Surface errors without semantic impairment in acquired dyslexia: a voxel-based lesion–symptom mapping study

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Patients with surface dyslexia have disproportionate difficulty pronouncing irregularly spelled words (e.g. pint), suggesting impaired use of lexical-semantic information to mediate phonological retrieval. Patients with this deficit also make characteristic ‘regularization’ errors, in which an irregularly spelled word is mispronounced by incorrect application of regular spelling-sound correspondences (e.g. reading plaid as ‘played’), indicating over-reliance on sublexical grapheme–phoneme correspondences. We examined the neuroanatomical correlates of this specific error type in 45 patients with left hemisphere chronic stroke. Voxel-based lesion–symptom mapping showed a strong positive relationship between the rate of regularization errors and damage to the posterior half of the left middle temporal gyrus. Semantic deficits on tests of single-word comprehension were generally mild, and these deficits were not correlated with the rate of regularization errors. Furthermore, the deep occipital-temporal white matter locus associated with these mild semantic deficits was distinct from the lesion site associated with regularization errors. Thus, in contrast to patients with surface dyslexia and semantic impairment from anterior temporal lobe degeneration, surface errors in our patients were not related to a semantic deficit. We propose that these patients have an inability to link intact semantic representations with phonological representations. The data provide novel evidence for a post-semantic mechanism mediating the production of surface errors, and suggest that the posterior middle temporal gyrus may compute an intermediate representation linking semantics with phonology.

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Abbreviation: VLSM = voxel-based lesion-symptom mapping
Introduction

Pioneering work over the past half century has provided abundant evidence for at least two distinct processes in reading aloud (Marshall and Newcombe, 1973; Coltheart et al., 1980; Patterson et al., 1985). The first of these, relevant mainly in alphabetic writing systems, makes use of learned correspondences between letters or letter clusters (graphemes) and consonant or vowel sound speech sounds (phonemes), allowing pronunciation to be ‘assembled’ phonetically from sublexical parts (Coltheart et al., 1993). In addition to handling known words, such correspondences permit the pronunciation of novel letter strings, like *kint*, based on letter-sound correspondences learned from similar examples, like *hint, lint, mint, tint, kick, kid, kin, kiss*, etc. The second process, central to logographic writing systems, involves retrieving the pronunciation of a word ‘as a whole’. Rather than assembling the pronunciation from sublexical correspondences, the sound of the whole word is accessed from a mental store of word forms (Coltheart et al., 1993) or meanings (Plaut et al., 1996). In alphabetic writing systems, this holistic access process is thought to aid pronunciation of words that ‘violate’ familiar letter-sound correspondence patterns, like *pint*. Although rare or non-existent in some languages, such violations are commonplace in English, which has many ‘irregular’ words like *done, have, some, plaid, sew, shoe, sweat, wand*, and so on, with pronunciations that are inconsistent with other, similarly spelled words. Selective impairment of whole-word access produces special difficulty in pronouncing such words, a pattern called surface dyslexia (Patterson et al., 1985). This impairment results in over-reliance on the intact sublexical assembly process, producing characteristic ‘regularization’ errors, in which an irregular word is pronounced using more typical grapheme–phoneme correspondences (e.g. *soot* pronounced as *suit*).

Surface dyslexia is often observed in patients with the semantic variant of frontotemporal dementia (Patterson and Hodges, 1992; Woolfam et al., 2007), suggesting that a common semantic impairment may underlie both syndromes. Semantic dementia is associated with patho- logical changes concentrated most heavily in the anterior half of the temporal lobe (anterior temporal lobe), and evidence has been presented linking surface dyslexia with anterior temporal lobe pathology in these patients (Brambati et al., 2009). Other studies, however, have linked surface dyslexia with more posterior temporal lobe damage (Vanier and Caplan, 1985; Ripamonti et al., 2014) and with impaired functional activation in the posterior temporal lobe (Wilson et al., 2009). Functional imaging studies have implicated both posterior (Graves et al., 2010) and anterior (Hoffman et al., 2015) temporal regions, specifically in irregular word reading.

Our aim in the present study was to clarify the neural correlates of whole-word reading processes by identifying damage associated with the production of regularization errors. Previous correlation-based lesion studies used overall irregular word accuracy (Brambati et al., 2009; Ripamonti et al., 2014), or accuracy on irregular words relative to regular words (Fiez et al., 2006; Rapcsak et al., 2009; Henry et al., 2012; Ripamonti et al., 2014) as behavioural indices of damage to these processes. A potential problem with this approach is that irregular words place higher demands on working memory and other domain-general processes compared to regular words (Binder et al., 2005; Graves et al., 2010; Cattinelli et al., 2013; Taylor et al., 2013), thus overall accuracy measures may not accurately index the specific process of interest, i.e. holistic mapping from orthographic to phonologic representations. Across the present sample of patients with left hemisphere stroke, for example, non-word and irregular word reading accuracy was strongly correlated (*r* = 0.82, *P* < 0.001), presumably due to impairments affecting shared phonological, working memory, or articulatory processes. As an alternative approach, the present study uses regularization errors to target a specific processing impairment. In theory, regularization errors should not occur unless patients have greater damage to lexical-semantic than to sublexical reading processes, resulting in over-reliance on sublexical grapheme–phoneme mapping. Lesion sites producing this error type were identified using voxel-based lesion-symptom mapping (VLSM).

Another goal of the study was to specify more precisely the underlying processing deficit giving rise to regularization errors in these patients. Although regularization errors occurring in semantic dementia have been proposed to arise from damage to the semantic system, such errors could also arise from an inability to access intact semantic information from written input, or from impairment in mapping from intact semantic information to a phonologic representation (Shallice and Warrington, 1980). We assessed these possibilities by correlating the rate of regularization errors with performance on semantic matching tasks using words and pictures, two tests widely used to assess semantic memory (Howard and Patterson, 1992; Bozeat et al., 2000; Adlam et al., 2010).

Materials and methods

Participants

The participants were 45 patients with focal encephalomalacia from chronic left hemisphere stroke (21 females, 24 males). Participants had to have at least minimal ability to read aloud, defined as ≥10% accuracy in single word reading, but were otherwise included regardless of behavioural profile. All participants were at least 180 days post-stroke, native English speakers, and premorbidly right-handed according to the Edinburgh Handedness Inventory (Oldfield, 1971) handedness quotient [mean = 89.4, standard deviation (SD) = 21.6]. Lesions included 36 middle cerebral artery infarcts, one anterior choroidal infarct, three combined middle/anterior cerebral artery infarcts, two posterior cerebral artery infarcts, one...
combined middle/posterior cerebral artery infarct, and two cases of chronic encephalomalacia from lobar haemorrhage. Other participant data are listed in Table 1. The rate of regularization errors was not correlated with age, education, time from onset, or overall lesion volume. Patients were enrolled prospectively using a written informed consent procedure approved by the Medical College of Wisconsin Institutional Review Board and undertaken in accord with the Declaration of Helsinki.

**Oral reading test**

The task was administered on a laptop computer connected to a touch-sensitive LCD monitor (ELO model 1522L) and programmed in the ‘Runtime Revolution’ environment (www.runrev.com). Testing occurred in a quiet closed-door testing room. Participants wore a headphone set with a built-in microphone (Sennheiser model PC 166 USB). They initiated each trial by touching an empty green square on the computer screen. Manual and vocal responses were automatically recorded.

Participants read aloud a set of 224 pronounceable letter strings that included 188 English words and 36 pronounceable non-words (pseudowords). Non-words (e.g. *heak*, *prng*, *blance*, *replain*, *overchife*) were derived using a Markov chain-procedure based on position-specific English trigram probabilities (Medler and Binder, 2005). None were homophones of English words. The words included four-length- and imageability-matched sets of 36 monosyllabic items each that crossed spelling-sound consistency (regular versus irregular) with word frequency (high versus low). This factorial design allows separate scores to be computed, for example, for matched sets of low-frequency regular words and low-frequency irregular words. The remaining words included a set of 18 regular, multisyllabic words; 18 regular, monosyllabic ‘function’ words (pronouns, possessives, prepositions, conjunctions, quantifiers, auxiliary verbs); and eight irregular monosyllabic function words. Thus, there were 108 words with regular pronunciations (i.e. conforming to the most likely spelling-sound mapping) and 80 words with irregular pronunciations. Regular and irregular word sets were matched overall on length, bigram frequency, and word frequency. Table 2 lists some summary statistics for the word subsets and non-words. A complete list of the stimuli is provided in the Supplementary material.

The 224 items were presented in a different random order for each participant. On each trial, the item to be read appeared alone in the centre of the screen until a complete response was made or the participant declined to make any further attempt, at which point the examiner pressed a key to end the trial. No time limit for responding was imposed. At the conclusion of each trial a green square appeared in the centre of the screen, which the participant touched to advance to the next trial. Vocal responses were digitally recorded and scored offline.

Scoring was based on the first complete response. Responses on irregular word trials were scored as regularization errors if the response was an incorrect but plausible pronunciation derivable from typical grapheme–phoneme correspondences (Venezky, 1970).

**Semantic memory tests**

Additional tests were obtained to further characterize the patients’ deficits and their relationship with regularization errors. Although regularization errors indicate a relative inability to use whole-word information during reading, this impairment could arise from damage to the semantic memory system, from an impairment in mapping orthographic input to semantic information, or from damage to a non-semantic store of whole-word forms (Shallice and Warrington, 1980; Patterson et al., 1985). Integrity of the semantic memory store was assessed with a 120-trial picture matching test similar to the ‘Camel and Cactus’ test (Bozeat et al., 2000; Adlam et al., 2010). On each trial, patients were presented with three colour photographs of objects, arranged such that a sample picture was positioned above two choice pictures. The choices appeared on the screen surrounded by green squares indicating that they could be selected by touching the screen (Pillay et al., 2014). The task was to indicate which of the choices was most similar to the sample. Integrity of orthography-semantic mapping was assessed using an analogous 80-item test requiring matching of visually presented concrete nouns based on semantic similarity. In both tests, half of the trials were ‘easy,’ involving distractor choices from a different superordinate category than the sample and target (e.g. match *bee* with *wasp* or *lamb*), and half of the trials were ‘hard,’ involving three objects from the same superordinate category (e.g. match *shoes* with *sandals* or *boots*).

Relationships between each of these additional measures and the regularization errors of interest were assessed using Pearson correlation.

**Table 2** Descriptive statistics for subsets of the oral reading items

<table>
<thead>
<tr>
<th>Letter Type</th>
<th>n</th>
<th>Letters</th>
<th>BGF/1000</th>
<th>Log10 Freq</th>
<th>Imageability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regular</td>
<td>108</td>
<td>5.50 (1.39)</td>
<td>1.35 (1.16)</td>
<td>1.28 (0.75)</td>
<td>4.62 (1.54)</td>
</tr>
<tr>
<td>Irregular</td>
<td>80</td>
<td>4.95 (0.83)</td>
<td>1.61 (1.49)</td>
<td>1.17 (0.92)</td>
<td>4.39 (1.48)</td>
</tr>
<tr>
<td>Non-words</td>
<td>36</td>
<td>6.50 (1.70)</td>
<td>1.06 (0.79)</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

Values shown are mean (SD). Letters indicates number of letters. BGF/1000 indicates mean position-specific bigram frequency in thousands. Log10 Freq indicates base 10 logarithm of orthographic word frequency per million words (Baayen et al., 1995). Imageability indicates rated imageability on a scale from 1 to 7, compiled from published norms (Wilson, 1988; Bird et al., 2001; Clark and Pavio, 2004; Cortese and Fugget, 2004).
Lesion tracing

High-resolution T1-weighted MRI images were obtained in the chronic stage in all patients. MRI was performed at 3 T in 40 patients and 1.5 T in five patients. Voxel size was approximately $1 \times 1 \times 1\,\text{mm}^3$.

Lesioned areas were labelled using a semi-automated procedure, beginning with 6-way segmentation of the MRI volume using FSL Automatic Segmentation Tool (FMRIB Software Library, www.fmrib.ox.ac.uk/fsl). The purpose of the automated segmentation step was to identify tissue boundaries in the volume as objectively as possible. Boundaries between damaged and normal tissue are often indistinct, resulting in a degree of subjectivity in placing these boundaries manually. The segmentation step locates local 3D boundaries based on objective changes in image intensity. However, this process is not capable of distinguishing normal from damaged tissue because of extreme heterogeneity of intensity values within lesions, which can contain CSF, cystic tissue, ischaemic remnants of grey or white matter, and residual iron products. This heterogeneity produces overlap between the intensity distributions of normal and lesioned tissue, such that any given segment produced by the algorithm typically contains a number of bounded volumes, some of which contain damaged tissue and others of which contain normal tissue. Each segment was therefore visually inspected and manually edited by an experienced stroke neurologist (J.R.B.) to include only bounded volumes within the lesioned tissue. The six edited segments were then combined to make a complete lesion map (Fig. 1). Each patient’s anatomical image and associated lesion map were then morphed to a stereotaxic template (‘Colin n27’) using Advanced Normalization Tools software (http://stnava.github.io/ANTs/) with a constrained cost-function masking approach using the lesion volume as a mask, and resampling to a nominal $1 \times 1 \times 1\,\text{mm}^3$ voxel grid.

This non-linear registration process corrects for anatomical distortions that are common after focal brain damage, particularly local ventricular enlargement. Normalized total lesion size (in template voxels) was obtained in each patient from the template-registered lesion map.

Voxel-based lesion–symptom mapping

VLSM uses lesion status at each voxel as a grouping variable, then compares the lesioned and non-lesioned groups on any given dependent measure, producing an effect size statistic for each voxel. A custom Matlab script was used that implements VLSM as an analysis of covariance to account for within- and between-group variance of no interest. Only voxels lesioned in at least five patients were included. The main analysis of interest examined the rate of regularization errors (proportion of irregular word trials on which regularization errors occurred) as the dependent measure.

For comparison with the main analysis, an additional VLSM analysis explored the neural correlates of overall accuracy on irregular word reading, with overall accuracy on non-word reading included as a covariate to minimize non-specific phonologic and executive deficits as sources of variance.

Finally, additional VLSM analyses using the picture matching and word matching tasks as dependent variables (collapsing across hard and easy trials) were undertaken to compare the sites associated with deficits on these semantic tasks with those associated with regularization errors.

The resulting $t$-statistic maps were thresholded at a voxel-wise $P < 0.005$ and cluster-corrected at a family-wise error of $P < 0.05$ using a minimum cluster size criterion of 1400 $\mu\text{l}$, as determined by randomization testing with 10 000 permutations.

Results

Behavioural data

All participants readily understood the reading task. Mean overall reading accuracy was 66.1% (Table 3). Scores on regular words, irregular words, and non-words were all highly correlated (regular versus irregular: $r = 0.96$, $P < 0.001$; regular versus non-word: $r = 0.82$, $P < 0.001$; irregular
versus non-word: \( r = 0.83, P < 0.001 \)). Regularization errors occurred on an average of 5.9% of irregular word trials (SD 5.4, range 0–31) and comprised 28.8% of irregular word errors on average (SD 28.2, range 0–100). The rate of regularization errors tended to be positively correlated with overall reading accuracy. That is, patients who made more regularization errors tended to make fewer errors overall in reading. This relationship is notable because it supports the underlying hypothesis that regularization errors depend on an intact sublexical grapheme–phoneme mapping process. Also consistent with this hypothesis is the fact that the relationship was particularly strong for low-frequency regular words and non-words, which are especially dependent on sublexical grapheme–phoneme mapping.

Additional measures of semantic processing were obtained to enable interpretation of the regularization errors made by this sample of patients (Table 3). Production of regularization errors was not correlated with any of the semantic measures. In particular, the rate of regularization errors showed no correlation with accuracy in matching pictures based on semantic similarity, a measure that assesses integrity of the semantic memory store. Similarly, the rate of regularization errors showed no correlation with accuracy in matching words based on semantic similarity, a measure that assesses integrity of the semantic memory store as well as access to this store from orthographic input. These negative results should be considered with some caution because most participants performed fairly well on both semantic measures, which may limit the power to detect correlations with other tests. Notably, performances on the two semantic tests were highly correlated (\( r = 0.70, P < 0.001 \)), suggesting that the lack of correlation with regularization errors was not due primarily to insufficient variance. Furthermore, the group as a whole showed moderate deficits (mean 82.8%, chance = 50%) and substantial variance (range 57.5–97.5%, SD 8.5) on the hard version of the word matching task, yet there was no correlation between this measure and the rate of regularization errors.

### Voxel-based lesion–symptom mapping

Figure 2A shows the lesion overlap map thresholded to show only voxels damaged in at least five patients. As shown in Fig. 2B, regularization errors were associated with damage in a single region centred on the posterior half of the middle temporal gyrus, extending into adjacent middle occipital gyrus. Peak coordinates are given in Table 4. The region correlated with regularization errors notably spares adjacent posterior perisylvian structures linked with phonological processing, such as the supramarginal gyrus and posterior superior temporal gyrus (Indefrey and Levelt, 2004; Hickok and Poeppel, 2007; Buchsbaum and D’Esposito, 2008; Graves et al., 2008; Pillay et al., 2014). Addition of lesion volume as a covariate of no interest produced very similar results, though with generally stronger effect sizes, presumably due to removal of within-group variance associated with variation in lesion volume (Supplementary Fig. 1).

A second VLSM analysis used overall irregular word reading accuracy as the dependent variable of interest, while incorporating non-word reading accuracy as a covariate to account for effects of general phonologic, executive, and speech production impairments. After controlling for variance associated with non-word reading accuracy, no voxels associated with overall irregular word reading accuracy survived cluster size correction for family-wise error.

Finally, VLSM analyses were conducted using the semantic matching tasks as dependent variables to assess whether damage associated with impairments on these tasks overlapped with the region associated with regularization errors. However, these analyses produced very similar results, though with generally weaker effect sizes, presumably due to removal of within-group variance associated with variation in lesion volume. Overall, VLSM analyses suggest that regularization errors are associated with damage to a region in the posterior half of the middle temporal gyrus, extending into the middle occipital gyrus, implicating a role for this area in semantic processing and the regularization process.

### Table 3 Correlation of regularization error rates with other psycholinguistic measures

<table>
<thead>
<tr>
<th>Test measure</th>
<th>Mean (SD)</th>
<th>Correlations with regularization errors</th>
<th>Correlations with picture matching</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>( r ) \quad ( P )</td>
<td>( r ) \quad ( P )</td>
</tr>
<tr>
<td>Overall reading accuracy</td>
<td>66.1 (26.1)</td>
<td>0.34</td>
<td>0.021</td>
</tr>
<tr>
<td>Regular words, all trials</td>
<td>74.8 (26.6)</td>
<td>0.39</td>
<td>0.008</td>
</tr>
<tr>
<td>High-frequency regular</td>
<td>80.7 (24.4)</td>
<td>0.37</td>
<td>0.012</td>
</tr>
<tr>
<td>Low-frequency regular</td>
<td>70.9 (28.7)</td>
<td>0.40</td>
<td>0.006</td>
</tr>
<tr>
<td>Irregular words, all trials</td>
<td>65.1 (24.7)</td>
<td>0.23</td>
<td>0.123</td>
</tr>
<tr>
<td>High-frequency irregular</td>
<td>76.0 (24.7)</td>
<td>0.33</td>
<td>0.026</td>
</tr>
<tr>
<td>Low-frequency irregular</td>
<td>53.9 (26.7)</td>
<td>0.30</td>
<td>0.048</td>
</tr>
<tr>
<td>Non-words</td>
<td>41.4 (33.2)</td>
<td>0.39</td>
<td>0.009</td>
</tr>
<tr>
<td>Semantic picture matching %, all trials</td>
<td>92.8 (3.8)</td>
<td>-0.11</td>
<td>0.474</td>
</tr>
<tr>
<td>Easy trials</td>
<td>98.4 (3.7)</td>
<td>0.02</td>
<td>0.894</td>
</tr>
<tr>
<td>Hard trials</td>
<td>87.2 (5.3)</td>
<td>-0.17</td>
<td>0.263</td>
</tr>
<tr>
<td>Semantic word matching %, all trials</td>
<td>90.4 (5.5)</td>
<td>0.04</td>
<td>0.819</td>
</tr>
<tr>
<td>Easy trials</td>
<td>97.0 (5.1)</td>
<td>-0.02</td>
<td>0.905</td>
</tr>
<tr>
<td>Hard trials</td>
<td>82.8 (8.5)</td>
<td>-0.11</td>
<td>0.474</td>
</tr>
</tbody>
</table>

\*Significant at alpha < 0.05 after Holm-Bonferroni correction for family-wise error.
errors. As shown in Fig. 2C, impairment on the picture matching task was associated with damage to deep white matter in the occipital lobe. These fibres likely connect early visual cortex with lateral occipital regions involved in object perception (Grill-Spector and Malach, 2004) and include posterior elements of both the inferior fronto-occipital and inferior longitudinal fasciculi (Wakana et al., 2004). Overlap between this cluster and the region associated with regularization errors was minimal (Supplementary Fig. 2). Of the 13,645 voxels associated with either regularization errors (10,567 voxels) or picture matching impairment (3,221 voxels), only 143 voxels

**Figure 2** VLSM results. (A) Lesion overlap across all 45 patients, thresholded to include only voxels that were lesioned in at least five patients. Colours indicate the degree of overlap. Subscript numbers indicate the x-axis location of the slice in standard space. The same locations are used for the other sagittal series. (B) VLSM analysis using rate of regularization errors as the dependent measure. Colours indicate z-scores. Subscripts below the coronal images indicate the y-axis location of the slices. Green lines on the axial image indicate the locations of orthogonal slices. (C) VLSM analysis using accuracy on the semantic picture matching task as the dependent measure.

**Table 4** Peak coordinates of sites associated with regularization errors

<table>
<thead>
<tr>
<th>Regularization errors Structure</th>
<th>Z-score</th>
<th>Coordinates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posterior temporal white matter</td>
<td>5.653</td>
<td>34 -43 -0</td>
</tr>
<tr>
<td>Posterior temporal white matter</td>
<td>4.795</td>
<td>37 -34 -2</td>
</tr>
<tr>
<td>Posterior middle temporal gyrus</td>
<td>4.670</td>
<td>47 -61 -2</td>
</tr>
<tr>
<td>Posterior middle temporal gyrus</td>
<td>4.670</td>
<td>-62 -51 -4</td>
</tr>
<tr>
<td>Middle occipital gyrus</td>
<td>4.420</td>
<td>-42 -62 +4</td>
</tr>
<tr>
<td>Middle temporal gyrus</td>
<td>3.740</td>
<td>-53 -37 -6</td>
</tr>
</tbody>
</table>
(1.05%) were common to both lesions. No voxels associated with impairment on the word matching task survived cluster size correction for family-wise error. Relaxing the cluster size threshold revealed an occipital white matter focus that overlapped with the picture matching focus, and a separate focus in the temporal stem white matter that likely represents more anterior portions of the inferior fronto-occipital fasciculus (Supplementary Fig. 3).

Discussion

The present results provide the clearest evidence to date that ‘surface’ errors in reading can arise from a processing impairment outside the semantic system. There is general consensus that regularization errors indicate impaired access to whole-word knowledge, but such an impairment could arise from several sources (Shallice and Warrington, 1980; Patterson et al., 1985). According to one prominent theory known as the ‘triangle’ or ‘primary systems’ model, activation of a semantic representation (word meaning) plays a critical role in generating the correct phonological code for irregular words, particularly low-frequency irregular words (Shallice et al., 1983; Plaut et al., 1996; Woollams et al., 2007). Evidence for this semantic mechanism includes the frequent appearance of surface dyslexia in patients with semantic dementia, and a strong correlation between the severity of semantic deficits and impaired irregular word reading in these patients (Patterson and Hodges, 1992; Woollams et al., 2007).

An underlying semantic deficit, however, seems not to have been the cause of regularization errors in our stroke patient cohort. The rate of regularization errors made by the patients was uncorrelated with performance on semantic matching tasks using either pictures or words, suggesting that regularization errors arose from mechanisms unrelated to semantic processing or semantic access from orthographic input. This pattern is reminiscent of previously described patients with surface dyslexia from focal lesions who had intact access to word meanings, even for words they regularized in pronunciation (Kay and Patterson, 1985; Kremin, 1985; Margolin et al., 1985; Watt et al., 1997). According to one reading theory known as the dual-route model, this pattern arises from damage to a non-semantic store of phonological word forms that receives input directly from the orthographic system and mediates whole-word reading independent of semantics (Coltheart et al., 1993).

An alternative possibility consistent with the primary systems view is that the deficit in such cases arises from an impairment in mapping from semantic to phonological representations (Kay and Patterson, 1985; Margolin et al., 1985; Watt et al., 1997). Associating concepts with phonological representations is a difficult computational task due to the arbitrary nature of these relationships. Artificial neural networks are unable to perform such arbitrary transformations without a system of intermediary distributed representations that link combinations of input features with combinations of output features (Hinton and Sejnowski, 1986). Intermediate representations linking semantic to phonological representations would be neither semantic nor phonological, but would capture abstract information about both semantic and phonological structure. Damage to this intermediate system would disrupt the use of semantic knowledge during word pronunciation but would not impair semantic knowledge, access to semantics from print, or phonological tasks like repetition that do not require semantic input.

Although the present data cannot adjudicate between these dual-route and primary systems accounts, the deficit underlying regularization errors in our sample appears, in any case, to be independent of semantic access, and to reflect the same deficit previously labelled ‘post-semantic’ surface dyslexia (Margolin et al., 1985).

Neural correlates of whole-word phonological access

This is the first study to examine the lesion correlates of regularization errors. These errors are a cardinal feature of surface dyslexia and directly demonstrate an over-reliance on typical or expected grapheme–phoneme correspondences in patients who have lost access to whole-word phonology from orthography (Marshall and Newcombe, 1973). Previous group studies of the neural correlates of whole-word reading processes focused on overall irregular word reading accuracy rather than on specific error types (Brambati et al., 2009; Henry et al., 2012; Ripamonti et al., 2014). Brambati et al. (2009) used voxel-based morphometry (VBM) to examine anatomical correlates of irregular word reading impairment in 56 patients with various cortical degenerative syndromes, including semantic dementia (n = 14), primary progressive aphasia (n = 26), and various forms of generalized dementia. VBM showed a correlation between irregular word reading accuracy and grey matter volume throughout the anterior half of the left temporal lobe, including anterior superior temporal gyrus, middle temporal gyrus, inferior temporal gyrus, and fusiform gyrus. Henry et al. (2012) reported a similar VBM analysis in 11 patients with progressive aphasia syndromes (five with semantic dementia). Irregular word accuracy was correlated with grey matter volume along the entire length of the left lateral temporal lobe as well as part of the angular gyrus.

The only VLSM analysis of surface dyslexia in patients with stroke is a study by Ripamonti et al. (2014), which included five patients classified as surface dyslexia in a larger cohort of 59 patients (Ripamonti et al., 2014). Four of the surface dyslexia patients were also impaired on both a visual lexical decision task and a picture naming task, which the authors interpreted as a deficit affecting both orthographic and phonologic word representations (no specific semantic deficits were mentioned). A
lesion overlap subtraction analysis comparing the five patients with surface dyslexia with 33 phonological dyslexia patients showed a higher incidence of damage throughout the temporal lobe in the surface dyslexia group, including posterior temporal regions. VLSM on the entire sample identified a region involving deep temporal lobe white matter, insula, putamen, and inferior frontal gyrus where damage correlated with a measure of lexical reading impairment. An important caveat of this study is that the patients were speakers of Italian, a language that uses only regular orthography–phonology mappings. Whole-word orthographic knowledge was therefore assessed using a measure of syllabic stress assignment, which is unpredictable and unmarked in Italian, and thus depends on word-specific knowledge. It is unclear, however, whether this knowledge of word-specific stress sequences is entirely equivalent to knowledge of word-specific phoneme sequences.

The present results clarify the functional anatomy of whole-word reading in two ways. First, they provide strong evidence that damage in the posterior half of the temporal lobe can produce the regularization errors typical of surface dyslexia. Second, they demonstrate that lesions in this region selectively impair access to whole-word phonology without impairing semantic processing. These data, together with previous studies linking semantic dementia and surface dyslexia with anterior temporal damage, suggest at least two distinct lesion foci underlying two distinct subtypes of whole-word reading impairment. In the first subtype, typical of semantic dementia, progressive damage to the anterior temporal lobes (usually bilaterally) produces a semantic impairment and co-occurring surface dyslexia as a direct result of the semantic impairment, a combination dubbed ‘SD squared’ by Woollams et al. (2007). In the second subtype, described here, damage to the left posterior lateral temporal lobe produces surface errors without a corresponding semantic deficit. It is worth noting that the lesion coverage in our sample was limited to areas typically damaged in middle cerebral artery stroke. This coverage did not include ventral temporal lobe or temporal pole regions that likely play a large role in semantic processing (Patterson et al., 2007; Lambon Ralph et al., 2009).

The claim that reading irregular words depends on posterior temporal areas is supported by a functional MRI study by Graves et al. (2010), in which healthy participants read words aloud that varied in spelling-sound consistency. Consistency was parameterized as the number of words with the same ending letter sequence (known as the rime) and same rime pronunciation as the target word (termed the spelling-sound ‘friends’ of the target word) minus the number of words with the same rime and a different rime pronunciation (termed the spelling-sound ‘enemies’ of the target word). Thus, regular words like book have many friends (brook, cook, crook, hook, look, took, etc.) but relatively few enemies, whereas irregular words like kook and spook have many enemies and few friends. A posterior left temporal lobe region straddling middle- and inferior temporal gyri showed stronger activation when spelling-sound consistency was lower, suggesting activation of word-specific representations in this region. In contrast to inferior frontal gyrus regions typically activated by irregular words (Fiez et al., 1999; Binder et al., 2005; Graves et al., 2010), the middle/inferior temporal gyri region identified by Graves et al. (2010) showed no sensitivity to reaction time, suggesting a specific role in supplying information needed for orthography-phonology mapping rather than in executive control processes. As shown in Fig. 3, this region is immediately inferior to and overlaps with the inferior edge of the lesion site associated with regularization errors in the present study. The extent of overlap may be limited by the lack of lesion coverage inferiorly. These studies provide convergent evidence from activation data in healthy participants and patterns of impairment in focal lesion patients that access to whole-word knowledge in reading aloud depends on posterior lateral temporal lobe regions, particularly the posterior half of the middle- and inferior temporal gyri.

To be clear, we do not claim that only posterior temporal lesions can cause regularization errors or that anterior temporal areas play no role in reading. In addition to the
compelling evidence from patients with semantic dementia (Brambati et al., 2009; Woollams et al., 2007), a recent functional MRI study by Hoffman et al. (2015) provides the first evidence for selective engagement of the anterior temporal lobe during reading of irregular words relative to regular words. Although the effect in this anterior temporal lobe region was weak at the group level, participants who showed stronger reliance on semantic information during reading (based on assessment of consistency effects in a reading task outside the scanner) activated the region significantly more than participants with weaker semantic reliance. Thus, there is evidence that at least some readers selectively engage the anterior temporal lobe when reading irregular words.

Our VLSM analyses using picture and word semantic tasks as dependent variables failed to implicate anterior temporal lobe regions. This is likely due to poor lesion coverage in ventral anterior temporal and temporal pole regions, as shown in Fig. 2A and noted above. Sparing of these regions is consistent with the relatively mild single-word semantic deficits observed in the sample as a whole. Interestingly, the semantic deficits that did occur were associated mainly with damage to occipital lobe white matter pathways at the posterior-inferior edge of the middle cerebral artery territory. We speculate that damage to these tracts affects transfer of information between ventral visual systems involved in object recognition and the anterior temporal lobe, producing mild impairments in concept retrieval, particularly with picture input. Overlap between this lesion site and the one associated with regularization errors was minimal, consistent with the claim that regularization errors in our cohort arise from impairment outside of the semantic system.

Limitations

Although regularization errors are characteristic of surface dyslexia, the latter label is sometimes reserved for patients who show particular difficulty reading irregular words. Indeed, the emphasis in many studies is on overall accuracy in reading irregular words compared to regular words or non-words, regardless of the types of errors made. Our analysis using overall irregular reading accuracy, however, failed to show any reliable localization for this measure when non-word reading was incorporated as a control for general phonologic and executive processes. Thus, one caveat regarding the present study is that surface dyslexia, if this is defined as lower accuracy in reading irregular words, may not have a localization within the middle cerebral artery territory, and may only occur in patients with severe and relatively isolated semantic deficits.

On the other hand, the term surface dyslexia was originally coined to reflect the theoretical interpretation that patients with the syndrome rely on sublexical grapheme–phoneme mapping (i.e. ‘surface’ features) to compensate for impaired (or inaccessible) whole-word phonology. We argue that regularization errors are a direct and specific index of this over-reliance on grapheme–phoneme correspondences. This high degree of diagnostic specificity could explain why the VLSM using regularization errors produced such robust results, whereas the VLSM using simple accuracy measures was unrevealing. VLSM based on specific error types has also been used successfully to identify distinct semantic access processes during picture naming (Schwartz et al., 2009, 2011). These experiences suggest that diagnostic error types provide a useful dependent measure for studies aimed at localizing specific processing impairments.

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Supplementary material

Supplementary material is available at Brain online.

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