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Individual fMRI activation in orthographic mapping and morpheme mapping after orthographic or morphological spelling treatment in child dyslexics

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Abstract

Four sets of word-form tasks were administered during fMRI scanning to 18 child dyslexics and 21 controls to identify unique brain activation associated with four kinds of mapping—orthographic, morpheme with and without phonological shift, and phoneme—before treatment, and to measure the effect on each kind of mapping after orthographic and morphological spelling treatment (to which dyslexics were randomly assigned). Dyslexics and/or controls showed significant pretreatment activation in group maps in 18 brain regions during one or more of the mapping tasks. Average fMRI z-scores were used to determine for each kind of fMRI mapping which of the 18 brain areas (a) differentiated dyslexics and controls before treatment; (b) showed significant pre- to post-treatment activation change in dyslexics; (c) showed post-treatment 'normalization' of activation; and (d) changed differently for dyslexics as a function of the kind of treatment received. Dyslexics in orthographic treatment showed reliable change, normalization, and treatment-specific response in right inferior frontal gyrus and right posterior parietal gyrus. Implications of the findings of

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the combined group map and individual (region of interest) analyses for neurolinguistics, including assessment, treatment and brain plasticity, and the role of different word forms in spelling at a specific developmental stage, are discussed.

Keywords: Developmental dyslexia; Functional MRI; Brain response to spelling treatment; Orthographic word forms; Phonological word forms; Morphological word forms

1. fMRI and behavioral studies of word form

Dyslexia, which is unusual difficulty in learning to read and spell that may affect as many as one in six to one in five school-age children (Lyon, Shaywitz, & Shaywitz, 2003) has a brain basis (Démonet, Taylor, & Chaix, 2004). Behavioral studies of dyslexia show that measures of phonological, orthographic, and morphological word forms contribute uniquely to dyslexia in childhood, but that a second-order factor underlying the first-order factors for each of these word forms contributes uniquely in adults with dyslexia, suggesting that adults have created mapping relationships among these *three word forms* and their *parts* (Berninger et al., 2005). The research reported in this article is from a programmatic research program on the phonological, orthographic, and morphological word forms and their interrelationships in individuals with and without dyslexia.

1.1. Phonological word forms

Differences between developmental dyslexics and good readers in childhood and adulthood have been well documented in the neurolinguistic literature on fMRI tasks that require analysis of spoken word forms (e.g. Corina et al., 2001; Poldrack et al., 2001) and integration of letters and phonological units (e.g. Aylward et al., 2003; Shaywitz et al., 2002). Across languages that vary in conformity with regular spelling-sound mappings, dyslexics and good readers differ in their ability to process phonological word forms on fMRI tasks (e.g. Paulesu et al., 2001). Ability to analyze and reproduce phonological word forms and their parts has been shown in over 20 years of behavioral research to be involved in the causal mechanism(s) of dyslexia (e.g. Bishop & Snowling, 2004; Bradley & Bryant, 1983; Morris et al., 1998; Wagner & Torgesen, 1987). Thus, fMRI brain imaging and behavioral measures converge on the importance of phonological word forms in explaining reading and its disorders.

1.2. Orthographic word forms

Neuroimaging studies have also provided evidence for the role of the visual word form (e.g. Dehaene, Le Clec'H, Poline, Le Bihan, & Cohen, 2002; Cohen et al., 2002; Posner & McCandliss, 1993; Posner, Petersen, Fox & Raichle, 1988). We refer to the visual word form as the 'orthographic word form,' as a reminder that it involves visible language and is not a purely visual process (e.g. Polk et al., 2002). The fusiform gyrus is involved in processing the *orthographic word form* (Booth et al., 2002; Dehaene et al., 2002; McCandliss, Cohen, & Dehaene, 2003), which is sensitive to letter patterns rather than visual features of individual letters (Cohen et al., 2002; Polk et al., 2002). Children with dyslexia differ from good readers during orthographic processing (Siok, Perfetti, Jin, & Tan, 2004). Richards et al. (2005) also found group differences during tasks that require access to precise spelling patterns, when controlling for processing of letter patterns alone. Behavioral studies also show that individual differences in processing orthographic word forms in working memory are related to reading development in typically developing children (Berninger, 1987; Berninger, Yates, & Lester, 1991), at-risk readers (Nagy, Berninger, Abbott, Vaughan, & Vermeulen, 2003), and dyslexics (Berninger, Abbott, Thomson, & Raskind, 2001; Olson, Forsberg, & Wise, 1994). Thus, fMRI and behavioral studies also converge on the contribution of orthographic word forms to reading and its disorders.

1.3. Morphological word forms

Semantic processing is mediated by a network of spreading activation that includes expectancy based and postlexical access checks (Plaut & Booth, 2000), and contributes early in processing to understanding word meaning (Pulvermüller, Assadollahi, & Elbert, 2001). Morphological word form (base words and pre- and post-affixes) is a different mechanism that contributes to understanding word meaning (Berninger et al., 2005; Berninger & Richards, 2002; Nagy, Berninger, & Abbott, 2005). In the brain/mind, word meaning may be represented and accessed in two ways: (a) in networks that represent semantic features and underlying concepts and are accessed through spreading activation, and (b) discrete representations in the mental lexicon that are accessed through morphological word forms. The network representation may have the advantage of linking language meaning to non-language concepts, and the discrete morphological representation may have the advantage of linking language forms for word meaning to language forms for phonological and orthographic representations. Both may contribute to vocabulary learning and language comprehension.

Aylward et al. (2003) identified brain activation unique to the morphological word form when controlling for general semantic knowledge (synonyms); the task required decisions about semantic relatedness on the basis of derivational suffixes that mark grammar as well as meaning. Aylward et al. also identified unique brain signatures for phonological and morphological word forms, adding to the comparable findings of Crosson et al. (1999) for phonological and semantic (not morphological) processing. In the Aylward et al. study, the stimuli used for the morphological word form task did not require phonological shifts (transformations of the vowels or consonants in the base word when one or more affixes are added). Richards et al. (2005) extended that work to show that orthographic, phonological, and morphological word forms have unique neural signatures and that good readers are equally good at processing morphological word forms with and without phonological shifts, but dyslexics are not—they have more difficulty with the morphological word forms with phonological shifts. Behavioral studies have also confirmed the contribution of the morphological word form to typical reading development (Nagy et al., 2005), at-risk reading and writing (Nagy et al., 2003), and dyslexia (Berninger et al., 2005). Thus, as with the other word forms, results of fMRI and behavioral studies converge in showing that morphology contributes to reading and its disorders.

2. Linking instructional treatment and brain

Berninger and Richards (2002) proposed that the reading brain is initially constructed as children learn to relate existing phonological word forms to orthographic word forms, and during this process create memories of written word forms. In research on learning and teaching spelling, this stage is referred to as the phonological stage of spelling (Moats, 2000; Templeton & Bear, 1992). This phonological stage involves encoding of phonemes into graphemes (1- and 2-letter spelling units). In the process of repeated encodings, typical spellers begin to create precise representations of all the constituent letters in the written word spelling (whether or not the letters relate to a phoneme in a one-to-one way). With sufficient practice in spelling written words, these representations in long-term memory organize as an *autonomous orthographic lexicon* that can be accessed automatically without the intervening phonological encoding process. Mental computations of the interrelationships among phonological, morphological, and orthographic words forms create mental maps of the word-specific orthographic word forms that underlie this autonomous orthographic lexicon (e.g. Berninger, Abbott, Billingsley, & Nagy, 2001; Nagy et al., 2003). Thus, triple word form theory (Richards et al., in press) is relevant to understanding how the autonomous orthographic lexicon underlying automatic spelling and fluent reading emerges from the earlier phonological stage—instead of relying only on phonological–orthographic mappings, children begin to rely on phonological–morphological–orthographic mappings. When children rely on the autonomous orthographic lexicon rather than phonological encoding, they have entered the orthographic stage of spelling development (see Moats, 2000; Templeton & Baer, 1992). However, mature spelling requires an additional stage of spelling development. Because English is a morphophonemic language (Venezky, 1970; 1999), English spelling relies greatly on morphological rules that require analysis of vowel and consonant patterns at the end of base words that influence whether letters are dropped or added when adding suffixes (e.g. Dixon & Englemann, 2001). Nagy and colleagues (e.g. Nagy et al., 1993) have conducted programmatic research for nearly two decades on the typical developmental course from simple to complex morphological processing that affects word reading and spelling and have shown that the morphological processing begins to contribute in a substantial way around grade 4 but continues to develop through the high school years and possibly even beyond.

In the research reported here, we used fMRI measures that correspond to each of the three word forms—phonological, morphological, and orthographic word forms. For the phonemes in the phonological word form, we used the phoneme mapping task in Aylward et al. (2003). However, in the current study, we included two morpheme mapping tasks—one with stimulus pairs that did not involve phonological shifts as in Aylward et al. and one that did. A ‘phonological shift’ occurs when pronunciation changes occur in a base word as the result of the addition of a morpheme. For example, the sound of the vowel ‘a’ in ‘nation’ changes when the suffix ‘al’ is added to create the word ‘national.’ Morpheme mapping with phonological shift requires the coordination of both morphological and phonological word forms, while morpheme mapping without phonological shift requires processing the morphological word form only. However, because the goal of this research was to investigate brain response to instructional interventions designed to facilitate the transition from the phonological to orthographic stage of spelling development, we also added an orthographic mapping task, designed to assess the functioning of the autonomous orthographic lexicon that is accessed through precise written spellings that may include some parts that are not phonologically encodable.

3. Plasticity of brain response

Both biological and environmental variables influence reading development (e.g. Eckert, Lombardino, & Leonard, 2001). Although neurological variables may explain why individuals with dyslexia struggle more than children without dyslexia in learning to read, the dyslexic brain may still show plasticity in response to instructional interventions. Specific language processes may normalize after short-term treatment, suggesting that if appropriate instruction is sustained, this treatment may lead to full compensation (full recovery of normal reading). Evidence for such brain plasticity in individuals with dyslexia, which is associated with differences in *occipital–temporal*, *temporal–parietal*, and *frontal* brain systems (e.g. Shaywitz & Shaywitz, 2003), has been reported following treatment. fMRI tasks have shown pre- to post-treatment changes in brain activation levels and patterns in frontal systems (Aylward et al., 2003; Richards et al., 2000, 2002; Temple et al., 2000, 2003; Shaywitz et al., 2004), temporal–parietal regions (Aylward et al., 2003; Eden et al., 2004; Shaywitz et al., 2004; Simos et al., 2002; Temple et al., 2003), and occipital–temporal regions (Aylward et al., 2003; Shaywitz et al., 2004). Plasticity of brain response has been observed *across the life span*: (a) in younger students in response to explicit phonological awareness and phonics instruction (Shaywitz et al., 2004; Simos et al., 2002), (b) in upper elementary and middle school students in response to instruction designed to increase the precision of phonological and orthographic word representations and the efficiency of the working memory architecture (Aylward et al., 2003; Richards et al., 2000, 2002), and (c) in adults in response to explicit instruction in sound and articulatory awareness and phonics training (Eden et al., 2004). Brain plasticity has also been demonstrated for normal adolescents learning non-word associations (Molfese et al., 2002) and normal adults learning a miniature visual language (McCandliss, Posner, & Given, 1997). See Richards et al. (in press) and Berninger (in press) for additional details of these studies, which varied in imaging modality, imaging tasks, age of participants, and nature of the treatment.

Given the well-documented disruption to the posterior word form center (e.g. Shaywitz et al., 2002; Temple et al., 2001), one of the goals of our research group has been to disentangle the brain basis of three word forms—phonological, orthographic, and morphological—that contribute to effective remediation of word reading and spelling (Berninger, Abbott, Billingsley et al., 2001; Berninger, Abbott, Thomson et al., 2001; Berninger & Hidi, in press; Berninger et al., 2003; Berninger & Richards, 2002; Henry, 2003). Because the existing fMRI studies have focused primarily on the phonological word form (see review in Berninger & Richards, 2002), it is possible that other regions besides the left posterior ones are involved in processing orthographic and morphological word forms.

Often dyslexics respond early in schooling to phonologically driven instruction aimed at decoding in reading (Shaywitz et al., 2004; Simos et al., 2002). However, dyslexics tend to have spelling problems that persist beyond their initial problems in phonological decoding (Berninger, Abbott, Thomson et al., 2001), and effective treatments for spelling as well as decoding require investigation. Because orthographic, phonological, and morphological processes are involved in spelling (Bryant, Nunes, & Bindman, 1997; Carlisle, 1994; Moats, 2000), we designed fMRI tasks that assess each of these language processes and extended Crosson et al.'s (1999) study with adults to children. Like Crosson et al., we included imaging tasks that assess phonological and orthographic word forms, but we used a task that assessed morphological word forms (over and beyond general semantic knowledge) rather than semantic processing that may rely on interrelated networks rather than discrete representations as discussed earlier. We compared (a) child dyslexics and age- and IQ-matched good readers on these fMRI tasks, and (b) dyslexics before and after they received alternative treatments, each linked conceptually to one of the tasks.

In contrast to previous studies that evaluated effects of phonological treatment on the basis of brain response to phonologically based reading instruction, we investigated the brain's response to spelling instruction. Effects of spelling instruction were of interest because during the past decade participants in the family genetics study showed plasticity in their response to reading instruction on both behavioral and brain measures but sought continuing assistance with spelling that was not remediated on the basis of reading instruction alone. In a recent study, we documented that children with dyslexia in our sample ($n = 122$) met both absolute criteria (skill falls at or below 90 standard score or the 25th percentile) and relative criteria (skill falls one or more standard deviations below Verbal IQ and below the population mean) on behavioral measures of spelling but that adults with dyslexia were not impaired in spelling based on either absolute or relative criteria (Berninger & O'Donnell, 2004). These findings suggested that (a) dyslexia is a disorder of spelling as well as word reading/decoding, and (b) the brains of individuals with dyslexia may also be responsive to spelling instruction.

We evaluated two spelling treatments—one developmentally appropriate for the children in grades 4–6 and one that would be more appropriate for children in the next step in spelling development whether or not they have dyslexia. We tested the hypothesis that an orthographic treatment, which is theoretically linked to the spelling stage beyond the phonological stage and developmentally appropriate for the grade level of students in the current study, might result in greater brain change related to orthographic word form than would morphological treatment that would be appropriate at the next stage of spelling development. In addition, we tested the hypothesis that brain activation patterns would not change during the fMRI phoneme mapping because treatment relevant to that process was not intensive. Although many children above the fourth grade level have mastered the phonological stage of spelling, many children with dyslexia have not because processing the phonological word form and its parts is an area of deficit associated with dyslexia (see earlier section on phonological word form) and their brain activation patterns are unlikely to change without more systematic, intensive treatment of the underlying phonological problems. Results supporting both hypotheses would provide construct validity for the evaluation of instructional treatment with specific fMRI tasks—because a specific instructional treatment results in brain changes only on a theoretically linked fMRI task and not on fMRI tasks that are linked to a contrasting treatment, which is provided but is not developmentally appropriate (related to morphological word form), or is not provided in sufficient intensity to overcome deficits that interfered with mastering an earlier skill in development (related to phonological word form).

Treatment effectiveness was assessed by determining whether the treatment (a) produced reliable pre- to post-treatment change in regions where dyslexics and controls differed significantly prior to treatment during specific kinds of language mapping, (b) eliminated preexisting dyslexic-control differences for specific kinds of language mapping in specific brain regions, and (c) showed differential brain response as a function of the kind of treatment received. Instead of using a control treatment hypothesized to be unrelated to spelling, we used alternative treatments (each serving as the control for the other).

4. Methods

4.1. Participants

Eighteen children with dyslexia (5 girls, 13 boys) and 21 normal spellers (8 girls, 13 boys), participated in this study. Of the 18 dyslexics, who were randomly assigned to one of two treatments, eight completed the orthographic treatment and 10 completed the morphological treatment and the brain scans at time 1 and time 2.

The dyslexics, who were recruited for persisting spelling problems, were probands that met inclusion criteria for a family genetics study of dyslexia (Berninger, Abbott, Billingsley et al., 2001; Berninger, Abbott, Thomson et al., 2001; Berninger et al., 2005): (a) Verbal IQ of >90 (top 75% of the population), and (b) unexpectedly low reading and spelling achievement (below the population mean and at least one standard deviation below their Verbal IQ). The controls met the inclusion criteria of reading and spelling above the population mean. Exclusion criteria for both dyslexics and the control group of good readers and spellers included left-handedness and non-removable metal, such as oral braces, and hearing or vision problems. The Human Subjects Institutional Review Board where the study was conducted approved this study, and each participating child (as well as parent/guardian) gave written informed consent.

The dyslexic and control groups did not differ significantly on sex or age (Table 1). The average Verbal IQs for both groups were well above the population mean (although there was a reliable but slight difference between them). At the initial scan, the children with dyslexia were on average about one standard deviation below the population mean for age on the Word Identification (reading real words) and Word Attack (reading pseudowords) subtests of the Woodcock Reading Mastery Test (Woodcock, 1987) and on the Wide Range Achievement Test, Third Edition Spelling subtest (Wilkinson, 1993). Scores on these tests were significantly below the dyslexic's mean Verbal IQ. All control subjects

Table 1
Descriptive data for the control ($n=21$) and dyslexics subjects ($n=18$) before instructional treatment

Demographic and test data	Dyslexics, mean ± SD	Control, mean ± SD	p-Value
±	130.8±12.1	132.6±10.6	0.6
Verbal IQ[a]	114.2±8.5	120.6±7.5	0.02
Word identification[a]	84.83±11.3	114.9±7.7	<0.0001
Word attack[a]	86.8±11.0	110.3±6.7	<0.0001
WIAT II spelling[a]	82.4±7.8	118.0±10.4	<0.0001
CTOPP elision[b]	8.3±2.2	12.05±2.2	<0.0001
TOWRE phonemic decoding[a]	84.4±9.6	119.9±8.3	<0.0001
Wolf RAN (letters)[c,d]	2.14±1.7	−0.9±1.1	<0.0001
Wolf RAN (number–letter)[c,d]	3.02±1.8	−0.8±1.3	<0.0001
PAL expressive coding[c]	−1.26±0.7	0.91±0.48	<0.0001
UW morphological signals[c]	−0.26±0.7	0.71±0.65	<0.0001

[a] $M=100$, SD=15.

[b] $M=10$, SD=3.

[c] $M=0$; SD=1.

[d] Time score so + is below mean.

were at or above the population mean on these same reading and spelling tests. The controls had substantially higher phonological, orthographic, and rapid automatic naming processing skills. The controls and dyslexics differed significantly in age-corrected standard scores for the following tests (see Table 1): WRMT-R Word Identification and Word Attack (Woodcock, 1987), WIAT II Spelling (Wechsler, 2001), TOWRE Rate of Phonological Decoding of Written Words (Torgesen, Wagner, & Rashotte, 1999), CTOPP Elision (Wagner & Torgesen, 1999), PAL Expressive Orthographic Coding (Berninger, 2001), UW Morphological Signals (Nagy et al., 2003), Wolf RAN (Letters) (Wolf, 1986; Wolf, Bally, & Morris, 1986), and Wolf RAS (Numbers and Letters) (Wolf, 1986; Wolf et al., 1986). In addition, when we compared the dyslexia treatment groups to which the dyslexics were randomly assigned, at pretest, the orthographic treatment group ($n=8$) and the morphological treatment group ($n=10$) did not differ significantly in any of the measures in Table 2.

4.2. Acquisition of MRI and fMRI scans and tasks

4.2.1. Scan acquisition

Structural and functional MR imaging were performed on a 1.5 T MR imaging system (General Electric, Waukesha, version 5.8). Scanning included a 21-slice axial high resolution set of anatomical images in plane with functional data (TR/TE 200/2.2 ms; fast spoiled gradient echo pulse sequence; 6 mm thick with 1 mm gap; 256×256 matrix). This anatomical series was followed by four fMRI series using 2-dimensional gradient echo echoplanar pulse sequence (TR/TE 3000/50 ms, 21 slices; 6 mm thick with 1 mm gap, 64×64 matrix, 114 volumes total). Each functional MRI scan lasted 5 min and 42 s. The four series were administered to the subjects in this order: (1) Phoneme Mapping; (2) Morpheme Mapping without phonological shift; (3) Morpheme Mapping with phonological shift; and (4) Orthographic Mapping.

Table 2
Descriptive data for the dyslexic subjects in the morphological treatment group ($n=10$) and dyslexics subjects in the orthographic treatment group ($n=8$) before instructional treatment

Demographic and test data	Morphological treatment Grp., mean + SD	Orthographic treatment Grp., mean + SD	p-Value
Age, mo	131.7 ± 13.0	129.7 ± 11.65	0.74
Verbal IQ[a]	113.9 ± 9.2	114.6 ± 8.3	0.87
Word Identification[a]	84.2 ± 12.7	85.6 ± 10.4	0.80
Word attack[a]	85.8 ± 11.6	88.0 ± 11.0	0.69
WIAT II spelling[a]	81.3 ± 9.6	83.7 ± 5.0	0.52
CTOPP elision[b]	8.1 ± 1.9	8.6 ± 2.6	0.63
TOWRE phonemic decoding[a]	83.4 ± 7.8	85.6 ± 12.0	0.64
Wolf RAN (Letters)[c,d]	1.9 ± 0.6	2.5 ± 2.6	0.44
Wolf RAN (number–letter)[c,d]	3.0 ± 2.0	3.0 ± 1.7	0.98
PAL expressive coding[c]	−1.2 ± 0.6	−1.3 ± 0.8	0.68
UW morphological signals[c]	−0.17 ± 0.58	−0.37 ± 0.95	0.57

[a] $M=100$, SD = 15.
[b] $M=10$, SD = 3.
[c] $M=0$; SD = 1.
[d] Time score so + is below mean.

4.2.2. fMRI tasks

Each of the four series consisted of a pair of on and off tasks. See Table 3 for description and examples of each set of on–off tasks and processes thought to be isolated by comparison of the on- and off-tasks. For each series, the two contrasting tasks were alternated, with four repetitions of each task lasting 30 s each. In addition, a fixation condition (cross-hair), lasting 18 s, was presented at the beginning, in the middle, and at the end of the series in order to provide a standard baseline. A slide with instructions appeared for 6 s before each condition. Visual word pairs were presented for 6 s, with no interstimulus interval. For all tasks, children indicated a 'yes' response by pressing a button held in the dominant hand. The button press had to occur during the 6-s stimulus presentation to be counted as correct. For each task condition half of the items had 'yes' as the correct answer. Stimuli were presented and responses were recorded using Eprime software (Psychology Software Tools, Pittsburgh, PA). The subject viewed the visual stimuli through a pair of goggles that was connected via high-resolution fiber optic cables to two Infocus projectors, which were, in turn, connected to the Eprime computer. Magnet-compatible earphones were used for auditory presentation of words for the Morpheme Mapping tasks. Before each scan, the children were thoroughly trained on each task to ensure that they understood what they would be asked to do inside the scanner.

A set of MRI-compatible head phones were placed over both right and left ears for each child and before the fMRI experiment began, a set of words were presented over the earphones and the child was asked if he could hear the words. The auditory intensity was adjusted to make sure the child could hear the words well but no exact measure of auditory intensity was measured.

Table 3
Description and examples of on and off conditions for each set of language tasks and the process isolated by significant differences between on and off conditions

Orthographic mapping	
On task	Stimuli were pairs of words, presented visually, one above the other. The child pressed a button if two words were real words spelled correctly (e.g. *bead-feel*). No button press if one of the words was spelled incorrectedly (e.g. *bead-feal*)
Off task	Stimuli were non-pronounceable letter strings containing approximately the same number of letters as words in the on task. The child pressed a button if two letter strings (e.g. *szpy* and *sxpy*) matched exactly. This control task required attention to all letter positions, but did not involve any phonological processing.
Isolated process	Comparison of activation during these two tasks isolated the brain areas specifically related to the construct of mapping the orthographic word form onto letter strings apart from processing letter strings alone. Letter strings do not correspond to a real word with meaning or predictable pronunciation.
Morpheme mapping without phonological shift (Aylward et al., 2003)	
On task	Stimuli were pairs of real words, presented visually, one above the other, and simultaneously presented auditorially. The top word contained a letter string sometimes used as a morpheme (i.e. conveying meaning in some words; e.g. '*er*'). The child pressed a button if the top word came from (was related in meaning to) the bottom word (e.g, *builder- build*) but did not press the button if the words were not related (e.g. *corner-corn*). For this version of the Morpheme Mapping task, the top word, if related to the bottom word, did not involve a phonological transformation of the bottom (base) word. For example, *builder* comes from *build* and adding the suffix (*er*) did not change how any sound is pronounced in the transformed word compared to the original word.
Off task	Stimuli were pairs of real words, presented visually, one above the other, and simultaneously presented auditorially. The child pressed a button if the two words were synonyms (shared the same meaning) (e.g. baby–infant), but did not press the button if they were not (e.g. mother–father).
Isolated process	Comparison of activation during these two tasks isolated the areas of activation specifically related to the construct of mapping the morphological word form (base + suffix) onto word. meaning apart from word meaning (semantic features) alone
Morpheme mapping with phonological shift	
On task	Stimuli and task were the same as for the Morpheme Mapping task without Phonological Shift, with one exception. For the Phonological Shift version of the task, the top word, if related to the bottom word, did involve a phonological transformation of the bottom (base) word. For example, *national* comes from *nation,* and adding the suffix (*al*) does change how the '*a*' in nation is pronounced in the transformed word compared to the original word.
Off task	Stimuli and task were the same as for the off task of the Morpheme Mapping task without Phonological Shift
Isolated process	Comparison of activation during these two tasks isolated the areas of activation related to morpheme mapping as in the previous task comparison.
Phoneme mapping (Aylward et al., 2003)	
On task	Stimuli were a pair of non-sense words, each containing a letter or group of letters printed in pink, presented visually, one above the other. The child pressed a button if the pink letters in the top pseudoword could represent the same sound as the pink letters in the bottom pseudoword (e.g. pl*ea*k-l*ee*ze), but did not press the button if the pink letters could not stand for the same word (e.g. *ph*eak-*p*anch.
Off task	Stimuli were a pair of non-pronounceable letter strings. The child pressed a button if the top string of letters matched the bottom string of letters (e.g. *szpq–szpy*).
Isolated process	Comparison of the activation during these two tasks isolated brain areas specifically related to the construct of mapping phonemes onto letters apart from letter processing alone in a word-like context.

4.3. Instructional treatments

Dyslexics were randomly assigned to either the orthographic or morphological spelling treatment. One hour of each of 14 sessions over a 3-week period was devoted to one of these spelling treatments. In addition, each student received one hour of common instructional components (alphabetic principle, 10 min; composition, 50 min).

4.3.1. Orthographic spelling treatment

Taught words were selected from high frequency words in graded lists (Instant Words in [Fry, 1996)]. A different list of words was used in each lesson, but each word in the list was practiced using each of two orthographic strategies.

The goal of the *first orthographic strategy* (Photographic Leprechaun) was to create a precise representation of all the letters in a written word in memory including those that could be phonemically recoded and those that could not. The teacher directed children to look at and name each word on the list, one word at a time. Children were encouraged to look carefully at and name each letter in the word from left to right and then to close their eyes and look at the snapshot that their photographic leprechaun had taken of the word in their mind's eye. Next the teacher asked them to direct their attention to one or more letter positions in the word and raise their hand when they could name the letter(s) in those positions (e.g. first, last, third and fourth). Letter positions were chosen that corresponded to silent letters, schwas (reduced vowels), or spelling units that had alternative plausible spellings for the same phoneme.

The goal of the *second orthographic strategy* (Proofreader's Trick) *was to strengthen further the precise representation of the written words in working memory.* The teacher explained that proofreaders find typos by spelling words backwards. Children were directed to (a) take a good look at a target word on the list and name all the letters in it, (b) close their eyes again, picture the word in their mind's eye, look at all the letters in the word, and then while they held the word in memory spell it backwards, quietly naming each letter in reverse order, starting with the last letter and ending with the first letter. They were instructed to open their eyes when they named the first letter in the word. Then they checked their reverse spelling against the target word before the group moved to the next word.

In addition, children completed visual search (circle letters that spell a real word), anagrams (rearrange the letters to spell a real word), and proofreading (correct the spelling errors) activities in the *SRA Morphograph Spelling Program* (Dixon & Englemann, 2001). Later in the session, students were asked to spell dictated words from the word set that they had practiced with two strategies earlier in the session. Percent correct was graphed for a visible record of progress.

4.3.2. Morphological spelling treatment

High frequency words containing high frequency morphemes were selected from *Spelling with Morphographs* (Dixon & Englemann, 2001). The goal of the *first morphological strategy* (Word Building) was to synthesize word parts to generate morphologically complex words. The teacher said a word part by part and asked the children to use these word parts to build a whole word and then write it on the response sheet.

For the *second morphological strategy* (Word Dissecting), the goal was to analyze the whole word and decompose it into its meaning parts. The teacher said a word and asked children to break it down into its component meaning parts, which are morphemes or word parts that convey meaning and grammar signals. Children were instructed to write each word part in the word on a worksheet leaving spaces between the word parts.

In addition to these strategies, children completed word-contracting and spelling-rule activities from *SRA Spelling Morphographs* (Dixon & Englemann, 2001). Later in the session, students were asked to spell dictated words that had been practiced with the morphological strategies. Percent correct was graphed for a visible record of progress.

This morphological treatment differed in substantial ways from the one (Berninger et al., 2003) provided for children in Aylward et al. (2003). That morphological treatment emphasized reflection and application of morphological awareness to phonological decoding (overt pronunciation of written words) and meaning judgments. It consisted of seven activities only two of which overlapped with the current treatment—dissecting words into base words and affixes and generating new words from these word parts. Other activities included (a) finding word parts for meaning in the orthographic word form, (b) sorting to categorize words according to written word parts that do and do not share morphemes and phonemes, (c) deciding if word pairs are related in meaning based on whether spelling parts also function as morphemes, (d) selecting word parts that fit a sentence context on the basis of derivational suffixes that mark grammar as well as meaning, and (e) transferring morpheme knowledge to decoding (pronouncing) morphologically complex written words. In contrast, the morphological treatment in the current study emphasized application to spelling, especially spelling rules (based on vowels and consonants at the end of base words (Dixon & Englemann, 2001) and transferring to written spelling of morphologically complex words. On one hand, the morphological treatment for reading did not emphasized rules but rather linguistic awareness and the morphological treatment for spelling emphasized articulation and application of rules. On the other hand, they contrasted in how morphological knowledge was applied—to reading written words (translating letters into over pronunciations) or to written spelling (translating spoken or orthographic word forms into written spellings). Given that spelling is not an inverse of reading (see Berninger & Richards, 2002), these morphological treatments may differ in significant ways.

4.3.3. Alphabetic principle taught in the phoneme to spelling direction

Both treatments began with a 10-min warm-up in which the substitutions (alternative 1- to 2-letter spelling units for representing each phoneme) were practiced using a substitution chart that listed the possible spelling units for each phoneme. The warm-up consisted of the teacher saying a pictured word, making the target phoneme in it, and naming the letter or letters in the corresponding spelling unit. Children then imitated saying the word, making the phoneme, and naming the letters. The teacher and children alternated turns in this modeling-imitating process for a set of phoneme-spelling unit substitutions in each lesson. Following the modeling, children were given pictured words with target phonemes and were asked to write all the possible spelling units (alternations) that might go with the target phoneme. This treatment, which was brief and focused on automaticity, differed in important ways from that provided in Aylward et al. (2003) for reflective, phonological awareness, which was more intensive lasting an hour in each session and consisting of seven activities described in Berninger et al. (2003) and Richards et al. (in press). Those activities were designed to (a) develop precise representation of the number of syllables and phonemes in spoken words, (b) generate new words from phoneme units, (c) parse words into graphemes and blend corresponding phonemes to create phonological word forms, (d) transfer taught grapheme–phoneme correspondences to new word contexts, (e) decide if graphemes could stand for the same phoneme, (f) sort words by phonemes regardless of their graphemes, and (g) choose phonemes that fit word contexts to create real words.

4.3.4. Composition

The rest of each session for *both treatments* was devoted to a writers' workshop based on the theme of Mark Twain's life and his work as a writer. For further details about this aspect of the intervention, see Berninger and Hidi (in press).

4.3.5. Training words

Training words for the morphological treatment were all real words that contained prefixes and/or suffixes (e.g. disliked, careless). The training words for the orthographic treatment were all real words that contained some spelling units that corresponded to more than one phoneme or did not correspond to any phoneme (e.g. e*x*amples, languag*e*). The words in both treatments were polysyllabic and had generally the same number of letters.

4.4. Data analyses

4.4.1. Image processing and MEDX analyses

fMRI scans were analyzed using MEDX (version 3.4.1) (Sensor Systems, Sterling, VA). Scans were considered acceptable for analysis if at least two of the four alternating cycles within the scan had less than 3 mm of movement. The data were motion corrected, linear detrended, and a t-test was performed contrasting the two conditions within each scan, expressed as a z-score. Each subject's activation z-maps were spatially smoothed with a 4 mm Gaussian filter. The individual's activation z-maps were converted to standard stereotaxic space of Talairach (Talairach & Tournoux, 1988) using FLIRT (www.fmrib.ox.ac.uk/fsl/).

4.4.2. Group fMRI analysis

MEDx was used to generate group maps (Bosch, 2000) for each fMRI task using a random effects model and a z score threshold of 2.4 to identify clusters greater than 20 voxels that were significantly more activated for the group for the on vs. off conditions. In the pretreatment scans, 18 brain regions (36 regions total for both left and right sides) were found that were significantly activated for at least one of the fMRI tasks for either the dyslexic or control groups (or both): superior frontal gyrus (SFG), middle frontal gyrus (MFG), inferior frontal gyrus (IFG), orbital frontal (Orb), supplementary motor (Suppl motor), anterior cingulate (Ant Cing), superior temporal gyrus (STG), middle temporal gyrus (MTG), inferior temporal gyrus (ITG), fusiform gyrus (FG), lingual gyrus (Ling), posterior parietal lobe including angular gyrus (post-parietal incl ANG), anterior parietal lobe including supramarginal gyrus (Ant Parietal incl SMG), anterior insula (Ant Insula), precentral gyrus (PreC), occipital gyrus (Occ Gyrus), thalamus, and cerebellum (see Table 4).

4.4.3. Individual brain region of interest fMRI activation analyses

For the 18 regions that showed significant activation on group z maps for either dyslexics or controls prior to treatment, outlines were drawn separately for right and left sides on a three-dimensional standardized brain (normal child, 10 year old subject's brain placed in Talaraich space). Fifteen of these regions were outlined on the standardized brain using the software program MEASURE (Barta et al., 1997; Buchanan, Vladar, Barta, & Pearlson, 1998). Masks for the other three regions (orbital frontal, thalamus, and supplementary motor area) were derived from the anatomical atlas supplied with the MRIcro software (these regions were adjusted to match the child standardized brain and anatomically fit well into place compared with the other 15 regions). Software was developed in our laboratory to apply the same anatomical mask for z-maps for all subjects' brains and automatically calculate the mean z-score within each ROI.

Table 4
Regions of significant fMRI activation (on task > off task) based on group maps at Time 1 for dyslexics and controls during four language tasks (R = Right, L = Left, B = Bilateral, M = Midline or Medial)

	Orthographic Mapping		Morphological Mapping (without Phonological Shift)		Morphological Mapping (with Phonological Shift)		Phoneme Mapping	
	Dyslexic	Control	Dyslexic	Control	Dyslexic	Control	Dyslexic	Control
SFG		M	R	M	M		LM	M
MFG		B	B	L	L	L	L	L
IFG	B	B	B	L	B	L	B	L
Orb	R	R	L	R	B		L	B
Supl Motor	M	M	R		M		M	M
Ant Cing	M	B					M	B
STG		L			L		L	
MTG		B	R				L	L
ITG		L	B	L	L	L	B	B
FG	B	B	B	B	B	B	B	B
LING	B	B	B	B	B	B	B	B
Post parietal incl ANG		R	B	B		B	B	B
Ant parietal incl SMG			L					
Ant insula	B	B			L			
PreC	B		B	B	L	B	L	B
Occ Gyrus	B		B	B	B	B	B	B
Thalamus			B		B		L	B
Cerebellum	B		B	L	B	L	B	B

4.4.4. Statistical analyses

As indicated above, we used both group maps and region of interest methods (from hereon referred to as 'individual brain analysis') to analyze fMRI data. For the individual brain analysis method, data consisted of z scores for each subject for each region of interest. Group differences between dyslexics and controls at Time 1 were assessed using one-way ANOVA. ANOVA was used to confirm that the two dyslexia treatment groups did not differ in these regions prior to treatment. For the regions that significantly discriminated between these groups at Time 1, change over time (pre- to post-treatment) was assessed for the dyslexic subjects using repeated measures ANOVA, with pre- and post-treatment z scores used as the repeated measures. For regions that were identified as changing significantly over time for the dyslexic subjects, one-way ANOVA was used to determine whether dyslexics and controls differed on Time 2 measures. Regions were assumed to have 'normalized' as result of treatment if (a) they had showed differences in activation between dyslexics and controls at Time 1, (b) changed significantly in dyslexics from time 1 to time 2, and (c) did not show differences in activation between dyslexics and controls at Time 2. Finally, for the regions that showed normalization, another repeated measures ANOVA was performed, with pre- and post-treatment z-scores for the specific language mapping task in the normalized brain region used as the repeated measure, and treatment group (orthographic vs. morphological) as the between-group measure. Of interest was whether the time by treatment group interaction was significant for a certain kind of language mapping in a specific brain region, which provides evidence for treatment-specific brain responding. Causal inferences about treatment and brain response are stronger if two treatments lead to two different kinds of brain response (fMRI language mapping process in a specific region) than if both treatments lead to the same brain response.

4.4.5. Behavioral analyses

Psychometric, normed measures of spelling were given to evaluate whether spelling achievement improved significantly as a result of either of the spelling treatments. Both spelling real words and spelling pseudowords from dictation were evaluated. Repeated measures analyses of variance were used to determine whether treatment was associated with increased performance on these tests.

5. Results

5.1. Group analyses

5.1.1. Differences in brain activation among the four kinds of language mapping

Table 4 summarizes results for regions shown to be significantly activated in MEDX group analyses. Results of the group analyses displayed in Table 4 can be summarized as follows. For the control children who were good readers and spellers, both common and unique patterns of brain activation were observed for the four kinds of language mapping: orthographic, morpheme without phonological shift, morpheme with phonological shift, and phoneme mapping. Common regions of activation were observed in the left inferior frontal gyrus, lingual gyrus (both sides), fusiform gyrus (both sides), and left inferior temporal gyrus. Areas uniquely activated during the Orthographic Mapping included the right middle frontal gyrus, left superior temporal gyrus, right middle temporal gyrus, and bilateral anterior insula. For Morpheme Mapping (with or without phonological shifts), only left cerebellum activated; but for Phoneme Mapping, cerebellum activated bilaterally. The areas uniquely activated during Phoneme Mapping included left orbital frontal, bilateral thalamus, right inferior temporal gyrus, and right cerebellum. Controls did not activate any brain regions during Morpheme Mapping with phonological shifts that they had not activated during Morpheme Mapping without phonological shifts. For good readers and spellers, Morpheme Mapping and Phoneme Mapping did not activate a set of completely identical brain regions but Morpheme Mapping activated the same regions whether or not phonological shifts were involved.

Fig. 1 shows examples of four brain slices where unique and common brain activation was observed for controls during the four tasks used in the current study. For phoneme mapping, left inferior temporal gyrus had also been uniquely activated during this task in Aylward et al.'s (2003) sample of dyslexics ascertained using the same inclusion criteria.

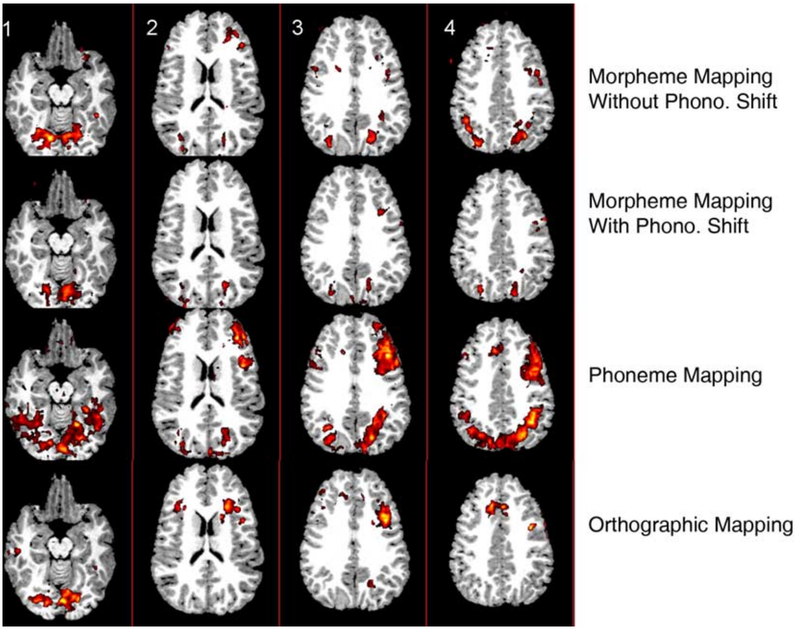

Fig. 1. Functional MRI of the controls (normal readers) at time 1 for four different language tasks—morpheme mapping without phonological shift (row 1); morpheme mapping with phonological shift (row 2); phoneme mapping (row 3); orthographic mapping (row 4). Each column shows a different anatomical axial section of brain in Talaraich space—Column 1 is at the level of the fusiform and lingual gyrus; column 2 is at the level of the inferior frontal gyrus (triangularis), middle frontal gyrus, occipital gyrus; Column 3 is at the level of the inferior frontal gyrus, middle frontal gyrus, parietal lobe, angular gyrus, precentral gyrus; Column 4 is at the level of the middle frontal gyrus, parietal lobe, angular gyrus, precentral gyrus, and anterior cingulate.

For morpheme mapping without phonological shifts, left cerebellum had also been activated during this task in Aylward et al.'s sample.

5.1.2. *Differences in activation between dyslexics and controls*

Different patterns of activation were observed for dyslexics and controls on the four fMRI mapping processes (see Table 4, which lists 18 regions on the left and 18 regions on the right). For Orthographic Mapping, dyslexics activated in 11 (counting both left and right as separate regions) of the 20 regions in which controls activated and activated in six regions where controls did not. Thus, dyslexics' significant activation consisted of both absence of activation where controls activated and presence of activation where controls did not. For Morpheme Mapping without Phonological Shifts, dyslexics showed different patterns of activation than the controls in 11 regions. For Morpheme Mapping with Phonological Shifts, dyslexics showed different patterns of activation than controls in 13 regions. For Phoneme Mapping, dyslexics and controls both activated in 21 brain regions; however, dyslexics activated in the right and left inferior frontal gyrus, whereas controls activated in only left inferior frontal gyrus. Dyslexics activated in left thalamus and left precentral gyrus, whereas controls activated bilaterally in both these regions, suggesting that the bottlenecks in language processing may have subcortical and cortical origins. Also for Phoneme Mapping, dyslexics activated in the left superior temporal gyrus and controls did not.

On one hand, dyslexics did not appear to use completely different neural regions for the language processes investigated than controls did—because many common regions were activated for each language process. On the other hand, sometimes dyslexics did not activate where controls did and sometimes controls did not activate where dyslexics did. The underactivation may indicate inability to engage the necessary neural circuits. The activation of extra neural regions may indicate either alternative pathways or inefficiency in the system.

5.2. *Individual brain and region of interest analyses*

Because the specific aim of our research program is to evaluate brain response of individual students to alternative treatments, individual brain regions of interest were also analyzed. The results of the MEDX individual fMRI z-scores maps were transformed into Talaraich space using FLIRT (see Section 4). Then the resulting individual quantitative values for fMRI tasks in specific brain regions were evaluated in sequential analyses for (a) pretreatment differences between dyslexics and controls, (b) significant changes in dyslexics from before to after treatment, (c) elimination of pretreatment differences, and (d) evidence of treatment-specific brain responding.

5.2.1. *Comparison of dyslexics and controls before treatment*

Significant differences between controls and dyslexics were found in 10 brain regions using the individual ROI analyses at time 1 (see Table 5 for means and standard deviations). For *Orthographic Mapping* before treatment, controls had significantly greater activation than dyslexics in right inferior frontal gyrus, $F(1,37)=3.84$, $p=.05$, and right posterior parietal gyrus, $F(1,37)=3.92$, $p=.05$. For *Morpheme Mapping without*

Table 5
Means and standard deviations for regions showing significant differences between dyslexics and controls at Time 1 in average z scores. The last column shows the p value for the dyslexic versus control comparison of regional z score

	Dyslexics		Controls		p
	M	SD	*M*	SD	
Orthographic Mapping					
Right Inferior Frontal Gyrus	−.154	.527	.178	.527	.05
Right Posterior Parietal Gyrus	−.758	.820	−.306	.602	.05
Morpheme Mapping with phonological shift					
Right anterior cingulate	.017	.371	−.251	.498	.05
Phoneme Mapping					
Right Anterior Insula	−.077	.485	.316	.499	.018
Left Anterior Insula	.192	.453	.591	.504	.014
Left Fusiform Gyrus	.364	.443	.831	.551	.006
Left Inferior Frontal Gyrus	.581	.529	1.006	.594	.027
Left Inferior Temporal Gyrus	.146	.277	.354	.347	.048
Right Lingual Gyrus	.141	.453	.3582	.738	.007
Left Lingual Gyrus	.243	.490	.8769	.626	.001

phonological shift, the dyslexics and controls did not differ significantly in activation in any of the regions at Time 1. For *Morpheme Mapping with phonological shift*, the controls had significantly greater activation than dyslexics in right anterior cingulate, $F(1,37)=4.11$, $p=.05$ at Time 1. For *Phoneme Mapping*, the controls had significantly greater activation than dyslexics in seven regions: right anterior insula, $F(1,37)=6.16$, $p=.018$, left anterior insula, $F(1,37)=6.67$ $p=.014$, left fusiform gyrus, $F(1,37)=8.33$, $p=.006$, left inferior frontal gyrus, $F(1,37)=5.48$, $p=.027$, left inferior temporal gyrus, $F(1,37)=4.18$, $p=.048$, right lingual gyrus, $F(1,37)=6.20$, $p=.017$, left lingual gyrus, $F(1,37)=12.109$, $p=.001$. For significant comparisons, the controls had more BOLD activation than did the dyslexics. Thus, all pretreatment differences between dyslexics and controls involved underactivation of the dyslexics in specific brain regions during specific fMRI language mapping processes. Overall, when all 36 brain regions for the four language mapping processes were evaluated, only a few instances of significant differences between dyslexics and controls were found, suggesting that a small set of brain regions may be interfering with normal spelling development.

5.2.2. Comparison of pre-treatment and post-treatment activation for dyslexics

The two regions of significant BOLD activation differences between dyslexics and controls at Time 1 on *Orthographic Mapping* did show *reliable change from Time 1 to Time 2 in dyslexics*. In right inferior frontal gyrus, the dyslexics showed significantly greater activation after treatment ($M=0.068$, $SD=0.579$) (see Fig. 2) than before treatment ($M=-0.154$, $SD=0.527$; $F(1,16)=4.34$, $p=.05$). In right posterior parietal gyrus, the dyslexics showed significantly more activation after treatment ($M=-0.335$, $SD=.590$) (see Fig. 3) than before treatment ($M=-0.758$, $SD=0.820$; $F(1,16)=7.44$, $p=.015$). For these regions, control children had also showed stable activation during

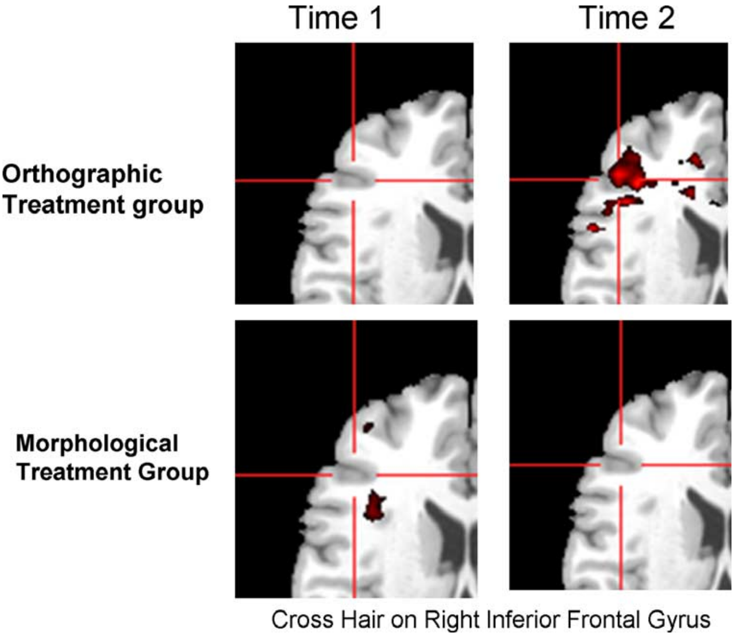

Fig. 2. Functional MRI images (group maps) during the Orthographic Mapping task for the two different treatment groups of dyslexics. The red areas indicate regions where brain activation was greater for the on task than for the off task, and there is visually far more activation at Time 2 for the orthographic treatment group in the right inferior frontal gyrus compared to the morphological treatment group.

Orthographic Mapping, with no significant change in activation from Time 1 to Time 2. However, the BOLD activation in dyslexics did not change significantly over time for (a) right anterior cingulate on Morpheme Mapping with phonological shifts, or (b) any of the regions of significant BOLD activation differences between dyslexics and controls at Time 1 on Phoneme Mapping.

As hypothesized, the effectiveness of the orthographic treatment for increasing brain activation during the Orthographic Mapping task, to which it is theoretically linked, was demonstrated. In contrast, morphological treatment was not effective in leading to significant change on the Morpheme Mapping task. Anterior cingulate, a region associated with conflict management (Mesulam, 1990), did not change in activation on Morpheme Mapping with Phonological Shifts, suggesting that the dyslexics did not change in response to treatment for a task that required coordination of word forms and possible conflict. Neither treatment was effective in leading to significant change in phoneme mapping. Because the primary treatments were orthographic or morphological, it is not surprising that they did not lead to change in phoneme mapping, which is usually mastered earlier in development but not necessarily for older children with dyslexia. The differences in treatment effectiveness may also be due to fact that little instructional time was devoted to alphabetic principle and none to reflective, phonological awareness as in Aylward et al. (2003).

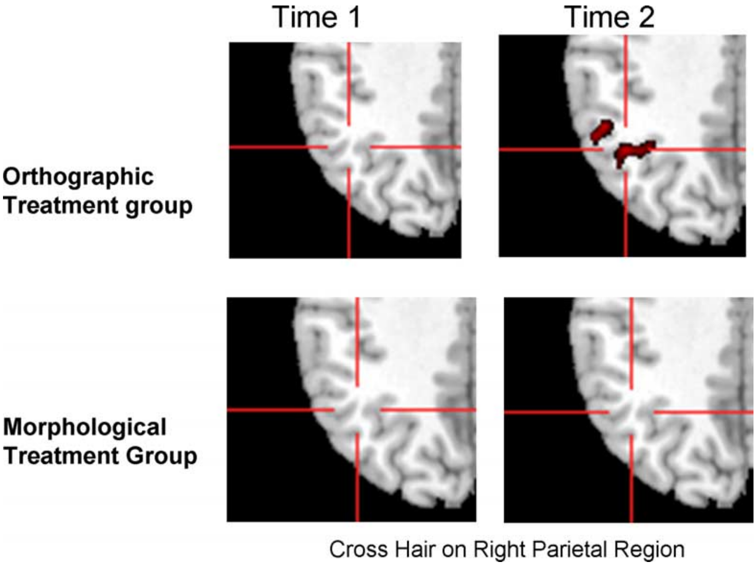

Fig. 3. Functional MRI images (group maps) during the Orthographic Mapping task for the two different treatment groups of dyslexics. The red areas indicate regions where brain activation was greater for the on task than for the off task, and there is visually far more activation at Time 2 for the orthographic treatment group in the right parietal region of the brain compared to the morphological treatment group.

5.2.3. Treatment-specific brain activation

The time by treatment interaction during Orthographic Mapping was significant in right inferior frontal gyrus, $F(1,16)=9.57$, $p=.007$, and in right posterior parietal gyrus, $F(1,16)=5.00$, $p=04$. In right inferior frontal gyrus, the orthographic treatment was associated with a significantly greater increase in activation (from $M=-0.363$, $\mathrm{SD}=0.372$ at Time 1 to $M=0.296$, $\mathrm{SD}=.410$ at Time 2), than was the morphological treatment ($M=0.014$, $\mathrm{SD}=0.589$ at Time 1 and $M=-0.115$, $\mathrm{SD}=0.648$ at Time 2). Likewise, the orthographic treatment resulted in significantly greater increased activation in right posterior parietal gyrus, from $M=-0.928$, $\mathrm{SD}=0.586$ at Time 1 to $M=-0.081$, $\mathrm{SD}=0.460$ at Time 2, than did the morphological treatment, $M=-0.622$, $\mathrm{SD}=0.978$ at Time 1 and $M=-0.538$, $\mathrm{SD}=0.625$ at Time 2. Group maps shown in Figs. 2 and 3 (see also Table 4) confirm these treatment-specific findings based on individual brain analyses in the right inferior frontal gyrus and the right posterior parietal region. Table 6 shows the quantification of the post-treatment fMRI cluster analysis for the orthographic treatment group map. Plots of average z-score (Fig. 4 for the right inferior frontal gyrus and Fig. 5 for the right posterior parietal gyrus) versus time show that the z-scores for dyslexics in the orthographic treatment group approached the same value as controls after treatment whereas this effect was not observed for morphological treatment group.

5.2.4. Normalization of brain activation

The dyslexics and controls did not differ in BOLD activation in right inferior frontal gyrus (see Fig. 4) or posterior parietal regions (see Fig. 5) on the Orthographic Mapping

Table 6
Quantification of fMRI cluster results from the orthographic treatment group map during the orthographic task

Cluster index	Voxels	*p* Value	Max *Z*	COG *x* (mm)	COG *y* (mm)	COG *z* (mm)
5	18,535	1.15×10^{-8}	4.54	46.5	7.23	17.8
4	14,673	3.58×10^{-7}	5.16	−1.33	20.4	42.3
3	12,168	3.64×10^{-6}	5.3	18.3	−77.2	−8.68
2	5705	0.00416	4.27	−18.7	−81.7	−4.37
1	4331	0.0249	3.55	−40.2	19.3	19.9

Voxels = number of significant voxels within the cluster; *p* value = probability that the fMRI cluster occurred by chance; Max *Z* = maximum *z*-score within the cluster; COG *x*, *y*, *z* = center of gravity coordinates *x*, *y*, *z* in Talaraich space in millimeters.

task following orthographic treatment, indicating that the ability to map the orthographic word form onto letter strings may have normalized in these regions after theoretically linked treatment.

5.3. Behavioral changes in spelling achievement

A significant main effect for time showed that spelling improved for the dyslexics as a group: in real word spelling on the Wechsler Individual Achievement Test, Second Edition (WIAT II) (Wechsler, 2001), $F(1,15)=6.959$, $p=.019$ (from a mean standard score of 86.1, SD = 13.7, to a mean standard score of 93.1, SD = 8.8), and in pseudoword spelling on the Woodcock Johnson Third Edition (WJ III) (Woodcock, McGrew, & Mather, 2001) Spelling Sounds subtest, $F(1,15)=13.895$, $p=.002$ (from a mean standard score of 81.8, SD = 8.9, to a mean standard score of 85.5, SD = 9.5). Both before and after treatment, this sample is relatively better at spelling real words than pseudowords. For pseudoword spelling, a significant time × treatment interaction occurred, $F(1,15)=7.173$, $p=.017$,

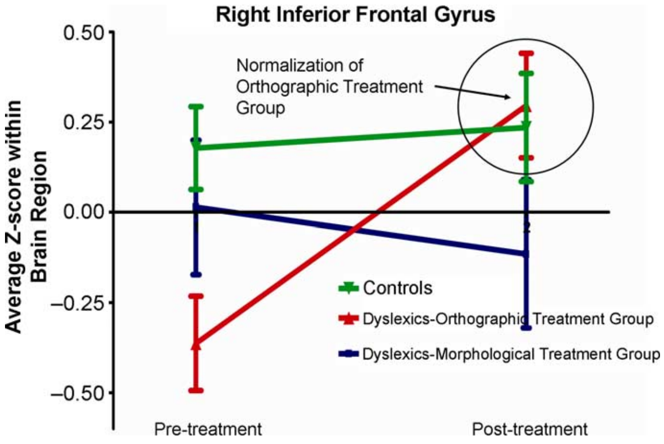

Fig. 4. Plot of average fMRI *z*-score within the right inferior frontal gyrus for the orthographic treatment group (red line); morphological treatment group (blue line); and control group (green line) during the orthographic task. The average fMRI *z*-scores were taken from the region of interest analysis.

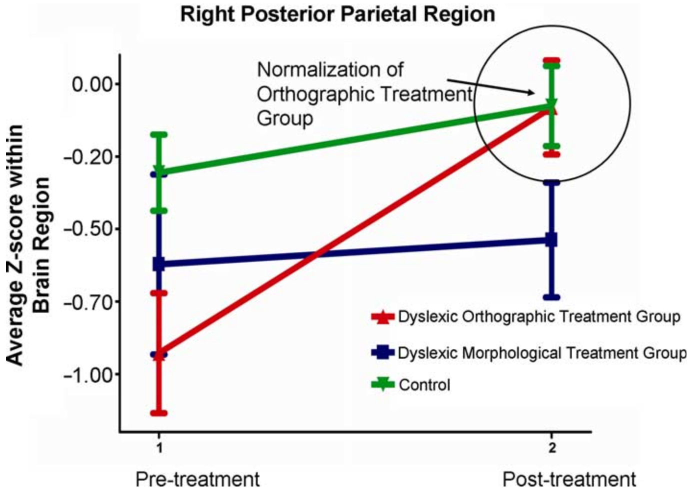

Fig. 5. Plot of average fMRI z-score within the right posterior parietal region for the orthographic treatment group (red line); morphological treatment group (blue line); and control group (green line) during the orthographic task. The average fMRI z-scores were taken from the region of interest analysis.

with greater improvement for the morphological treatment group than for the orthographic treatment group. This interaction is consistent with Triple Word Form theory (see introduction), which hypothesizes that computations among the morphological, phonological, and orthographic word forms contribute the encoding process of spelling by phonological encoding, which precedes spelling by accessing the autonomous orthographic lexicon. For real word spelling, the time × treatment interaction approached but missed conventional significance; 75% of the individuals in the orthographic treatment compared to 55% of the individuals in the morphological treatment improved on this outcome measure. Taken together these findings suggest that the children with dyslexia in this study are still constructing the orthographic word forms in the autonomous orthographic lexicon. The benefits of the orthographic treatment are first evident on the fMRI orthographic mapping task. Only with sustained treatment over time is reliable, substantial improvement in spelling real words on psychometric test as a function of word-specific orthographic training likely to be realized.

6. Discussion

6.1. Methodological and applied significance

In this study we combined standard group mapping analysis of fMRI activation and individual brain fMRI activation (region of interest) analyses. The advantage of group analyses is that reliability of measurement of regions of significant brain activation is increased by taking into account data from many subjects. However, results of group analyses do not always generalize to all the individuals contributing to them. One reason for group results not applying to individuals is that individuals may use unique strategies for performing tasks during scanning (e.g. Burton, Noll, & Small, 2001). The advantage of individual analyses is that they may support the application of research paradigms to clinical practice in diagnosing differences between child dyslexics and normal spellers/readers and in evaluating individual brain response to spelling treatment for dyslexia. By identifying regions that were reliably activated in individual controls from time 1 to time 2, we increased the probability that changes in brain response were related to common mechanisms across participants rather than to idiosyncrasies in strategies used by individuals.

6.2. Theoretical significance for neurolinguistics

Each of three word forms—phonological, orthographic, and morphological—showed distinct patterns of BOLD brain activation in good readers and spellers (see Fig. 1). Although many of the common and unique regions of activation on these word form tasks were in the posterior regions (e.g. lingual, fusiform, inferior temporal gyrus, and insula), it was also the case that some activation was in the frontal (e.g. inferior frontal gyrus, middle frontal gyrus, and orbital frontal cortex) and subcortical (e.g. cerebellum and thalamus) regions. Moreover, these regions specific to word form processing were not always on the left—sometimes they were on the right and sometimes bilateral (see figures and Section 5). Thus, word form processing draws greatly on specific areas of posterior regions, especially but not exclusively on the left, but it also draws on selected regions of frontal cortex and subcortical structures, also sometimes on the right as well as the left. Researchers should be cautious in attributing word form processing exclusively to the left posterior regions.

Richards et al. and colleagues extended these analyses of one word form at a time to the relationships between two word forms at a time (Richards et al., 2005) and effects of a treatment aimed at one word form on contrasting word form (Richards et al., in press). In future research, BOLD activation associated with single word forms, cross-word form mapping, or effects of word-form treatment, could be used in conjunction with neural modeling to identify which regions are involved in neural computations underlying word reading and word spelling, both in populations of typically developing readers/spellers and dyslexics.

Phonological, orthographic, and morphological word forms that are represented in the brain/mind are not synonymous with the phonological, orthographic, and morphological stages of spelling development (Moats, 2000; Templeton & Baer, 1992). Normal spelling goes through three typical stages: an initial phonological stage (strategic mapping of phonemes onto written graphemes in words not yet represented in the autonomous orthographic lexicon) during the primary grades, followed by an orthographic stage (automatic retrieval of the orthographic word form) during the upper elementary grades, followed by a morphological stage (using morphemes to spell new transformations of bases and spelling rules for adding inflectional or derivations suffixes to base words) during the middle school years (Moats, 2000; Templeton & Bear, 1992). Both future fMRI studies and behavioral studies of spelling (and reading) might investigate processing of single word forms, cross-word form mapping, and treatment designed to improve phonological, orthographic, or morphological processing at specific stages of spelling development. Moreover, research is needed on whether stages of spelling development are discrete stages or overlapping, cascading phases of progression from phonological to orthographic to morphological processing and whether the progression is parallel or distinct for reading and spelling.

6.3. Significance for children with dyslexia in middle childhood

Results of the group and individual analyses converged (see Figs. 2 and 3 and Table 4) in identifying two brain regions during orthographic mapping—right inferior frontal gyrus and right posterior parietal regions—in which dyslexics (a) differed from good spellers prior to spelling treatment, (b) changed reliably after treatment, (c) normalized, and (d) showed evidence of treatment-specific responding during orthographic mapping following orthographic treatment. One of these regions—right inferior frontal gyrus contains the right pars triangularis where dyslexics of the same age in a structural imaging study differed from controls; and a behavioral measure of orthographic coding was correlated with the size of the surface area of this structure (Eckert et al., 2003).

In another treatment study for children with dyslexia at the same grade levels as the current study, decreases in activation in right inferior frontal gyrus following phonological or morphological treatment was associated with improvement in phonological word decoding, suggesting that, as children were able to attend to other sources of linguistic information and not just orthographic information they were better able to compute the phonological, morphological, and orthographic relationships underlying decoding (see Richards et al., in press). Changes before and after treatment were also observed in correlations between fMRS lacate activation, an indicator of neural metabolism (Serafini et al., 2001), and structural MRI measures in the right pars triangularis in this region, suggesting that brain structures were recruited in a more efficient manner after treatment (Richards et al., in press). In functional connectivity studies, adult males with and without dyslexia differed in the fMRI functional connectivity between right inferior frontal gyurs and the left posterior word form centers but not between left inferior frontal gyrus or cerebellum and the left posterior word form regions (submitted). Thus, research evidence is accumulating that right inferior frontal gyrus is important in written word learning and may differ from normal controls in structural MRI, functional MRI, functional MRS, and fMRI functional connectivity (to word form regions).

Left inferior frontal gyrus, which is where changes in phoneme mapping were observed following reading treatment (Aylward et al., 2003), may be more important in phonological processing. Brain changes were probably not observed on this task in the current study because the brief treatment in automatizing alphabet principle was not sufficient nor did either treatment provide substantial training in phonological awareness. In contrast to the changes in right superior parietal regions observed in Aylward et al. (2003) during phoneme mapping, in the current study changes were observed in the right posterior parietal regions following treatment designed to improved processing of the orthographic word form. The effects of such orthographic treatment on right inferior frontal gyrus and right posterior parietal regions add to the growing literature documenting that brain regions on the right, and not only regions on the left, contribute to language processing (Poeppel & Hickok, 2004).

One approach to evaluating effective treatments is to compare a treatment group to a control group that receives no experimental treatment. Another approach is to compare two different types of instructional treatment (alternative treatments control design) that are hypothesized to affect brain activation differentially in specific regions and behavioral response. The alternative treatments control design has advantages over a treatment group-control group design in that it can be used to test theoretical relationships between instruction and brain response on tasks that are conceptually linked to the treatment. This design moves research that combines brain imaging and instruction beyond merely evaluating the effectiveness of a treatment to investigating relationships between specific kinds of treatment and the nature of the observed brain change(s). It is no longer news that dyslexic brains may normalize in specific language processes as a function of receiving treatment (see introduction). Treatment-specific brain responding provides stronger evidence of the link between teaching and brain response than experimental designs that have only one instructional treatment. Studies that combine different kinds of brain imaging tasks and different kinds of language instruction, both of which are linked theoretically or empirically, for well-defined populations have great promise in developing a knowledge base for educational science that is grounded in cognitive neuroscience and neurolinguistics.

Treatment-specific brain responding is necessary to establish the construct validity of treatments validated on the basis of brain response for specific populations at specific developmental stages on specific fMRI tasks. The current study provides *construct validity* for the orthographic treatment in changing the brain on a fMRI orthographic mapping task requiring access to a precise orthographic word form and *discriminant validity* for morphological treatment—it does not result in brain change during fMRI orthographic mapping—and for brief phonological treatment for automatizing alphabetic principle—it does not result in brain change as more systematic, intensive phonological training did (Richards et al., in press). As research that combines brain imaging tasks and instructional treatments increases, these issues of construct and discriminant validity are as important as they are for psychometric testing with behavioral measures.

6.4. Significance for other brain imaging studies of spelling

Most of the brain imaging research on spelling to date has been done with normal adults or adults who have lost spelling function. In one brain imaging study of normal spelling (Mennon & Desmond, 2001), adult participants spelled auditorially dictated sentences by writing small letters on a 10×10 cm^2 piece of paper on their right thigh. When compared to fixation (a control that requires only focal visual attention), spelling increased activation mostly in left superior parietal lobe but also in nearby left dorsal inferior parietal cortex. Ojemann et al. (1998) used a word completion paradigm in which three-letter strings (word stems for highly predictable words) are presented and the task is to complete the stem to spell a real word. Normal adults increased activation in left frontal and supplementary motor areas and right cerebellum and decreased activation in right parietal regions and right insula. In another word completion paradigm study with adults, Dhond, Buckner, Dale, Marinkovic, and Halgren (2001) identified temporal stages in the unfolding neural events, which proceeded from the back to the front of the brain: The orthographic word form was initially processed in the visual association areas, but later multi-modal coding (mapping) took place in Wernicke's area in the left temporal region and subsequently was completed in Broca's area in the left frontal region. Lee et al. (1999) showed that silent spelling activated the left inferior frontal gyrus in normal adults, in contrast to right inferior frontal gyrus that we observed in normal children and treated dyslexics. Booth et al. (2002) reported spelling-related brain activity in the fusiform. That was certainly a region of significant activation across all four fMRI language tasks (see Table 4); it may play a greater role in learning to spell words than was assessed by our orthographic mapping task that required access to orthographic representations in long-term memory.

Our study adds by extending functional brain imaging research to spelling in children who are normal spellers (and readers) and children who have dyslexia, a disorder of reading and spelling despite normal intelligence. Regions involved in spelling may change over development. Both good spellers and dyslexics in this study of upper elementary grade children activated the right IFG and right parietal regions including angular gyrus, whereas adults in the studies discussed earlier tended to activate the left side of these regions. Results based on group maps (see Table 4) in our child sample converge with some of the regions of activation reported for adults but are not identical. Although good spellers showed hardly any differences in brain activation for morphological word forms that did and did not involve phonological shifts (see Table 4), dyslexics showed many differences in brain activation during these two kinds of morpheme mapping (Table 4). Taken together, results (Table 4) for the four language mapping processes (Table 3) reported in this article and other research that is cited suggest that phonological, orthographic, and morphological word forms are involved in learning to spell in ways that change over the course of development.

7. Summary and conclusions

This study found evidence for differences in brain activation patterns during orthographic mapping between child dyslexics and matched controls who were good readers and spellers in right inferior frontal gyrus and right posterior parietal regions including angular gyrus. Dyslexics who received orthographic treatment improved reliably on orthographic mapping in both of these regions and did not differ in these regions from good spellers at time 2 after the dyslexics had received orthographic treatment. Thus, the individual brain responding of child dyslexics appeared to be changed and to normalize for regions that prior to orthographic treatment differentiated the dyslexics from controls and that were stable from time 1 to time 2 in the controls.

In no way does this imply that their spelling problems were fully remediated. Rather, the results show that an instructional component that emphasizes orthographic strategies may be effective in changing the orthographic mapping related to spelling at the orthographic stage of spelling development. However, the child dyslexics also appear to need specialized instruction for the phonological processes involved in spelling to normalize their phoneme mapping. The benefits of morphological treatment for spelling may not be detected in brain response of child dyslexics in the upper elementary grade levels, at least not until they master or reach reasonable proficiency in the earlier phonological encoding and orthographic spelling stages. The measured effectiveness of the treatment will also likely depend, to a large degree, on the nature of the phonological, orthographic, or morphological treatment given and the nature of the fMRI phonological, orthographic, and morphological tasks used to assess brain response.

Good spellers may be taught, not born, as is often assumed. More research evidence, based on brain and behavioral data, is needed regarding the optimal developmental sequence and mix of the phonological, orthographic, and morphological instructional components for both dyslexics and normally developing spellers.

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