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Anatomic, clinical, and neuropsychological correlates of spelling errors in primary progressive aphasia

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ABSTRACT

This study evaluates spelling errors in the three subtypes of primary progressive aphasia (PPA): agrammatic (PPA-G), logopenic (PPA-L), and semantic (PPA-S). Forty-one PPA patients and 36 age-matched healthy controls were administered a test of spelling. The total number of errors and types of errors in spelling to dictation of regular words, exception words and nonwords, were recorded. Error types were classified based on phonetic plausibility. In the first analysis, scores were evaluated by clinical diagnosis. Errors in spelling exception words and phonetically plausible errors were seen in PPA-S. Conversely, PPA-G was associated with errors in nonword spelling and phonetically implausible errors. In the next analysis, spelling scores were correlated to other neuropsychological language test scores. Significant correlations were found between exception word spelling and measures of naming and single word comprehension. Nonword spelling correlated with tests of grammar and repetition. Global language measures did not correlate significantly with spelling scores, however. Cortical thickness analysis based on MRI showed that atrophy in several language regions of interest were correlated with spelling errors. Atrophy in the left supramarginal gyrus and inferior frontal gyrus (IFG) pars orbitalis correlated with errors in nonword spelling, while thinning in the left temporal pole and fusiform gyrus correlated with errors in exception word spelling. Additionally, phonetically implausible errors in regular word spelling correlated with thinning in the left IFG pars triangularis and pars opercularis. Together, these findings suggest two independent systems for spelling to dictation, one phonetic (phoneme to grapheme conversion), and one lexical (whole word retrieval).

1. Introduction

1.1. Agraphia

Damage or atrophy in the left hemisphere causes a variety of language deficits. While often not the main complaint of patients with language impairment, these individuals often complain about or demonstrate difficulty in spelling, known as agraphia.

According to cognitive models, linguistic information can take multiple routes to get from input to output (Ellis & Young, 1988). In the case of spelling by dictation, a heard word may either be recognized, and the spelling retrieved from long term memory, or sounded out, mapping each sound onto a written symbol (a process referred to as *phoneme-to-grapheme conversion*). We will refer to the former as the lexical or whole-word route to spelling, and the latter as the phonologic route.

Lexical agraphia is based on failure to access orthographic whole-word forms (Beauvois & Derouesne, 1981), while the phonetic route remains relatively intact. Regular words (e.g. "cat") contain predictable mappings of phoneme to grapheme, and may thus be spelled by either the lexical or phonologic route, while exception words (e.g. "freight") violate these standard mappings and therefore can only be correctly spelled via the lexical route. Hence, the spelling of regular words would be spared, while spelling of exception words would be impaired. Additionally, misspelled words would likely be spelled in a phonetically plausible manner, leading to regularization of irregular words (e.g., misspelling "was" as "wuzz"), known as surface agraphia.

In *phonologic* (*or phoneme-to-grapheme*) *agraphia*, the primary deficit is in the ability to convert phonemes into corresponding orthographic symbols (Roeltgen, Sevush, & Heilman, 1983; Shallice, 1981). If the phonologic route is selectively affected, the spelling of familiar and regular words should be relatively spared, as patients still have access to whole word representations. However, the patient will be unable to spell unfamiliar words or

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stimuli that are not real words (nonwords), which rely on phoneme-to-grapheme conversion. Additionally, when these patients make errors they tend to be phonologically implausible, such as "quand" for "queen" (Rapcsak et al., 2009).While these patterns were initially described in patients with focal brain damage such as vascular lesions, both phonologic and lexical agraphia have also been described in patients whose cognitive deficits are caused by neurodegeneration (Neils-Strunjas, Groves-Wright, Mashima, & Harnish, 2006; Rapcsak, Arthur, Bliklen, & Rubens, 1989).

1.2. Localization of agraphia

Gerstmann (1957) described agraphia related to damage to the left angular gyrus, as part of the syndrome now known by his name. However, further investigation has shown that written language impairments do not localize specifically to the angular gyrus, but instead appear to be related to left parietal damage in general (Benton, 1961; Critchley, 1953). In fact, study of spelling deficits in general has shown that a widespread network of brain regions are involved in spelling including areas in all lobes of the left hemisphere and numerous subcortical areas (Cloutman et al., 2009).

While these findings show that many areas of the brain are involved in written language, they do not address critical areas specifically involved in spelling. For this, analysis by type of agraphia has been more telling. In patients with damage in the left perisylvian cortex, including the inferior frontal gyrus and surrounding cortex, and the temporoparietal junction, spelling was more affected than reading, and the agraphia followed the phonologic pattern (Alexander, Friedman, Loverso, & Fischer, 1992; Marien, Pickut, Engelborghs, Martin, & De Deyn, 2001; Rapcsak et al., 2009). In patients with lexical agraphia, structural lesions were located in the left temporo-occipital cortex (Rapcsak & Beeson, 2004).

These findings demonstrate two routes for processing of spelling with different neural substrates: a phoneme to grapheme route, and a whole word route. As described by Saur et al. (2008), this model places lexical and "higher level" language processes in a ventral pathway, involving extrasylvian areas of the temporal lobe (anterior and inferolateral temporal cortices) and ventrolateral prefrontal regions. Phonologic and articulatory information is subserved by a separate pathway, the dorsal pathway, involving the superior temporal lobe and the premotor cortex (perisylvian regions). In the context of spelling, phonologic agraphia is thus caused by dysfunction of the dorsal pathway while lexical agraphia is caused by dysfunction of the ventral pathway.

1.3. Primary progressive aphasia

Mesulam presented six cases of isolated language decline in 1982 and named the syndrome primary progressive aphasia in 1987, as a dementia syndrome marked by prominent and isolated language deficits (Mesulam, 1982, 1987). While other cognitive domains such as memory, visuospatial skills, and executive abilities may be affected, especially later in the disease process, language remains the most salient feature of the disease process. This specificity for language is echoed by a predominance of atrophy in the left hemisphere in areas implicated in language (Gorno-Tempini et al., 2004; Mesulam et al., 2009; Rogalski et al., 2011). The neurodegeneration of these regions provides a unique opportunity to study the language network because atrophy occurs in patterns that are different from those commonly found in patients with vascular or surgical lesions (Rogalski et al., 2011). In contrast to stroke-induced lesions where the damaged area is completely destroyed, neurodegenerative diseases kill only a fraction of neurons even within areas of significant atrophy. Since the residual neurons maintain some functionality (Sonty et al., 2003), clinicoanatomical correlations can reveal more subtle relationships than in patients with stroke. Based on the pattern of language impairments, three variants have been identified: agrammatic (PPA-G), logopenic (PPA-L), and semantic (PPA-S) (Mesulam et al., 2009, Gorno-Tempini et al., 2011). Each has a different pattern of language deficits, outlined in Table 1.

1.4. Agraphia in primary progressive aphasia

In contrast to lesion patients and dementia of the Alzheimer type, there are very few published studies focusing on agraphia in PPA. Noble, Glosser, and Grossman (2000) described a pattern of regularization errors in spelling (surface agraphia) in patients with a diagnosis of semantic dementia (a syndrome that partially overlaps with the PPA-S variant), which was not found in those with other forms of PPA, nor in those with dementia of the Alzheimer type. Sepelyak et al. (2011) analyzed patterns of spelling errors in PPA, and found several discrete patterns of deficits variably involving phoneme to grapheme conversion, lexical access, and working memory. While this study successfully links identified patterns of spelling errors to a model of spelling, it does not directly compare types of words misspelled or types of errors to neuropsychological measures, clinical diagnoses, or atrophy patterns.

In a recent study, Henry, Beeson, Alexander, and Rapcsak (2011) evaluated various written language measures in 15 PPA patients and 15 controls. Each was given a battery of words to spell and to read, including nonwords, exception, and regular words. Complex composite scores were calculated for semantic and phonetic components of reading and writing. Comparison with gray matter volume using voxel based morphometric MRI analyses (VBM) revealed correlations with semantic scores in the extrasylvian left temporal lobe and angular gyrus, whereas phonetic scores correlated with the perisylvian system, specifically in the inferior frontal lobe and supramarginal gyrus.

The present study compares spelling deficits in each of the clinical PPA subtypes, and correlates spelling scores and error types to cortical thinning (atrophy) and neuropsychological language measures of confrontation naming, repetition, syntax, lexical-semantic processing, and overall language processing using a larger group of PPA patients ($n=41$) than used in previous studies. One goal of this study was to see if these patterns of agraphia in our sample of PPA patients confirm our current understanding of the neural substrates of spelling and other language processes. Our anatomical findings using cortical thickness correlations should complement previous VBM finding. Additionally, we set out to show that specific measures of spelling may be useful in probing the variable language deficits in patients with PPA.

Table 1
Key neuropsychological features of PPA subtypes (adapted from Rogalski et al., 2011 to reflect recent subtyping consensus paper Gorno-Tempini et al., 2011).

PPA-G	Abnormality of syntax or motor speech impairments with relatively preserved single word comprehension. Fluency is impaired
PPA-L	Intermittent word finding hesitations. Repetition is impaired
PPA-S	Abnormality of single word comprehension with relatively preserved grammar and fluency. Naming is severely impaired

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2. Methods

2.1. Participants

The data we report here were collected from 41 patients with a diagnosis of PPA and 36 age-matched healthy controls. The descriptive clinical diagnosis of PPA-G, PPA-L or PPA-S was made in all cases by the same neurologist (MMM) based on clinical history and exam, following the recently published consensus criteria (Gorno-Tempini et al., 2011). These clinical features are outlined in Table 1. Six patients were not assigned any one of the three subtypes due to having features of multiple subtypes or having deficits that were too mild or too severe to characterize by the consensus criteria. All subjects were evaluated at the Cognitive Neurology and Alzheimer's Disease Center at Northwestern University. Informed consent was obtained from all participants, and Institutional Review Board of Northwestern University approved the study.

Demographic information and neuropsychological tests scores for each patient subtype and controls are presented in Table 2. All participants were right handed native English speakers. All groups were equivalent in terms of years of education ($F_{(3,73)}=0.27$, $p=0.85$) and age ($F=2.36$, $p=0.08$). Among the subtypes of PPA patients, there were no significant differences in terms of duration since diagnosis ($F=1.32$, $p=0.28$), or WAB-AQ ($F=1.86$, $p=0.17$), a global language measure from the Western Aphasia Battery (Kertesz, 1982).

2.2. Neuropsychological tests

All participants underwent a large battery of neuropsychological language test. Single-word comprehension was evaluated using a 36-item subset of moderately difficult items from the Peabody Picture Vocabulary Test (PPVT-IV) (Dunn, 2006), in which the subject is read a word, and then asked to pick which one of four pictures portrays that word. The Western Aphasia Battery (WAB) was also administered, from which a global aphasia quotient and separate subscores were obtained, including one measuring repetition. For syntactic processing, we used a subset of 10 questions from the Northwestern Anagram Test (NAT), which in the past has been highly correlated with other measures of sentence production (Weintraub et al., 2009). In this test, a subject is given a picture showing an action, and tiles with words that are used to construct sentences describing the picture. Confrontation naming was tested using the Boston Naming Test (BNT) (Kaplan, 2001). In this test, line drawings of objects are presented to the subject, who is then asked to say the name of the object.

2.3. Spelling measures

We used single word spelling to dictation for 10 regular words, 10 exception words, and 10 nonwords, all selected from the Psycholinguistic Assessments of Language Processing in Aphasia (PALPA) (Kay, 1992). All three categories of words were matched in both number of letters ($F_{(2,27)}=1.15$, $p=0.32$) and number of phonemes ($F=1.18$, $p=0.33$). The regular and exception words were matched for imageability ($t=1.99$, $p=0.06$) and frequency ($t=0.08$, $p=0.94$) using norms from the MRC psycholinguistic database (Coltheart, 1981).

Words in each list were read aloud by the experimenter, and participants were asked to write each word on paper. Spelling errors were scored by a rater blinded to the identity and subtype diagnosis of the participant (HS). For nonwords, the spelling was considered correct if the participant's written spelling could be pronounced as the target, using standard English phonetic rules or by analogy to other English words. For instance, for the word "nar", acceptable spellings would include "narr", "knar", and "gnar".

In addition to overall accuracy for each word type, the types of errors were also further categorized. If the subject wrote an actual English word, but not the correct one, it was categorized as a lexical error. These were uncommon. The remaining spelling errors were categorized as being either phonetically plausible (i.e., what the subject wrote could feasibly be pronounced as the target word), or phonetically implausible.

2.4. MRI methodology

Brain magnetic resonance images (MRI) were obtained on 36 of the PPA patients. Scans were obtained during the same 2 d during which they underwent spelling and other neuropsychological testing. T1-weighted three-dimensional MP-RAGE sequences (2300 ms; echo time, 2.86 ms; flip angle, 9°; field of view, 256 mm) recording 160 slices at a slice thickness of 1.0 mm were acquired on a 3T Siemens TRIO system using a 12-channel birdcage head coil. Imaging was performed at the Northwestern University Department of Radiology Center for Advanced MRI (CAMRI).

MR images were processed using the image analysis suite FreeSurfer (version 4.5.0), which is documented and freely available for download online (〈http://surfer.nmr.mgh.harvard.edu/〉). Cortical thickness estimates were calculated by measuring the distance between representations of the white-gray and pial-CSF boundaries across each point of the cortical surface. This method has been demonstrated to be reliable across scanning protocols and platforms in comparisons of cognition and cortical thickness (Dickerson et al., 2008). The procedures have been described previously by Fischl and Dale (2000).

An a priori region of interest (ROI)-based approach was used to analyze quantitative relationships between cortical thickness in left hemisphere areas and spelling scores. Each ROI was defined as described in the Desikan atlas (Desikan et al., 2006). The regions chosen have been implicated in semantic and phonetic processing, including the fusiform gyrus, temporal pole, inferior frontal gyrus, and temporoparietal junction. Each part of the inferior frontal gyrus comprised its own ROI (pars opercularis, pars triangularis, pars orbitalis), and were analyzed separately. We specifically chose to include the pars orbitalis due to growing evidence that this region is functionally involved in heteromodal language processes with the rest of the inferior frontal gyrus. Hagoort coined the term, "Broca's complex" because cytoarchitectonic similarities suggest that the pars orbitalis likely shares functionality with the remainder of the Hagoort (2005). Furthermore, resting-state functional connectivity studies have shown that not only are the three parts of the inferior frontal gyrus heavily interconnected, but that they connect to heavily overlapped areas of temporal and parietal cortex (Xiang, Fonteijn, Norris, & Hagoort, 2010). The temporoparietal junction was sampled using the supramarginal gyrus and the angular gyrus. ROIs were first delineated on the template cortical surface, and then registered from that surface space to the individual subject's surface. Mean cortical thickness in each region was calculated from the thickness at each vertex within the ROI. This mean thickness was correlated to spelling errors using Pearson correlation analyses. All statistical analyses were performed using PASW 18.0 (SPSS).

3. Results

3.1. Spelling by clinical subtype

Spelling performance was analyzed via ANOVA including group as a between-subjects factor and word type (regular/exception/nonword) as a within-subject factor. As seen in Fig. 1, all three subtypes of PPA patients had poorer accuracy in spelling compared to controls (ANOVA collapsed across word type: vs. PPA-G, $F_{(1,54)}=52.6$, $p<0.001$; vs. PPA-L, $F_{(1,40)}=11.3$, $p<0.01$; vs. PPA-S, $F_{(1,43)}=53.9$, $p<0.001$). Spelling of regular words did not

Table 2
Demographic and neuropsychological scores for PPA patients and controls.

	Agrammatic $n=20$	Logopenic $n=6$	Semantic $n=9$	All PPA $n=41$	Control $n=36$
PPA subtypes					
Age (years)	64.1 ± 9.2	66.2 ± 8.1	57.2 ± 4.2	63.2 ± 8.4	62.2 ± 6.8
Education (years)	16.2 ± 2.2	16.5 ± 1.2	15.9 ± 2.1	16.0 ± 2.3	15.8 ± 2.4
Duration (years)	3.7 ± 1.9	2.5 ± 0.5	3.8 ± 1.7	3.5 ± 1.9	–
WAB-AQ (%)	77.5 ± 19.5	92.8 ± 4.2	72.6 ± 27.9	81.9 ± 15.4	–
BNT (%)	65.8 ± 30.5	91.1 ± 5.5	13.2 ± 18.6	58.2 ± 35.0	97.3 ± 3.1
PPVT (%)	77.6 ± 15.9	88.3 ± 1.3	28.6 ± 2.0	74.9 ± 27.9	81.3 ± 37.0
WAB-Rep (%)	72.7 ± 24.3	86.5 ± 7.1	80.0 ± 30.4	79.8 ± 19.6	95.6 ± 18.1
NAT-10 (%)	60.5 ± 27.2	96.7 ± 5.2	80.0 ± 32.8	75.2 ± 28.4	98.8 ± 4.2

NAT-10=Northwestern Anagram Test subset of 10 items. WAB-Rep=Western Aphasia Battery, Repetition subscore. PPVT=Peabody Picture Vocabulary Test. BNT=Boston Naming Test. WAB-AQ=Western Aphasia Battery Aphasia Quotient.

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differ significantly among the three PPA subgroups ($F_{(2,32)}=0.92$, $p=0.41$). However, PPA-S patients were significantly worse than the other subtypes in exception word spelling (vs. PPA-G, $t=-2.43$, $p=0.02$; vs. PPA-L, $t=-2.09$, $p=0.02$) whereas PPA-G patients were significantly worse at spelling nonwords than PPA-S ($t=-2.23$, $p<0.01$).

Evaluation of the types of errors made in spelling real words (regular and exception words) showed distinct patterns by subtype as well, particularly in PPA-G and PPA-S, as seen in Fig. 2. The PPA-G patients made significantly more phonetically implausible than plausible errors ($t=2.27$, $p=0.04$). In contrast, PPA-S patients made significantly more phonetically plausible errors than implausible ($t=2.36$, $p=0.046$). No such pattern was seen in PPA-L patients, where error types were made equally in both categories ($t=1.00$, $p=0.36$). Error types in spelling nonwords were also examined, but lexical errors were too rare to demonstrate any pattern by subtype.

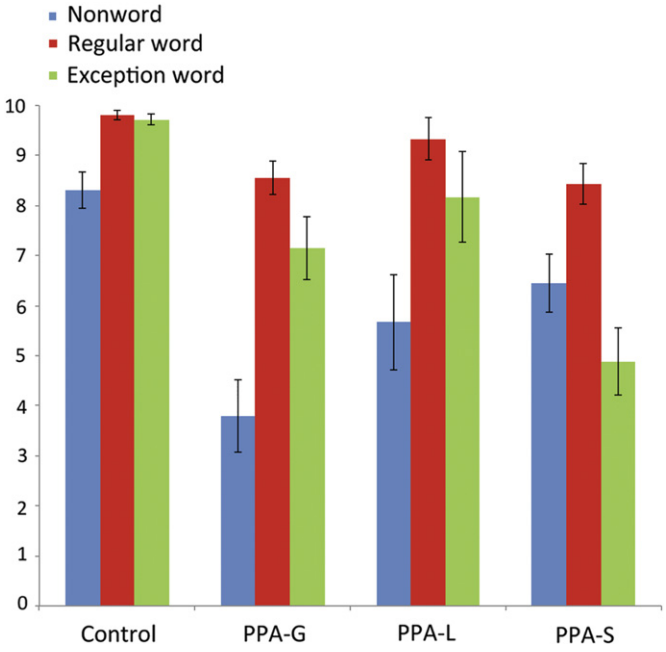

Fig. 1. Spelling accuracy of word types by clinical diagnosis.

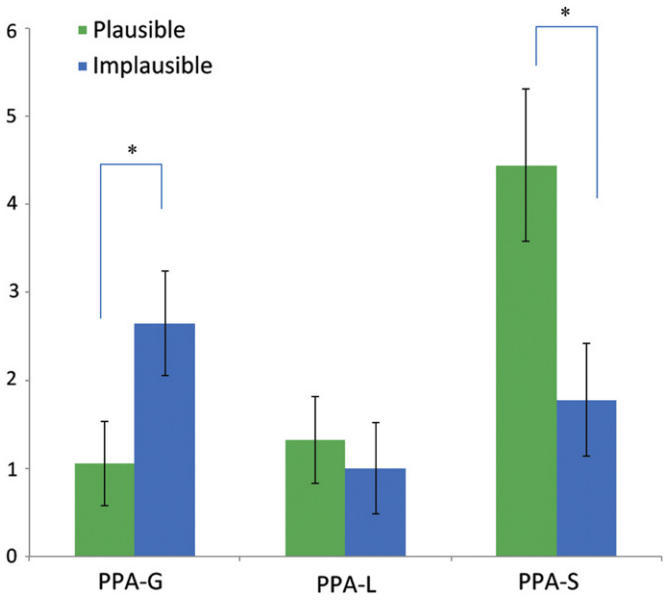

Fig. 2. Error types in spelling real words by subtype. * $p<0.05$.

Table 3
Correlation between neuropsychological language tests and spelling accuracy by word type (Pearson's *r*).

	Grammar	Repetition	Comprehension	Naming	Global Language
	NAT-10	WAB-Rep	PPVT	BNT	WAB-AQ
Nonword	0.42*	0.60***	−0.25	−0.16	0.15
Regular Word	0.09	0.19	0	0.13	0.29
Exception Word	0.06	0.05	0.35*	0.38*	0.29

* $p<0.05$.
*** $p<0.001$.

3.2. Correlations between spelling and other neuropsychological measures

Correlations between spelling accuracy and neuropsychological languages scores are shown in Table 3. Nonword spelling (i.e., the phoneme-to-grapheme route) correlated positively with grammar (NAT) and repetition (WAB-Rep) scores. Exception word spelling (i.e., the whole word route) correlated with the single word comprehension (PPVT) and confrontation naming (BNT) scores. The WAB overall score (WAB-AQ) did not correlate significantly with any of the spelling scores. Regular word spelling did not correlate significantly with any of the other neuropsychological measures examined.

3.3. Correlations between spelling and cortical thickness

Correlations between cortical thickness and spelling errors are presented in Fig. 3. The number of regular word errors did not significantly correlate with cortical thickness in any of the ROIs examined. Nonword spelling errors correlated negatively to cortical thickness (i.e., more errors with thinner cortex) in the left supramarginal gyrus and the left IFG pars orbitalis. Exception word spelling errors, on the other hand, correlated with cortical thinning in the left temporal pole and fusiform gyrus. No significant correlations were found between overall spelling scores by word type and cortical thickness in the angular gyrus or in the IFG pars opercularis and pars triangularis.

Since we did not find any significant correlations to regular word spelling, we also examined error types in regular word spelling. Phonetically implausible errors correlated negatively with the IFG pars opercularis and pars triangularis. Phonetically plausible errors did not correlate significantly with any of the ROIs examined.

4. Discussion

The purpose of this study was to examine the relation between types of spelling errors and measures of related language functions, clinical diagnosis, and patterns of atrophy. The results of this investigation demonstrate two distinct patterns of spelling errors in our PPA patients.

The first pattern is marked by an inability to use phoneme to grapheme conversion to spell a word, and could be described as a phonologic agraphia. In this pattern, nonword spelling is the most impaired because, while real and familiar words can still be spelled using the whole word approach, this is not possible with nonwords. In fact, real word spelling was not affected as severely in patients with phonological agraphia since the orthographic

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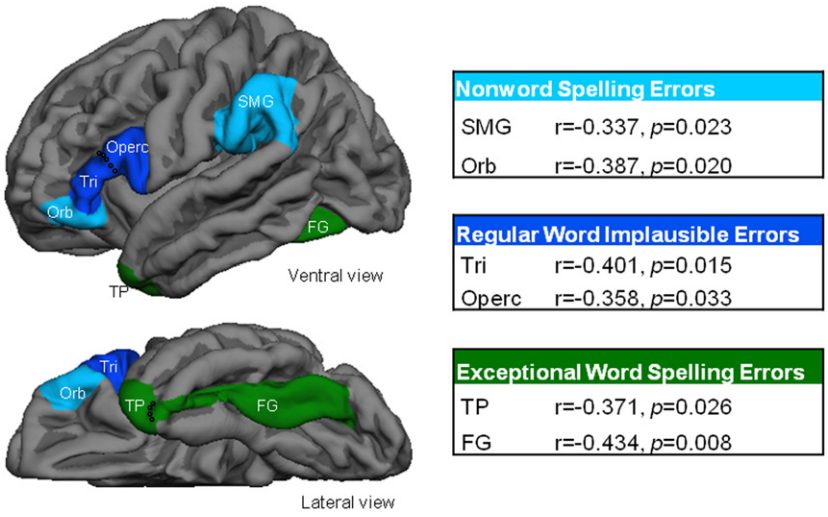

Fig. 3. Left hemisphere regions of interest with significant correlation between cortical thickness and spelling errors showing the differential involvement of perisylvian areas (inferior frontal gyrus, supramarginal gyrus) and extrasylvian temporal areas (fusiform gyrus, temporal pole) in phonetic (phoneme to grapheme, light and dark blue) and lexical (whole word, green) spelling, respectively.

forms of these words can also be accessed through the whole word route. Additionally, in real word spelling, the patients with phonologic agraphia make errors that tend to be phonetically implausible, another sign of phonologic processing deficits. The areas of cortical atrophy associated with phonologic agraphia (IFG, and the SMG of the inferior parietal lobule), are constituents of the perisylvian phonologic system. This pattern was seen primarily in patients with PPA-G.

The second pattern of spelling errors in our patients is a lexical agraphia. In these patients, exception word spelling is poor because of a selective impairment of the whole word route. Attempts to rely on the phonological route are not useful since the canonical rules of phoneme-to-grapheme conversion do not apply to the spelling of exception words. In contrast, nonword spelling, is relatively preserved since it can be achieved through the phoneme-to-grapheme route. Areas of atrophy associated with this pattern were located in extrasylvian temporal areas that are associated with visual word-form and semantic processing, namely the fusiform gyrus and temporal pole. This pattern was seen primarily in patients with PPA-S.

Our investigation suggests that the language network contains two distinct but interactive routes associated with spelling. The inferior parietal lobule and the inferior frontal gyrus, two areas known to be interconnected by components of the arcuate fasciculus (Catani & Mesulam, 2008), are major components of the dorsal route, which mediates phoneme-to-grapheme conversion. This route is also critically important for the phonological loop (Amici et al., 2007) and morphosyntax (den Ouden et al., 2012; Wilson et al., 2011), explaining why nonword spelling, the one type of spelling that most heavily relies on the phonological route, was significantly correlated with task of repetition and grammaticality. The correlation of phonological agraphia with atrophy in the inferior parietal lobule and the inferior frontal gyrus is also consistent with the known prominence of agraphia in Broca's aphasia and the Gerstmann syndrome. The phonological route of spelling relies on knowledge of the canonical rules that transform phonemes into the arbitrary symbols of that language. Once the rule is acquired, it enables accurate spelling of any heard real word or nonword that obeys the rule. It appears that the dorsal route, encompassing the inferior parietal lobule and the inferior frontal gyrus, is critical for applying the canonical rules of phoneme-to-grapheme conversion.

The ventral route, encompassing the fusiform gyrus and the temporal pole, has different functional properties. It plays a critical role in the whole word approach to spelling where the orthographic form cannot be deduced from phoneme-to-grapheme conversion. Instead, each word seems to present a special relationship of orthography to pronunciation. The spelling of such a word requires access to a unique audiovisual word-form representation. The fusiform gyrus plays a critical role in the encoding and recognition of behaviorally relevant percepts, including faces, objects, and word-forms (Allison, McCarthy, Nobre, Puce, & Belger, 1994). The temporal pole has been attracting increasingly more attention as an area of confluence for the language and object recognition networks (Simmons & Martin, 2009). These two areas may mediate the whole-word approach to spelling through their involvement in encoding and accessing audiovisual representations of exception words and linking them to graphomotor output patterns. In keeping with the importance of ventral route components to word and object knowledge, lexical agraphia in our patients was significantly correlated with poor performance in tests of object naming (the BNT) and word comprehension (the PPVT).

One phenomenon that these findings help to explain is gogi aphasia, a syndrome first described by Tsuneo Imura in 1943 (Sasanuma & Monoi, 1975; Yamadori, 2011). Unlike English, Japanese uses a variety of scripts in everyday written language. These include *kanji*, based on ideograms adapted from Chinese, where each symbol represents a unit of meaning, and the *kana*, which are specific to Japanese, and are syllabaries, with each symbol representing a syllable phonetically. In gogi aphasia, the ability to read and write using the *kana* was preserved, but affected patients were unable to read and write using *kanji*. In the context of this investigation, *kanji* is analogous to exception words, in that they must be written or read at the level of recognizing the character or word as a whole. Thus, gogi aphasia can be described as a lexical agraphia and dyslexia. Indeed, recent investigation shows that gogi aphasia is a clinical manifestation of anterior temporal atrophy as seen in PPA-S (Ichikawa et al., 2011; Jibiki & Yamaguchi, 1993; Sakurai et al., 2006). The same pattern is seen in Korean speakers with lexical impairments, which also uses Chinese-based ideograms, *hanja*, and a native phonetic writing system, *hangeul* (Suh et al., 2010).

We have couched these findings in the framework of a ventral and dorsal stream model of language processing, but it is important

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to recognize that this study is not designed to evaluate, and does not address the validity of other language models. Connectionist models (Plaut, McClelland, Seidenberg, & Patterson, 1996; Seidenberg & McClelland, 1989; Welbourne & Lambon Ralph, 2007) focus on a single route for conversion of phonemes to letters, regardless of word type. These models demonstrate that accurate regular word, exception word and nonwords spelling can be accomplished using a single phonologic system, but also generally include a semantic system which can interact with this system. Conversely, so-called "dual-route" models (Coltheart, Rastle, Perry, Langdon, & Ziegler, 2001; Ellis & Young, 1988; Tainturier, 2001) posit two routes of lexical processing, one with semantic input, one without. Our study does not distinguish whether lexical route impairments can be seen in the absence of semantic impairments. Further probing whether or not these two types of impairments dissociate can be challenging in PPA because truly gauging comprehension of words can be difficult to determine in the setting of other language impairments.

The analysis of spelling errors we found in PPA reproduce those of Henry et al., but also extends their findings by using a larger number of PPA patients, and more extensive representation of the clinical subtypes. In addition to supporting our understanding of perisylvian and extrasylvian language networks, this study also suggests that analysis of spelling can help to clinically differentiate distinct aphasia syndromes. This can be done, as in this study, by using a short battery of words, or by analyzing samples of the patient's writing. While regular word spelling errors in general were not helpful in distinguishing the two groups, spelling of exception words and nonwords, and phonetically implausible errors in regular word spelling were diagnostic.

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