	9.4 (1.1)

Dot counting (n correct)	10	4.1 (3.3)	54 (90.0%)	9.9 (0.2)
A Cancellation: completion time	90s	76.3 (34.9)	50 (83.3%)	NAv
CORVIST reading test	16	13.1 (5.5)	NA	NAv

* Disease duration was ascertained by asking participants or their caregivers when they first experienced symptoms.
** Median value is reported
*** Number and proportion of patients scoring below 20.
NA – Not applicable
NAv – Not Available

2.1.2. Background neuropsychology tests

- MMSE (Folstein, Folstein, & McHugh, 1975) The test consists of a series of questions. It tests a number of different mental abilities, including a person's memory, attention and language. Score range: 0-30.
- Short Recognition Memory Test for words Warrington (1996). The test contains 25 words that are visually and orally presented at the rate of 1 every 3 seconds. Participants have to express a judgment about each one (pleasant or unpleasant). The participant is then shown (orally and visually) with pair of words: the target and a distractor. The task is to identify the already seen and heard word. Score range: 12 (chance) – 25.
- Concrete synonyms test (Orpwood, 1998). The test is constituted of 25 target words presented orally. Patients are required to indicate which, out of two alternative words, is most similar in meaning to the target word. Score range: 12 (chance) – 25.
- Naming (verbal description). The experimenter describes some objects and other items and the participant is required to name the target. The test is interrupted after 4 consecutive errors. Score range: 0-20.

- Cognitive Estimates (Shallice & Evans, 1978). Participants are asked 30 questions for which a cognitive estimate, rather than a specific number, is required as a response. Each response can be scored between 0 (within the correct range) and 3 (extremely distant from a correct estimate). Score range: 30 - 0
- Graded difficulty calculation test. Patients are asked to sum up two numbers. The time cut-off is set to 30s for items 1-12 and to 30s for items 13-26. The first 12 items are administered irrespective of performance. From item 13the test is interrupted after 3 consecutive errors.
- Spelling. See the following section (2.1.3.).
- Gesture production test. The patient is asked to produce gestures such as use a toothbrush, a hammer and a trowel, wave and flick something away. 3 points are given if the gesture is correctly produced in the first instance, 2 points for the 2nd attempt, 1 point for the 3rd attempt and 0 for failure. Score range: 0-15
- Digit Span forward. 16 strings of numbers (length= 2-9, two strings for each length) are presented to the patient at the rate of 1/s. The patient is asked to repeat the string of numbers in the same order. The scores are represented by the total number of strings correctly reported and the maximum number of number in a string that the patient could correctly recall. Score range: 2-9.
- Digit Span backward. The test is administered as for the digit span forward. The only differences are the following: the patient is asked to repeat the sequence backwards and the length of the strings is 2-7, for a maximum of 14 strings administered. Score range: 2-7.
- Visual acuity (CORVIST) (James, Plant, & Warrington, 2001). The test measures visual acuity using three different shapes (triangles, squares and circles). Six rows, one for each size, each constituted of six items, are used. The score is given by the lowest row on which the participant responds to all 6 items accurately. Score range: 6/60 – 6/9.

- Figure-ground discrimination (VOSP) (Warrington & James, 1991). Patients are required to detect the presence of an X on speckled squares. 20 items are used and the target is present half of the times. Score range: 10 (chance score) - 20
- Shape discrimination – Efron squares (Efron, 1969). Patients are required to discriminate between a square and an oblong, which are randomly presented 10 times each. Score range: 10 (chance score) – 20
- Hue discrimination (CORVIST) (James et al., 2001). Patients are required to discriminate, among nine squares of similar colours, which of them is of a different hue. Score range: 0-4.
- Object decision (VOSP) (Warrington & James, 1991). Patients are required to identify, among 4 silhouettes, which one represent a real object (rather than a made-up one). Score range: 5 (chance score) – 20.
- Usual/Unusual views (Warrington & James, 1988). Patients are required to identify 20 pictures of objects taken from unusual prospective. Pictures taken from a usual perspective are re-presented for the objects which cannot be identified in the unusual perspective. Score range: 0-20.
- Fragmented letters (VOSP) (Warrington & James, 1991). Patients are asked to identify twenty capital fragmented letters, presented one at the time. Score range: 0-20.
- Number location (VOSP) (Warrington & James, 1991). Patients are required to look at sheets where there are two squares, exactly the same size. The top square contains numbers, all in different places. The bottom square just has a single dot in it. Patients are then asked to look at where the dot is in the bottom square, and indicate which number is in the same place in the top square. Ten trials are administered. Score range: 0-10.

- Dot counting (VOSP) (Warrington & James, 1991). Patients are required to indicate how many dots (range: 5-9) are represented on each of the 10 pages used. Reaction time is recorded. Score range (accuracy): 0-10.
- A cancellation (Willison & Warrington, 1992). Participants are presented with an A4 sheet where 19 As are embedded among other (N=69) distractor letters. Participants' task is to mark all As. Max time allowed: 90s.
- Reading (CORVIST) (James et al., 2001). The test includes 16 words the patients is asked to read aloud. One point is given for each correctly read word. Score range: 0-16.

2.1.3. Spelling test: Stimuli and Procedures

We administered the first 20 items of the Graded Difficulty Spelling test (Baxter & Warrington, 1994), to 60 individuals with PCA (Version B: N=57; Version A: N=3; Versions A and B highly correlated: r=0.92). Stimuli had a mean length of 5.8 letters (SD = 1.5; range = 4-10). Mean frequency (CELEX, Baayen, Piepenbrock, & van H, 1993) was 185.4 (SD= 374.5; range = 1 – 1464.6). The test was terminated after 4 consecutive errors. Participants were administered the test as part of a longitudinal neuropsychological study, with individual participants completing between 1 and 5 annual assessments. We only considered the earliest spelling assessment at which a MRI brain scan was also available (first visit: N=47; second visit: N=9; third visit: N=4). T1-weighted volumetric magnetic resonance images were acquired on a Siemens Trio TIM 3T scanner for the majority (75%) of the patients while the other scans were acquired in a 1.5T scanner.

2.1.4. Data analysis

Spelling errors were classified as phonologically plausible (e.g., *bruse* instead of *bruise*) and phonologically implausible (e.g., *paple* instead of *people*). We excluded those responses where the patients reported only one or two letters of the target word or when no answer was given and classified these as ‘others’.

In a second-step analysis, the phonologically implausible errors were classified further into five subcategories and included: substitutions (e.g. *cought* instead of *caught*), deletions (e.g. *oce* instead of *once*), insertions (e.g. *skiort* instead of *skirt*), transpositions (e.g. *peolpe* instead of *people*) and mixed errors (a combination of different phonologically implausible errors was produced; e.g. *taivl* instead of *table*). Furthermore, we classified the letter substitution errors on the basis of their phonological similarities to the target letters. The phonological relation (or not) between substituted letters was established on the basis of international phonetic alphabet classification (‘m’ and ‘n’ are phonologically similar, whilst ‘m’ and ‘b’ are not).

Statistical analysis was carried out on error category using STATA 12 with a univariate analysis of variance (dependent variable: number of errors; independent variable: error category [phonologically plausible, phonologically implausible and others]. A similar subsequent statistical analysis was carried out within the five error subcategories, in which the independent variable was the error subcategory (insertion, deletion, substitution, transposition, mixed). For both analyses Tukey HSD post-hoc tests were used to elucidate differences within error categories and subcategories.

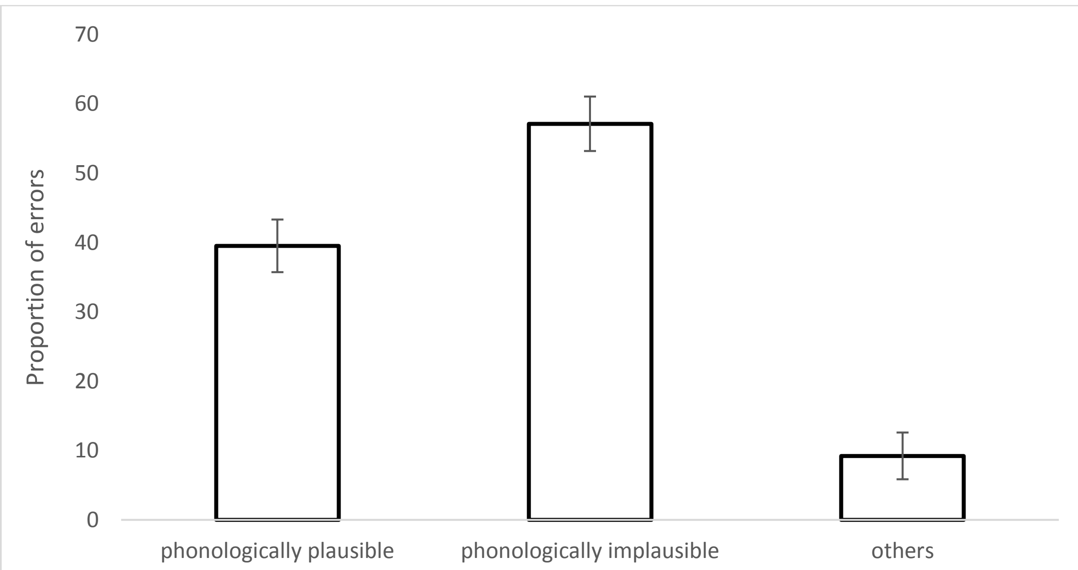
Analysis of neuroimaging data was carried out using voxel-based morphometry, performed in SPM12 (Statistical Parametric Mapping, Version 12; http://www.fil.ion.ucl.ac.uk/spm) running on MATLAB R2012a (http://www.mathworks.com). Images were rigidly orientated to standard Montreal Neurological Institute (MNI) space using the ‘New segment’ function in SPM12. Rigidly-orientated scans were segmented into grey matter, white matter and CSF. The Dartel toolbox (Ashburner, 2007) was used to perform spatial normalization, first aligning grey matter and white matter segmentations to their group-wise average (Ashburner & Friston, 2009), then combining this transformation with an affine mapping to MNI space. Normalized segmentations were modulated to preserve native-space tissue volumes and smoothed with a 6 mm full-width at half-maximum Gaussian kernel. A group-wise custom template in MNI space was created by arithmetically averaging the Dartel-normalized bias-corrected images of all 60 individuals with PCA. Associations between regional grey matter volume and spelling performance (number of correctly spelled words) were assessed using voxel-wise linear regression models in SPM12. Total intracranial volume, age, gender, MMSE and scan type score (3T or 1.5T) were included as covariates. A whole-brain grey matter mask was defined to include voxels for which the intensity was >0.1 in at least 80% of the images; this has been shown to be appropriate for participants with greater atrophy (Ridgway et al., 2009). A voxel-wise statistical threshold of $p<0.05$, family-wise error corrected for multiple comparisons was applied in all analyses. The resultant statistical parametric maps were overlaid on the custom template for display.

2.1.5. Results

Twenty-four out of 60 patients (40%) were impaired on the spelling assessment, falling below the 5th percentile. Some significant correlations were observed between the spelling performance and some of the background neuropsychological measures, such MMSE ($r=0.72$), concrete synonyms ($r=0.53$), naming ($r=0.63$), cognitive estimates ($r=0.59$), calculation ($r=0.69$) and reading ($r=0.58$; all $p<0.01$). All the other measures did not significantly correlate with the spelling performance.

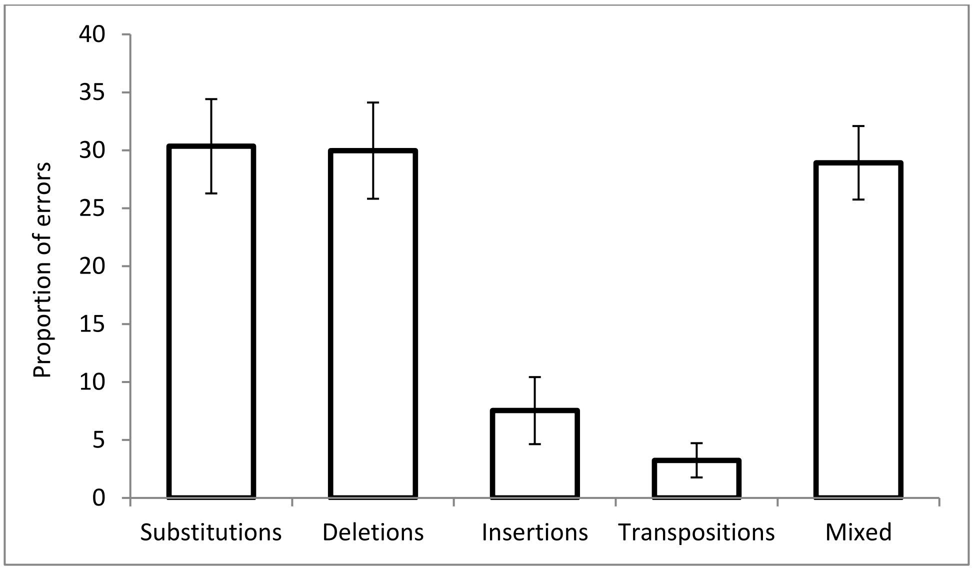
A total of 313 spelling errors, distributed within the three error categories described above (phonologically plausible, phonologically implausible, and others), were made by patients and are represented in Figure 1. The univariate analysis of variance indicated a main effect of error category [$F(2, 177)=32.5$, $p<0.0001$]. Phonologically implausible errors (N=176; 56.2%) were more frequent as compared to phonologically plausible errors (N=120; 38.3%, p=0.03) and both were more frequent than 'others' (N=17, 5.4%, both p<0.001). In terms of individual results, 61.7% of patients (N=37) showed a larger proportion of phonologically implausible vs. plausible errors, 13.3% of individuals (N=8) showed the same amount of the two errors' typology and 25% (N=15) of them showed a larger proportion of plausible vs. implausible errors.

Figure 1. Percentage of spelling errors classified in the different categories: phonologically plausible, phonologically implausible and others. Error bars represent standard errors.



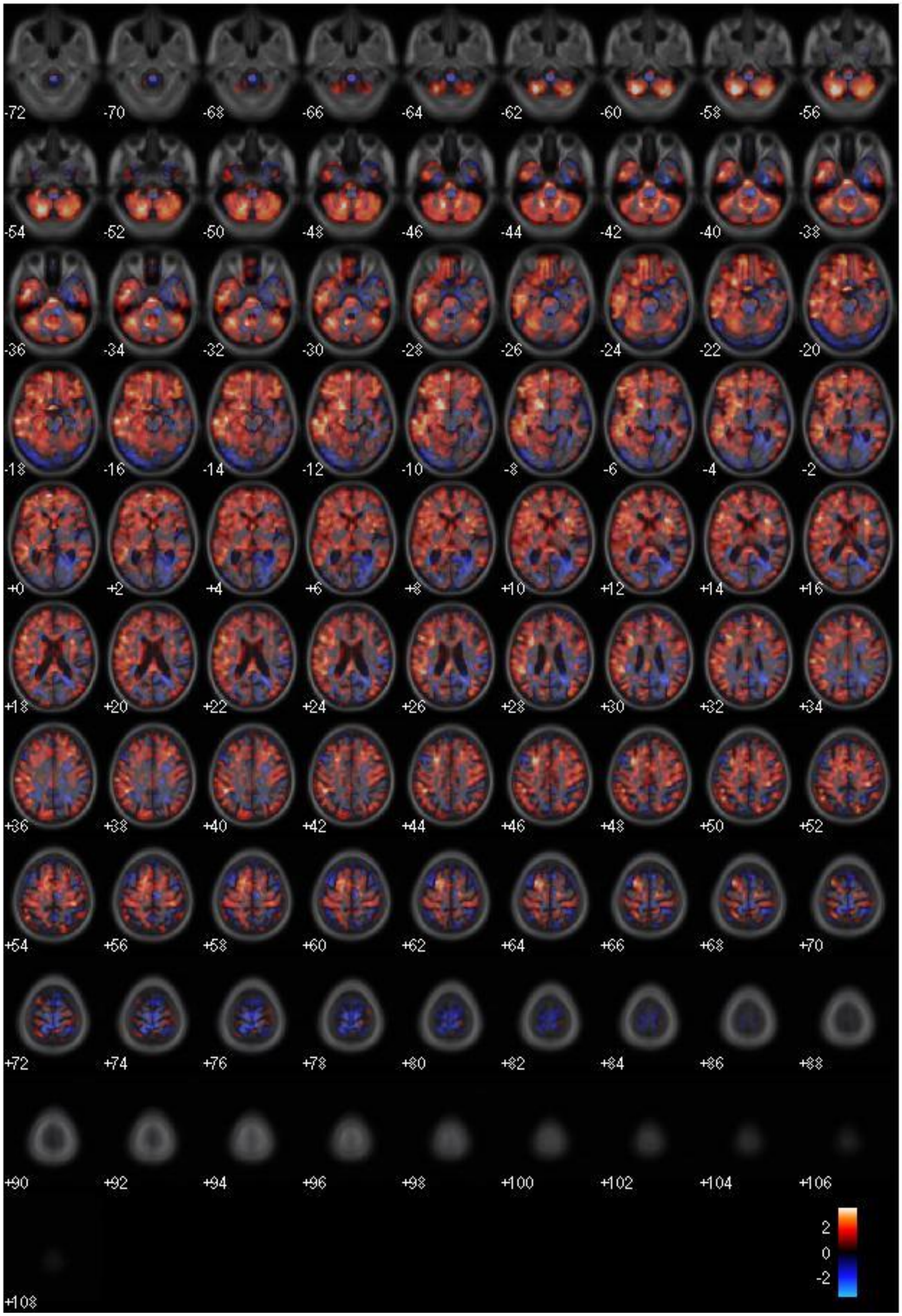
The number of substitutions, deletions, insertions, transpositions and mixed errors is shown in Figure 2. A significant main effect of error subcategory emerged [F(4, 295)=18.1, p<0.0001]. The Tukey HSD post-hoc test indicated that patients made a similarly high number of deletions (N=76, 30.0%) and substitutions (N=63, 30.3%; p=0.8) and a smaller number of insertions (N=12, 7.5%) and transpositions (N=6, 3.2%). The number of errors in these two categories is smaller as compared to deletions and substitutions (all p<0.001) but no significant difference emerged between the two (p=0.9). A large proportion of errors was characterized by phonologically mixed errors (N=74, 28.9%). This error category was as frequent as deletions and substitutions (both ps>0.1) but it was higher than both insertions and transpositions (both $p<0.001$). Finally, within the substituted letters, 17.2% (N=11) had a phonological relation with the target letter (e.g. *gause* instead of *gauze*).

Figure 2. Percentage of errors in the different error subcategories within the phonologically implausible errors: substitutions, deletions, insertion, transpositions and mixed errors. Error bars represent standard errors.



In terms of neuroimaging results, no significant associations between spelling performance and grey matter volume were found when correcting for multiple comparisons. A tendency toward an association with grey matter reduction in the left parietal and inferior temporal cortices and the frontal lobe can however be observed. T-contrast whole brain effect maps showing neuroanatomical associations between the number of correct responses in the spelling Baxter test and grey matter volume in individuals with PCA are displayed in Figure 3. The effect size map reported in Figure 3 was created on the basis of the correlation coefficient between spelling scores and brain atrophy.

Figure 3. T-contrast effect size maps showing uncorrected associations between a measure of spelling (proportion of correct responses) and grey matter volume displayed on axial sections. Warmer colours indicate stronger positive associations between a greater degree of impairment in spelling and lower grey matter volume, with cooler colours representing the reverse contrast. The colour-map indicates t-values for this association.


-72 -70 -68 -66 -64 -62 -60 -58 -56
-54 -52 -50 -48 -46 -44 -42 -40 -38
-36 -34 -32 -30 -28 -26 -24 -22 -20
-18 -16 -14 -12 -10 -8 -6 -4 -2
+0 +2 +4 +6 +8 +10 +12 +14 +16
+18 +20 +22 +24 +26 +28 +30 +32 +34
+36 +38 +40 +42 +44 +46 +48 +50 +52
+54 +56 +58 +60 +62 +64 +66 +68 +70
+72 +74 +76 +78 +80 +82 +84 +86 +88
+90 +92 +94 +96 +98 +100 +102 +104 +106
+108
2
0
-2

2.1.6. Comment

In summary, in the present experiment we explored the spelling pattern of errors in 60 patients with posterior cortical atrophy. Results indicated that patients made a larger proportion of phonologically implausible errors as compared to phonologically plausible errors. Moreover, patients mainly produced phonemes deletions and substitutions. A mix of different phonological errors on the same target word was also very frequent. Insertion and transposition errors were, instead, less frequent. The reported pattern of errors will be discussed in the General Discussion in terms of its relevance for the characterization of PCA.

2.2. Experiment 2

The second experiment was designed to test the details of the oral spelling impairment in PCA, including the effects of lexical, grammatical and phonological variables.

2.2.1. Participants

Eight individuals with PCA took part in Experiment 2. These were patients who were involved in the longitudinal study (Experiment 1) and then took part in an additional testing session.[1] The same selection criteria used in Experiment 1 were used in the present experiment. Patients' demographic information is reported in Table 2, left hand side.

[1] A large proportion of the patients who took part in Experiment 1, which was part of a longitudinal project, were recruited many years before the beginning of the detailed study on spelling abilities in PCA patients (Experiments 2 and 3). All the patients who were enrolled in the longitudinal study when Experiments 2 and 3 were running also took part in these.

Table 2. Demographic data and neuropsychological scores for the 8 individuals with PCA tested in Experiment 2 (left hand side) and for the 20 patients tested in Experiment 3 (right hand side).

		Experiment 2		Experiment 3	
	Max	**Mean**	**S.D.**	**Mean**	**S.D.**
Gender		M:F (3:5)	NA	M:F (7:13)	NA
Age (years)		64.6	7.0	66.1	7.2
Education (years)		15.6	2.6	15.3	2.3
Disease duration (years)		4.8	2.3	5.3	3.1
Background neuropsychology					
MMSE	30	21.9	4.6	23.3	4.0
Short Recognition Memory Test for words	25	20.7	3.1	18.4	5.8
Concrete Synonyms	25	22.5	2.0	22.2	2.1
Naming (verbal)	20	13.8	7.3	15.8	5.1
Cognitive estimates (errors)	30	10.3	7.0	9.0	5.7
Calculation (GDA)	26	6.7	7.2	7.4	6.7
Spelling (GDST - Set B first 20 items)	20	12.6	5.3	14.5	4.9
Gesture production test	15	12.3	2.7	13.1	2.4
Digit Span Forward (max)	12	5.9	1.2	5.9	1.2
Digit Span Backward (max)	12	3.8	1.4	3.5	1.4
Early visual processing					
Visual acuity (CORVIST): Snellen	6/9	6/9	NA	6/9	NA
Figure-ground discrimination (VOSP)	20	13.6	6.1	14.9	4.5
Shape discrimination - Efron squares	20	13.4	6.3	13.4	6.4
Hue discrimination (CORVIST)	4	2.4	1.8	2.2	1.5
Visuoperceptual processing					
Object decision (VOSP)	20	10.3	7.2	10.2	6.1
Fragmented letters (VOSP)	20	6.9	7.4	5.6	6.0
Visuospatial processing					
Number location (VOSP)	10	5.8	1.2	3.3	3.0
Dot counting (VOSP)	10	5.3	4.5	4.9	3.4

Dot counting (time s)	NA	6.6	2.9	8.7	4.5
A Cancellation: completion time (s)	90s	75.6	20.2	71.2	28.5
CORVIST reading test	16	12.3	5.0	13.9	3.7
Word minimal pairs discrimination	36	33.4	1.9	NAv	NAv
Upper to lower case letter matching	10	4.3	1.4	4.5	1.0
Single letter naming	41	19.2	6.0	NAv	NAv
Quantity facts test	20	12.3	5.7	NAv	NAv
Magnitude Judgments	10	9.0	1.9	NAv	NAv
Extended cognitive estimates	20	6.9	2.5	7.5	2.3

NA – Not applicable
NAv – Not Available

2.2.2. Background tests

All patients were administered the neuropsychological battery described in Experiment 1. Patients were also administered some further background tests, specifically aimed at assessing phonology, letter processing, numerical skills and quantity processing, including:

1. Phonology and letter processing tests

- *Word minimal pairs discrimination test* (N=36 items, from (*PALPA2;* Kay, Lesser, & Coltheart (1992): A phoneme perception test requiring a judgement as to whether pairs of spoken monosyllabic consonant–vowel–consonant words are the same (e.g., ‘coat’—‘coat’) or different (e.g., ‘tack’—‘cat’).
- *Single letter naming*: Patients were asked to read single letters presented at the centre of a computer screen (font: Courier New, letter height =1.2 deg from a viewing distance of 50 cm). Letters were presented within a central square fixation box subtending 2.5°/side to ameliorate the

effects of visual disorientation. All stimuli were presented in the first instance as capital letters. Those letters for which the visual form differs between upper and lower case were additionally presented in lower case (capital letters: N=26; lower case letters: N=15).

- *Letter imagery*: The examiner spoke the name of a letter and patients were asked to say if the pronounced letter had the same visual form in upper and lower cases. Ten letters were used, 5 in the same visual form condition (C, S, P, V, X) and 5 in the different visual form condition (H, R, N, B, D).

2. Numerical skills and quantity processing tests

- *Quantity facts tests* (N=20): Numerical semantics questions about quantity facts were presented (adapted from Crutch & Warrington, 2001; e.g. How many pence are there in a pound? How many days are there in a year?).
- *Magnitude judgments* (N=10): Patients were asked to decide which was the largest of two numbers spoken by the experimenter. Mean distance between numbers was 14.3, SD = 11.5, range = 2-40. The target largest number occurred 5 times as the first number presented and 5 times as the second number presented in pseudo-randomized order.
- *Extended cognitive estimates* (N=20): This test was composed of two parts, each including ten questions. For the first part the answer required the production of both a number and a unit of measurement (e.g., How heavy is the average British man?); for the second part just a number was required as a response (e.g., How many people are there in an orchestra?).
-

2.2.3. Spelling tests

For the spelling testing we administered 8 subtests from the PALPA test (Kay et al., 1992). The characteristics of the subtests were the following:

I. *Word length.* The subtest includes 24 monosyllabic words, ranging from 3 to 6 letters, 6 words for each length. Across each length condition, words are matched as closely as possible for frequency, imageability and morphemic complexity.

II. *Imageability and frequency.* Imageability (I) and frequency (F) are orthogonally manipulated so words could have high or low imagebility (I+ or I-, respectively) and high or low frequency (F+ or F-, respectively). 40 words are used: 10 I+F+, 10 I+F-, 10 I-F+, 10 I-F-.

III. *Regularity.* In order to investigate whether in PCA spelling to dictation is influenced by sound-spelling regularity, 20 regular and 20 exception words were used. Stimuli were matched (on an item-by-item basis) for word frequency, imageability, grammatical class and number of letters, syllables and morphemes.

IV. Nonwords. Made up words are a useful tool for assessing spelling skills (e.g., Bub & Kertesz, 1982)). Twenty-four 3 to 6 letter long nonwords were used, six for each length.

V. Homophones. Homophones are those words that share the same pronunciation with another word, but have different spelling and meaning. To disambiguate which is the word intended by the experimenter to be spelled, the patients were also given a short definition (e.g., '*bear*: Large animal with shaggy hair and claws'). Ten regular and ten exception homophones were used.

VI. *Lexical morphology*. Three sets of morphologically complex words were used: 10 words with regular inflections (e.g. *rocks*), 10 words with derivational endings (e.g. *cloudy*) and 10 irregularly inflected words (e.g. *mice*). Words were matched across the subsets for frequency and imageability. For each set of morphologically complex words, there was a corresponding set of mono-morphemic words which have the same final sound (e.g., tortured/orchard) for a total of 60 items. Morphologically complex words and their phonological controls were matched for frequency, imageability and syllable length.

VII. *Grammatical class I*. Sets of 10 nouns and 10 functors (e.g., prepositions, pronouns) were selected. Words were matched across groups (on an item-by-item basis) as far as possible for number of letters, syllables and morphemes. Nouns and functors were matched for imageability and frequency.

VIII. *Grammatical class II.* Sets of 5 nouns, adjectives, verbs and functors were selected. Words were matched across groups (on an item-by-item basis) as far as possible for word frequency, number of letters, syllables and morphemes. Nouns, adjectives and verbs were matched for imageability.

In order to improve the assessment of word length effect, a further set of 40 longer words (8, 9 and 10 letters-long words), extracted from Crutch & Warrington (2010) were included. Finally, 30 more geminate words (double letter words e.g. *summer*) were added to the original list in order to investigate the processing of words containing geminate letters. In total, each patient orally spelled 318 words. The number of letters, phonemes and syllables, frequency (total number of occurrences in the CELEX word frequency corpus divided by 17.9, Baayen et al., 1993), concreteness (MRC database [Coltheart, 1981]; range 100-700), imageability (imageability ratings from combined Bristol Norms [Stadthagen-Gonzalez & Davis, 2006] and MRC database [Coltheart, 1981]; range 100-700), orthographic and phonological neighbourhood size values (i.e., number of orthographic and phonologic similar words, see Wagenmakers & Raaijmakers, 2006) for the stimuli are reported in Table 3. For each stimulus, patients were asked to listen carefully to the stimulus, to repeat it so to ensure that it was heard correctly, and to spell it aloud.

Table 3. Means (and standard deviations) for length (expressed in letters, phonemes and syllables), frequency, concreteness, imageability, orthographic and phonological neighbours for words and nonwords used in Experiment 2. The same values are also separately reported for geminate words.

	Words (N = 294)	Nonwords (N = 24)	Geminate words (N = 70)
Length (letters)	5.6 (1.7)	4.5 (1.1)	6.0 (1.5)
Length (phonemes)	4.6 (1.6)	3.6 (07)	4.5 (1.3)
Length (syllables)	1.7 (0.8)	1.5 (0.5)	1.8 (0.6)
Frequency	68.6 (107.9)	NA	70.8 (91.9)
Concreteness	486.5 (129.2)	NA	501.5 (126.4)
Imageability	384.7 (230.2)	NA	382.3 (241.9)
Orthographic neighbours (N)	3.9 (4.9)	6.5 (6.1)	3.2 (3.7)
Phonologic neighbours (N)	9.7 (9.2)	8.5 (8.4)	9.1 (8.2)

NA: not applicable

2.2.4. Results

Results of the general neuropsychological assessment and the extra background tests for the 8 individuals with PCA are reported in Table 2, left hand side.

All patients correctly repeated the target stimulus before spelling it. The overall proportion of errors on the PALPA subsets was 26.5% (range: 4.1 – 59.3%). Results for individual PALPA subtests are reported in Table 4.

Table 4. Mean number of errors and standard deviations for the different PALPA spelling subset and relative conditions.

PALPA test results			
PALPA Subset	**Condition**	**Mean number of errors**	**S.D.**
Length (N=24)	3 letter words (N=6)	0.3	0.5
	4 letter words (N=6)	0.9	1.4

	5 letter words (N=6)	1.3	1.5
	6 letter words (N=6)	2.0	2.1
Imageability and frequency (N=40)	High Imageability (N=10)	2.8	2.6
	Low Imageability (N=10)	3.0	2.4
	High Frequency (N=10)	2.1	2.1
	Low Frequency (N=10)	3.0	3.2
Regularity (N=40)	Regular words (N=20)	2.4	3.6
	Exception words (N=20)	6.1	5.6
Nonwords (N=24)	3 letter nonwords (N=6)	0.8	0.9
	4 letter nonwords (N=6)	3.6	1.3
	5 letter nonwords (N=6)	2.8	2.1
	6 letter nonwords (N=6)	2.8	1.8
Homophones (N=20)	Regular (N=10)	0.6	0.5
	Exception (N=10)	6.1	5.2
Lexical morphology (N=60)	Morphological complex (N=30)	2.5	2.9
	Control (N=30)	3.6	2.5
Grammatical Class I (N=20)	Functors (N=10)	2.9	2.5
	Nouns (N=10)	2.5	2.8
Grammatical Class II (N=20)	Adjectives (N=5)	0.9	1.1
	Functors (N=5)	1.3	1.6
	Nouns (N=5)	1.0	1.6
	Verbs (N=5)	1.1	1.1

Paired one-tailed t-tests were run to compare the proportion of errors within each subtest or between subtests where appropriate.

I. *Word length.* As shown in the table, a progressively larger proportion of errors was observed with longer words. Statistically significant differences were observed between 3 *vs*. 5 and 3 *vs*. 6 letter words (p=0.05 and 0.02, respectively) and a non-significant trend towards a difference between 4 vs. 6 letter words (p=0.07).

II. *Imageability and frequency*. No significant differences emerged between high and low frequency words (p=0.1), nor in the comparison between high and low imageability words (p=0.3).

III. *Regularity*. A larger proportion of spelling errors was observed on exception words as compared to regular words (p=0.005).

IV. *Nonwords*. A larger proportion of errors was observed in 4, 5 and 6 letter stimuli as compared to 3 letter stimuli (all ps<0.05) and in 5-letter stimuli as compared to 4-letter stimuli (p=0.04). All the other comparisons within the nonword subset were not significant. We compared the proportion of errors made on nonwords and the matched words from the length subtest. Results indicated that a lexical effect was significant for 3 and 4 letter stimuli (p=0.05 and 0.001, respectively), marginally significant for 5 letter stimuli (p=0.06) and non-significant for 6 letter stimuli (p=0.2). Nonetheless, as reported below, individual results indicated that a significant lexical effect in shown in 5 out of 8 individuals with PCA.

V. *Homophones*. A larger proportion of errors was observed with exception vs. regular homophones (p=0.03).

VI. *Lexical morphology*. There was no significant difference in spelling accuracy for morphologically complex and mono-morphemic phonological control words (p=0.09).

VII. *Grammatical class I*. There was no significant difference in spelling accuracy between nouns and functors (p=0.24).

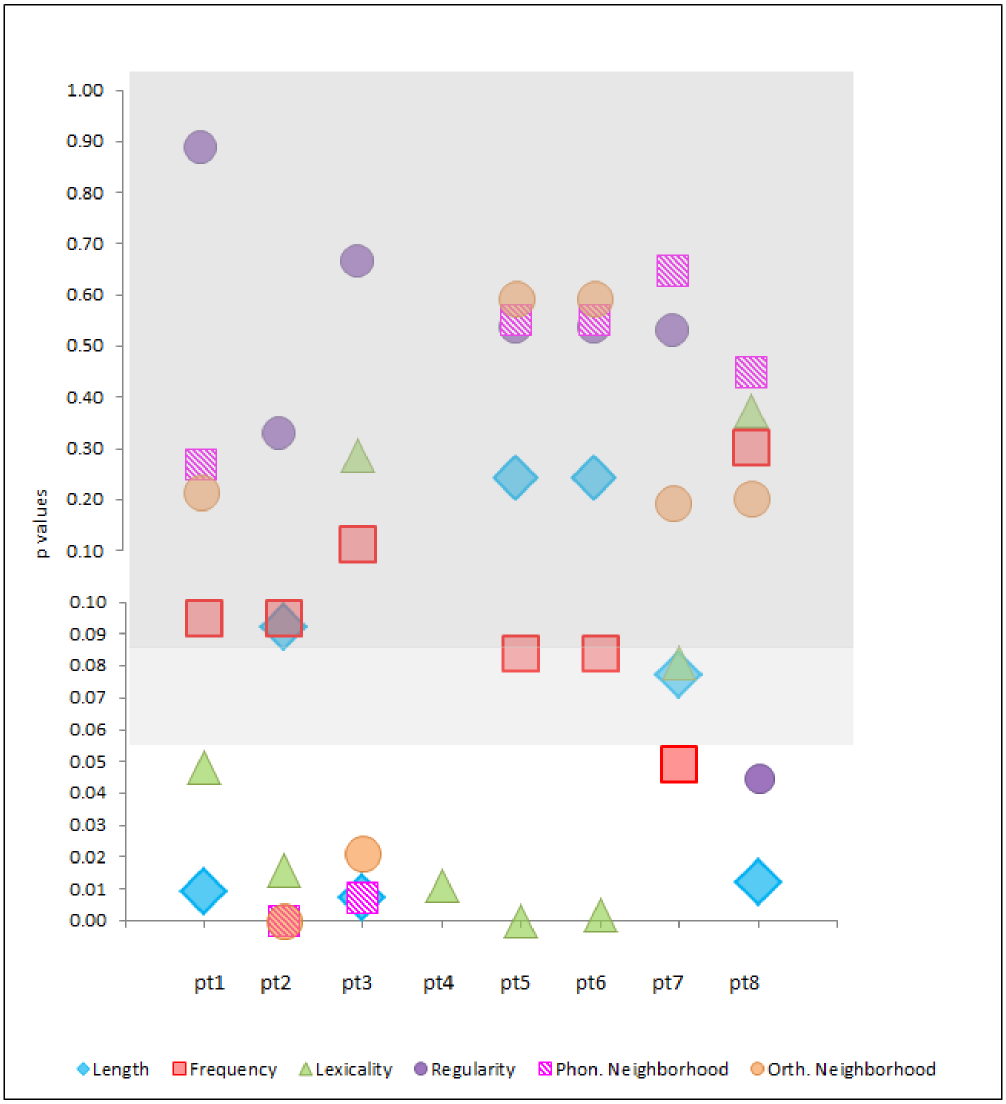
VIII. *Grammatical class II*. No significant differences emerged among the four grammatical classes in terms of proportion of spelling errors (all ps>0.1).

A logistic regression analysis of binary accuracy data was conducted on the entire dataset of words with number of letters, frequency, concreteness, imageability, orthographic and phonological neighbourhood size as independent variables and responses clustered by participants (STATA 12). Age and years of education were also included as nuisance variables.

Results showed length and frequency effects with an increase in the number of spelling errors on longer words ($z=8.48$, $p<.0001$) and on low frequency words ($z=4.36$, $p<.0001$). The frequency by length interaction was not statistically significant ($z=1.03$; $p=0.3$). Also the orthographic and phonological neighbourhood sizes were significant predictors of performance: more spelling errors were observed with smaller orthographic neighbourhood size ($z=-2.99$, $p=0.003$) and with words having larger phonological neighbourhood size ($z=3.41$, $p=0.001$). All the other variables did not play a statistically significant role in the spelling performance. A more in-depth qualitative error analyses on incorrect responses indicated that 85% of the errors on words resulted in nonwords (range: 65.8%-100%) and 52% of errors made on nonwords resulted in different nonwords (range: 30.8%-75.0%). Moreover, we explored the presence of illegal sequences in the patients' errors. We classified 2 and 3 letter sequences as illegal if the bigram or trigram frequency was equal to 0 (Jones & Mewhort, 2004; Davis, 2005). All but one patients produced responses including illegal sequences (Mean=5.5, SD=4.8, range =1-14). This is compatible with the hypothesis of a graphemic buffer damage (Caramazza, Miceli, Villa, & Romani, 1987; Hillis & Caramazza, 1989).

Moreover, individual logistic regression analyses of binary accuracy data have been run for each patient who took part in Experiment 2 in order to establish the co-occurrence or selective impairment of different domains contributing to the spelling performance. The individual regression analyses looked at the effects of length, frequency, concreteness, imageability, orthographic and phonological neighbourhood size. Lexicality has been tested by using one-tailed t-test between scores obtained in the PALPA subtests I and IV. Results of the analyses are reported in Figure 4, where the p-values for each effect and each patient are reported. Noteworthy individual differences are shown: the lexical effect is shown in 5 patients, the length effect in 3, the orthographic neighbourhood in 2, the regularity in 1, and the frequency effect in 1. Results also highlight that in half of the patients a combination of deficits affecting lexical and sublexical processes is evident.

Figure 4. Individual differences in the spelling performance from Experiment 2. P-values are reported for each patient and each effect studied: length, frequency, lexicality, regularity, phonological neighbourhood and orthographic neighbourhood. The white area represents the area where significant results were shown ($p<.05$), the light grey area represent a tendency to statistical significance ($.06<p<.08$) and the dark grey area represent non-significant values ($p>.08$).



In order to investigate the relationship between the patients' spelling performance (total number of correct responses on the stimuli used in the experiment) and other cognitive functions, correlations were performed with the results of the tests administered as part of the background cognitive assessment. Results showed that the spelling performance was significantly correlated (all $p<0.05$) with the Baxter spelling test ($r=0.98$) and the cognitive estimates test ($r=0.76$) but none of the other background measures. Among the extra background tests spelling performance was significantly correlated with the quantity fact test (r=0.70) and with extended cognitive estimate measures (r=0.86). All the other correlations were not statistically significant.

Within the spelling error dataset, we observed a high proportion of spelling errors regarding geminate words (36.3%) (proportion of errors on non-geminate words: 24.3%). Following Caramazza & Miceli (1990) we analysed the typology of errors made on geminate words. A list including the number and percentages of different typology of errors on geminate words is reported in Table 5. The most common error was the deletion of a geminate letter (55%). Given that Experiment 2 was not formally designed for testing differences between geminate and non-geminate words, no formal statistics were run. Experiment 3 (see Section 3) addressed this topic directly.

Table 5. For each typology of error concerning geminate words the total number, percentage, mean and standard deviation are reported.

Error typology	***Total number of errors***	***Percentage of errors***	***Mean***	***S.D.***
Deletion of a geminate letter (tummy --> tumy)	111	55.0	13.9	12.5
Substitution of one geminate letter (moon --> moun)	26	12.9	3.3	4.1
Duplication of a non-geminate letter (tunnel --> tuneel)	8	4.0	1.0	1.4
Deletion of one geminate letter and substitution of the other (crook --> crak)	5	2.5	0.6	1.1
Deletion of two geminate letters (cheese --> chse)	2	1.0	0.3	0.5
Substitution of two geminate letters (effort --> ephort)	2	1.0	0.3	0.7
Non-geminate duplication (door --> doorr)	1	0.5	0.1	0.4
Errors not related to the geminate letters (dummy --> dumme)	47	23.3	5.9	6.1

2.2.5. *Comment*

Results of Experiment 2 documented the presence of length and frequency effects in individuals with PCA, who produced a larger proportion of errors with longer and lower frequency words. Individual differences have also been described. Poor performance in spelling geminate words as compared to non-geminate words was observed. The prevalent typology of error concerning geminate words is represented by the deletion of one of the two geminate letters. Following Caramazza & Miceli's model of graphemic representation as multidimensional objects (1990), such a pattern of errors may indicate better preserved grapheme identity processing and a difficulty in processing the quantity information about the geminate feature. This is also compatible with the observed correlations between spelling performance and tests measuring quantity functions. Nonetheless such correlations should be interpreted cautiously given the small sample size and would need further exploration in a larger sample of patients.

3. Experiment 3

In order to further investigate the nature of the spelling impairment affecting geminate words, we directly compared two sets of matched geminate and non-geminate words in a larger sample of individuals with PCA.

3.1. *Participants*

In Experiment 3 we tested 20 individuals with PCA: 8 patients from Experiment 2 for whom we re-analysed a subset of their data as part of the present experiment (see below, 'Stimuli' section) and 12 patients (same selection criteria as per Experiments 1 and 2) who were tested ex-novo. Demographic information and the results from the background neuropsychological assessments are reported in Table 2, right hand side. A group of 9 healthy individuals with no history of neurological conditions took part in the experiment as controls. Controls were matched to individuals with PCA for age (mean: 67.5 years; SD: 7.5; range: 50-74; p=.6) and education (mean: 15.1 years; SD: 2.7; range: 12-19; p=.9).

3.2. Stimuli and procedure

From the original pool of words used in Experiment 2, we selected 60 stimuli, 30 geminate and 30 non-geminate words matched for number of letters, phonemes and syllables, frequency, concreteness, imageability, orthographic and phonological neighbourhood size and frequency, and regularity (see Table 6). The two lists were also matched in order to have a similar proportion of nouns, verbs, adjectives and functors and a similar proportion of regular and exception words. For each stimulus, patients were asked to listen carefully to the stimulus, to repeat it so to ensure that it was heard correctly, and to spell it aloud.

Table 6. Linguistic features of the geminate and non-geminate word stimuli used in Experiment 3 and comparisons (2-tailed t-tests; p values).

	Geminate Words (N=30)		**Non-Geminate Words (N=30)**		
	Average	SD	Average	SD	p values
Length (letters)	6.0	0.8	5.9	0.8	0.8
Length (phonemes)	4.4	0.8	4.9	1.4	0.1
Length (syllables)	1.7	0.5	1.8	0.8	0.6
Frequency	58.8	76.1	57.5	45.1	0.9
Concreteness	522.4	104.2	462.9	128.4	0.1
Imageability	496.5	124.8	482.3	114.6	0.7
Orthographic neighbours (N)	2.3	2.5	1.3	1.8	0.1
Phonologic neighbours (N)	7.0	5.2	5.5	6.1	0.3

3.3. Results

All participants correctly repeated the target stimulus before spelling it. Controls made an average of 1.3 errors (SD:1.7, range:0-5). None of the spelling errors made by healthy controls involved the deletion of a geminate letter. All controls also showed a high performance in the extended cognitive estimates test (mean score:19.6, SD:0.5, range:19-20) and in the upper to lower case letter matching test (mean score:9.4, SD:0.5, range:9-10). However, because of the ceiling performance and the consequent lack of variability, controls did not enter further statistical analysis.

Results for the 20 individuals with PCA are reported in Table 7. Patients showed an overall similar proportion of errors in spelling geminate and non-geminate words [$F(1, 38)=.006$, $p=.94$]. However, when looking closely at the geminate words, it emerged that a larger proportion of errors involved geminate letters as compared to non-geminate letters [$F(1, 38)=8.8$, $p=.005$]. Moreover error typology affected differently geminate and non-geminate letters: while deletions mainly involved geminate letters [$F(1, 38)=11.3$, $p=.002$] substitutions equally affected geminate and non-geminate letters [$F(1, 38)=1.6$, $p=.2$]. Within non-geminate words, letters were similarly affected by deletions and substitutions [$F(1, 38)=2.8$, $p=.09$].

Table 7. Proportion of errors made by individuals with PCA in Experiment 3 on geminate and non-geminate words, geminate and non-geminate letters.

	Average	**SD**
% Misspelled words (overall; N words=60)	25.3	19.8
% Misspelled geminate words (N words=30)	25.0	22.8
% Misspelled non-geminate words (N words=30)	25.5	18.8
GEMINATE WORDS (N words=30)		
% errors involving geminate letters (N letters=60)	9.8	10.4
% errors involving non-geminate letters (N letters=120)	2.7	2.9

% deletion of a geminate letter (N letters=60)	7.0	7.6
% deletion of a non-geminate letter (N letters=120)	1.2	1.4
% substitutions of a geminate letter (N letters=60)	2.8	4.3
% substitutions of a non-geminate letter (N letters=120)	1.5	2.4
NON-GEMINATE WORDS (N words=30)		
% deletion (N letters=178)	2.1	2.0
% substitutions (N letters=178)	3.6	3.4

The number of deleted geminate letters correlated significantly ($p<.05$) with MMSE ($r=0.73$), short recognition memory test for words ($r=0.62$), naming ($r=0.49$), cognitive estimates ($r=0.47$), calculation ($r=0.52$), spelling ($r=0.58$), object decision ($r=0.48$), fragmented letters ($r=0.44$), reading ($r=0.58$), upper-to-lower case matching ($r=0.73$) and extended cognitive estimates ($r=0.62$). Conversely, the deletion of non-geminate letters did not significantly correlate with any of the background neuropsychological measures available (all $p>.1$).

3.4. Comment

Experiment 3 clarified the nature of spelling errors concerning geminate features in PCA. Not only a larger proportion of errors concerned geminate as compared to non-geminate letters, but also a difference in terms of error type is observed. Geminate letters are more prone to deletions and non-geminate letters are more prone to substitution errors. Finally, the number of deleted geminate letters significantly correlated with multiple neuropsychology scores. This might suggest a broader association between disease severity and frequency of geminate letter deletion.

In the Discussion (Section 4) these results are discussed in terms of neuropsychological relevance and implications and in terms of the computational spelling models available to date.

4. Discussion

In the current paper we characterised the oral spelling profile in posterior cortical atrophy in terms of error frequency and error type. Consistent with early descriptions (Benson et al., 1988) and some diagnostic criteria (e.g. Mendez et al., 2002), spelling impairment was found to be frequently evident, with 40% of patients falling below the 5^{th} percentile on a standardised spelling test. In Experiment 1, a detailed analysis of the oral spelling error pattern in a sample of 60 individuals with PCA showed that the largest proportion of errors were phonologically implausible; specifically, a larger proportion of deletions and substitutions was observed. In Experiment 2, by using a larger set of stimuli, we explored psycholinguistic influences upon the spelling performance of individuals with PCA. In particular, at the group level marked length and frequency effects were evident whereby a larger proportion of errors was produced with longer and lower frequency words. Effects of regularity and orthographic and phonological neighbourhood sizes were also documented. At an individual level, however, a large heterogeneity among patients is described whereby some patients show effects indicative of a selective lexical or sublexical deficit while for others a combination of effects suggests the role played by multiple loci of impairment. Finally, significant positive correlations emerged between the spelling pattern and tests measuring abstract numerical or quantity knowledge (cognitive estimates and quantity fact tests), albeit in a small number of participants. Experiment 2 also highlighted particularly poor performance in spelling geminate words as compared to non-geminate words. The issue was further investigated in Experiment 3 where results indicated that geminate letters were more prone to errors as compared to non-geminate letters. Moreover, a difference in the types of errors emerged: geminate letters were more affected by deletions as compared to non-geminate letters by a factor of 2; conversely, errors on non-geminate letters mainly involved substitution errors.

Neuropsychological relevance and implications

To our knowledge this is the first group study investigating in detail the nature of the spelling impairment in a population of individuals with PCA. Graham (2000), in her review about spelling difficulties in the different types of dementia, highlighted that the spelling deficit in PCA has usually been attributed to a peripheral impairment. Indeed the dysgraphia has often been labelled as 'spatial', since problems with legibility and placement of letters on a page have had the focus of researchers' attention (Hecaen & Marcie, 1974; Ardila & Rosselli, 1993). Even though such a peripheral component is an important element of PCA, the present study, by focusing on oral spelling, demonstrates that the spelling deficit in PCA on the whole goes beyond a peripheral deficit and contains elements of a profound central dysgraphia. Some previous single case studies reported patterns of errors consistent with a central deficit, even though discrepancies were reported in terms of what was considered the be the specific locus of impairment. For example, the pattern of errors reported in the patients described by Ardila et al., (1997) is more consistent with a surface dysgraphia, while the one described by O'Dowd & Zubicaray (2003) could be classified as phonological dysgraphia. The present study helps to clarify this debate and shed some light on the characterization of spelling errors in PCA, whilst keeping in mind that owing to the large phenotypic heterogeneity in PCA, the nature of the impairment may vary among patients as shown by the reported individual differences in Experiment 2. The presence of lexical effect in a large proportion of PCA patients and the prevalence of phonologically implausible errors and in particular deletions and substitutions is compatible with a phonological dysgraphia. These effects have, in fact, been interpreted to reflect the selective breakdown of sublexical phoneme-grapheme conversion mechanisms. However, the lack of a strong benefit in spelling words as compared to nonwords for some of the patients and a more impaired performance in spelling irregular vs. regular words find a better explanation if an impairment of the lexical system is also taken into account, as for the case of surface dysgraphia (Baxter & Warrington, 1987; Behrmann & Bub, 1992). Finally, the marked length effect is compatible with a deficit to the graphemic buffer. The graphemic buffer is the dedicated short-term memory system which holds the abstract orthographic representations generated by the lexical and phonological processing during the operation of more peripheral output mechanisms. A deficit to this system yields strong length effects (Caramazza et al., 1987). The observed prevalence of nonword errors when spelling both words and nonwords and the presence of orthographically illegal letter sequences are compatible with the hypothesis of a lexical or a graphemic buffer damage (Caramazza et al., 1987; Hillis & Caramazza, 1989).

Moreover, although the spelling task administered in the present study systematically required a verbal response only, and the impact of peripheral components cannot be directly estimated, the role played by visuospatial components needs to be considered. In fact, the task's demands on visual imagery and spatial processing skills are substantial and a distorted mental imagery for letters and for their mutual spatial relationship within the target word may have had an impact. However, this possibility was not supported given the lack of significant correlations between the spelling performance and the visuoperceptual and visuospatial tests.

Elements of both phonological and surface dysgraphia and evidences of an impairment to the graphemic buffer seem to suggest that a multiple, rather than a single, locus of impairment can characterize the spelling pattern of this group of patients. More broadly, a hypothesis linked to the involvement of multiple cognitive processes in the production of the observed error pattern must be explored. This is even more evident if we take into account both the large heterogeneity but also the co-existence of lexical and sublexical effects within the same individuals.

The large proportion of phonological errors is compatible with the reported impairment of phonologically coded auditory verbal short term memory and a deficit in access to or retrieval of phonological information in a group of 15 individuals with PCA (Crutch, Lehmann, Warren, & Rohrer, 2013). The larger proportion of spelling errors observed with words having smaller orthographic but larger phonological neighbourhood sizes represents the pathological expression of common phenomena observed with normal controls: orthographic facilitation and phonological inhibition (Ziegler, Muneaux, & Grainger, 2003). The facilitatory effect of orthographic neighbours suggests that a more efficient processing strategy is in action with spoken words having a more common orthographic structure. Conversely, the phonological inhibitory effect has been attributed to a higher lexical competition between phonologically similar words.

According to the literature, substitutions and deletion errors have their origin in an orthographic impairment. The proportion of substitutions affecting geminate and non-geminate letters is similar and thus we can hypothesize that the same mechanism is responsible for the substitution errors observed in both cases. However, the particularly high frequency of deletion errors on geminate letters as compared to non-geminate letters might suggests the involvement of a further mechanism in which letter identity is partially preserved but 'quantity' features of the graphemic representation coding for the letter numerosity is more impaired. In particular, we suggest that a quantity processing deficit might exacerbate the proportion of geminate letter deletion errors which, as stated above, might occur even just as a consequence of the orthographic deficit.

However, despite the observed positive correlations between tests measuring abstract numerical or quantity knowledge (cognitive estimates, calculation and extended cognitive estimates) and deletion of a geminate letter the proportion of deleted geminate letters also correlated with multiple cognitive scores. This leaves open the possibility that the deficits in processing the quantity information about geminate letters and quantity information in general represent co-occurrences of two neuropsychological impairments. It is also possible that the deletion of geminate letters more frequently co-occurs with a higher degree of disease severity. Nonetheless, errors concerning geminate letter are particularly informative since they might reflect not only an impairment associated with the phonological route but also the abstract graphemic representation of letter numerosity. Implication of these results for cognitive spelling models are discussed below.

Although not statistically significant, the neuro-anatomical correlates derived from the VBM analysis are in accordance with the behavioural evidence of multiple loci of impairment and the previous literature on neural correlates of selective spelling impairments. Our results indicate a non-significant association between the spelling performance and the grey matter reduction in the left parietal, inferior temporal and frontal cortices. Previous literature has identified various neural correlates of specific spelling impairments. In particular, the left inferior temporal cortex has been shown to be involved in cases of surface dysgraphia and it has been considered as the neural substrate of the orthographic lexicon where the memory representations of written forms of familiar words are stored (Rapcsak & Beeson, 2004) and is crucial for lexical–semantic processing (Ralph, Sage, Jones, & Mayberry, 2010; Hickok & Poeppel, 2004). Left temporo-parietal involvement has also been described in patients with phonological dysgraphia (Rapcsak et al., 2009) while orthographic working memory deficits have been primarily attributed to lesions of the left parietal cortex (Rapp, Purcell, Hillis, Capasso, & Miceli, 2016). Finally, brain atrophy in the left frontal and temporoparietal regions has been significantly associated with impaired phonological skills (Henry et al., 2016). A cautious interpretation of our neuroimaging results is mandatory since only non-significant associations were observed. However, the fact that we find an, albeit weak, signal in multiple left fronto-tempo-parietal areas (rather than in a single brain area) that have already been individually associated with different spelling impairments is in agreement with the behavioural evidence of multiple loci of impairment involved in the PCA oral spelling deficit.

Finally, the present study is, to the best of our knowledge, the first group study looking at the spelling deficit in PCA patients as a group but also on individual basis and can provide a wider perspective on the large heterogeneity within the disease as compared to previous, single case studies. Phenotypical variability is a common finding in PCA and broadly in many neuropsychological conditions (Zillmer & Spiers, 2001). As in semantic dementia a case series approach has been required to address issues of heterogeneity (e.g. Lambon Ralph, Patterson, Garrard, & Hodges, 2003), we have to look at both group and individual performance to understand the multiple drivers of spelling performance in individuals with PCA. Indeed, the present results help to contextualise the existing single-case neuropsychological literature on spelling in PCA in which unitary explanations in terms of either a lexical or phonological impairment have been offered. Our data confirm that individual patients might show symptoms of a relatively isolated lexical or sublexical deficit. Nonetheless, despite the individual differences, we have also demonstrated that, within the same individuals, multiple loci of impairment can provide a better account for the spelling pattern of errors rather than a single deficit, at least in a proportion of patients.

Our results are overall in accordance with the broader literature on heterogeneity in PCA. A heterogeneous pattern of visual impairment among the PCA patients has already been described and the hypothesis according to which different presentations of PCA represent points in a continuum of phenotypical variation has been raised (Lehmann et al., 2011; Crutch et al., 2012). A similar phenotypical variability has been demonstrated by our data on the pattern of spelling errors and needs to be taken into account in the clinical and research settings.

Implications for cognitive models of spelling

The results coming from the present study are also relevant in terms of cognitive psychology and the available spelling models. According to a linear system of abstract letter identities for the representation of the graphemic elements (Wing & Baddeley, 1980; Caramazza et al., 1987) a similar number and typology of errors should be expected for all the graphemes in the strings of the target words. A different pattern of errors affecting geminate letters as compared to non-geminate letters is more compatible with a non-linear graphemic representation. In this context graphemes are regarded as multidimensional mental objects that separately encode information about grapheme identity and quantity (Caramazza & Miceli, 1990). The large proportion of deletion and substitution errors observed in Experiment 1 indicates a deficit in grapheme identity. However, this is not in contradiction with the hypothesis that a further deficit concerning the quantity feature of graphemic representation is an additional source of impairment. Indeed, the more fine grained analysis run in Experiment 3 showed that geminate letters are more prone to errors than non-geminate letters, mainly due to the correct reporting of only one of the two letters (deletion of one geminate letter). This is in accordance with the evidence reported about abstract quantity processing deficits not only restricted to calculation, but also evident in tasks where access to an internal representation of numbers is required, such as mental number bisection, approximation, estimation and semantic facts (Delazer et al., 2006). Such a difficulty in accessing the internal representation of quantity may thus determine an exacerbation of a specific error pattern in spelling geminate words which, as observed in our group of individuals with PCA, provide more information about the nature of the quantity feature of graphemic representations. Indeed, a larger proportion or errors affecting geminate vs. non-geminate letters and the deletion (rather than other typology of errors) affecting one of the geminate letters would be predicted and is observed.

This pattern might suggest that a further deficit in 'quantity' processing can have an impact on the pattern of spelling errors in individuals with PCA. This is particularly relevant in terms of the theoretical support it can provide to spelling models, strengthening the hypothesis according to which geminate letters have a special status in terms of graphemic representation and that such graphemic representations are indeed complex multidimensional structures (Caramazza & Miceli, 1990). In particular, we interpret the larger proportion of errors and the different typology of errors affecting geminate vs. non-geminate letters as an indication that information about identity and quantity are at least partially independently coded and can therefore be selectively impaired. A partial preservation of letter identity and a deeper damage to the respective quantity feature may shape a proportion of the results. The lack of a stronger and unique correlation between geminate letter deletions and processing of quantity information, however, implies a cautious interpretation and generalization of the data and stimulate further research on the topic.

Study limitations

Patients with very different levels of disease severity have been included in the study, and despite the fact that we looked at individual differences in Experiment 2, group analyses might have overshadowed some of them. Not all patients with PCA have a spelling impairment, and among those who do, the severity, nature and specific mechanism(s) involved might not be identical for all patients. Sample size is small in Experiment 2. For this reason, correlations have to be interpreted with caution. A larger sample of patients is required to further test the hypothesis of a link between abstract quantity processing and spelling of geminate words in individuals with PCA.

5. Conclusion

In conclusion the present study provides a detailed characterization of the oral spelling profile of posterior cortical atrophy, highlighting the central components of the deficit and the involvement of multiple cognitive processes. In particular, elements of phonological and lexical dysgraphia but also features of a graphemic buffer deficit are reported suggesting, despite a substantial individual variability, a multiple locus of impairment in at least a proportion of individuals with PCA. Moreover, the study provides further evidence to the hypothesis according to which graphemic representations are multidimensional mental objects that separately encode information about grapheme identity and quantity.

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