Common Neural Basis of Motor Sequence Learning and Word Recognition and Its Relation With Individual Differences in Reading Skill

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ABSTRACT

To investigate the neural basis of a common statistical learning mechanism involved in motor sequence learning and decoding, we recorded brain activation from participants during a serial reaction time (SRT) task and a word reading task using functional magnetic resonance imaging. In the SRT task, a manual response was made depending on the location of a visual cue, and the order of the locations was either fixed or random. In the word reading task, visual words were passively presented. In the inferior frontal gyrus pars triangularis (IFGpTr) and the insula, differences in activation between the ordered and random condition in the SRT task and activation to printed words in the word reading task were correlated with the participants' decoding ability. We speculate that extraction of statistically predictable patterns in the IFGpTr and insula contributes to both motor sequence learning and orthographic learning, and therefore predicts individual differences in decoding skill.

Introduction

Learning to read builds on multiple skills, such as phonemic segmentation and sequencing (Melby-Lervag, Lyster, & Hulme, 2012; Wimmer, 1996), detecting letter patterns (Cunningham, Perry, & Stanovich, 2001), and mapping from orthography to phonology (Ziegler & Goswami, 2005). In addition, substantial research suggests that sensitivity to orthographic structure, or the frequency of particular letter sequences, is an important aspect of learning to read. Indeed, Cunningham and Stanovich (1993) found that young children's sensitivity to frequency of certain letter sequences (e.g., "yikk" vs. "yinn") accounted for approximately 30% of unique variance in their word recognition ability. Bonte, Poelmans, and Blomert (2007) found that children with development dyslexia (DD) did not show comparable sensitivity to the phonotactic frequency of letter sequences of auditory nonwords compared to typically developing (TD) readers (see also Apel, Wolter, & Masterson, 2006). These findings suggest that the ability to extract statistical patterns based on the order and frequency information of letters or speech is an important factor in learning to read.

In addition to sensitivity to orthographic or speech sequences, nonlinguistic sequence learning has been associated with reading ability. In a typical serial reaction time (SRT) paradigm, participants press a button with different fingers according to the location of visual cues, which occur in two conditions: ordered and random. In the ordered condition, the order of the visual cues is fixed, and a sequential dependency occurs between neighboring elements (e.g., 1 is always followed by 2)

and is repeated across blocks (e.g., 1234, 1234). In the random condition, orders are not fixed and are not repeated across blocks (e.g., 3214, 2134). Howard, Howard, Japikse, and Eden (2006) compared TD and DD adults in a modified SRT task in which the sequential dependencies occurred in nonadjacent elements (e.g., 1r2r3r4, 2 is predicted by 1 and r is a random element). To determine the specificity of DD's learning impairment, Howard et al. also administered a spatial contextual cueing task (Chun & Jiang, 1998) in which participants judged the orientation of a target while a task-irrelevant spatial pattern either co-occurred with the target in the repetition condition or never occurred with the target before in the new condition. Learning was defined by the reaction time (RT) difference between the random condition and the ordered condition in the sequential learning task, and between the new condition and the repetition condition in the spatial contextual cueing task. Compared to TDs, DDs were inferior in motor sequential learning but better in the spatial contextual cueing task. Lum et al.'s (2013) meta-analysis showed the group effect (TDs outperform-ing DDs) on sequential learning in the SRT task holds regardless of task variation across studies. These findings suggest that basic nonlinguistic sequential coding may mediate the association between reading ability and orthographic or speech sequence learning.

The SRT task comprises multiple processes, including early visual-motor association, detection of serial order embedded in the motor response, and automatization of both the visual-motor associa-tion and the ordered motoric responses. As such, the correlation between sequence learning and reading ability could arise from individual differences in any of these processes. With respect to neurobiological correlates of these processes, Nicolson et al. (1999) conducted a functional magnetic resonance imaging (fMRI) study on TD and DD adults in motor sequence learning. The participants made a key-press response based on a specific auditory sound, with feedback indicating whether the response was correct. The same sequence was practiced for 2 hr; following this, the learned sequence and a new sequence of auditory tones were presented to the participants in the scanner. Behaviorally, DDs made more errors than TDs in performing the well-practiced sequence. The fMRI results showed that compared to TD, DD showed lower activation of the left cerebellum and the left cingulate cortex while performing the learned sequence and lower activation of the right cerebellum while performing the new sequence. Hence, the authors propose that both sequence learning and orthographic learning involve automatization in the cortical-cerebellar network, which requires substantial practice before performance becomes rapid and accurate (Nicolson & Fawcett, 2007). Menghini, Hagberg, Caltagirone, Petrosini, and Vicari (2006) found that adults with DD, relative to TD, showed reduced activation of the left supplementary motor area (SMA) during the early stages of sequence learning and enhanced activation of the bilateral cerebellum and the bilateral inferior parietal lobule during later stages. Although these fMRI findings demonstrated opposite activation patterns of the cerebellum in the TD/DD contrast, which may be due to differences in instruction (explicit learning with feedback vs. implicit learning without feedback), they together suggest altered cerebellar function for action execution and maintenance in DD.

Although several studies have found sequence learning and reading to be correlated, these processes rely on at least partly nonoverlapping neural circuitry (though shared pathways are suggested). Thus the few studies of TD/DD contrasts in sequence learning suggest prominent roles for the cerebellum, anterior cingulate, and premotor areas. On the other hand, studies contrasting TD and DD in reading and phonological processing tasks consistently implicate the fusiform visual word form area (VWFA), posterior superior temporal gyrus (pSTG), the angular gyrus, the middle temporal gyrus, and the inferior frontal gyrus (IFG) during processing of linguistic stimuli (Paulesu, Danelli, & Berlingeri, 2014; Pugh et al., 2010; Richlan, Kronbichler, & Wimmer, 2011), whereas cerebellar involvement is only sometimes reported (Fulbright et al., 1999; Preston et al., 2010). Moreover, other studies have found that some of these reading critical regions (e.g., the VWFA and IFG) are involved in statistical learning and sequence detection when linguistic stimuli are used (Binder, Medler, Westbury, Liebenthal, & Buchanan, 2006; Fiez, Balota, Raichle, & Petersen, 1999; Frost et al., 2005; Graves, Desai, Humphries, Seidenberg, & Binder, 2010; Herbster, Mintun, Nebes, & Becker, 1997; Mechelli et al., 2005; Vinckier et al., 2007). There is evidence for both shared

Table 1. Results of the Standardized Tests and Demographic Information Regarding the Participants.

Variable	Range	M	SD
WJ reading score	73–123[a]	102.16	11.63
WASI Performance IQ	75–139	103.43	14.87
Age	15–25	20.48	2.50

Note. WJ = Woodcock–Johnson Tests of Achievement; WASI = Wechsler Abbreviated Scale of Intelligence.
[a]The percentile score of WJ reading score ranges from 4 to 93.

and unshared circuits for linguistic processes and nonlinguistic sequence learning, raising the question of whether a subset of shared neurocognitive mechanisms gives rise to the observed correlations between reading and sequence learning (Pugh et al., 2013).

Although previous neuroimaging work implicates partially distinct and partially overlapping neural circuits for linguistic processing and nonlinguistic sequence learning, these studies were not designed to directly compare these circuits in the same individual and to link commonalities to behavioral variation. The present study directly compared these processes at the neurobiological level to determine whether any neural substrates are common to both the SRT task and linguistic processing tasks. Also, we treated individual differences in reading ability using a dimensional approach and examined whether activity in any overlapping regions was associated with individual differences in reading skill. To do this, we collected neuroimaging data during SRT task performance and during reading from a large sample of participants with substantial variability in reading ability (see Table 1 for more details). We hypothesized that if processes that detect order or regular patterns are common to reading and sequence learning, the IFG and VWFA should be commonly involved in both tasks, and their activation should scale according to individual differences in reading skill. Alternatively, if skill automatization is shared across reading and sequence learning, the cerebellum should be commonly involved in the two tasks and predict individual differences in reading skill.

Method

Participants

Eighty-nine adolescents (34 female, 55 male) who were native English speakers and had normal/corrected-to-normal vision and hearing were recruited for the current study. All participants completed a battery of standardized assessments for reading ability and two fMRI tasks. Specifically, the participants' reading ability was measured using composite age-adjusted standard scores of Word Attack (producing correct sounds of letters or pronounceable pseudowords) and Letter-Word Identification (identifying printed letters or words) from the Woodcock–Johnson III Tests of Achievement (Woodcock, McGrew, & Mather, 2001). The participants' nonverbal cognitive abilities were measured using composite scores of Block Design (making specific patterns using small blocks), Matrix Reasoning (identifying a constituent based on analogies to existing patterns), and Picture Completion (making a completed picture by filling in a missing element) from the Wechsler Abbreviated Scale of Intelligence II (Wechsler & Hsiao-Pin, 1999). The participants' performance in the standardized tests as well as some demographic information is summarized in Table 1. All participants were consented in compliance with Yale University's Institutional Review Board for protection of human participants.

Stimuli and procedure

Serial reaction time task

During fMRI scanning, participants were asked to perform a stimulus-response task in which they were required to press a button corresponding to the location of a visual stimulus in a display. At the beginning of each trial, a gray box appeared in the center of the monitor against a black background.
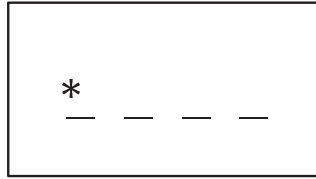
Figure 1. Illustration of the stimulus display in the serial reaction time task. *Note*. The four lines from left to right correspond to the four possible locations above which the asterisk could appear.

After 83 ms, an asterisk (1° × 1°) appeared for 750 ms in one of four locations within this gray box (Figure 1). Four straight lines beneath the asterisk indicated the four possible locations above which the asterisk could appear. Participants were asked to indicate the location (1, 2, 3, or 4) of the asterisk with their index finger, middle finger, ring finger, or pinky finger, respectively. In the ordered condition, 12 consecutive targets always appeared in a fixed first-order sequence: 121423413243. In the random condition, 12 consecutive targets appeared randomly. In total, participants completed 936 trials distributed evenly across three runs. Within each run, the two conditions alternated so that the random condition (24 trials) always preceded the ordered condition (96 trials).

Word reading task

During fMRI scanning, visual words were presented to participants without an explicit task to elicit processing more akin to natural reading. All words were one-syllable medium- to high-frequency (frequency range = 5,626 and 580,704) words according to the English Lexicon Project (Balota et al., 2007). On each trial, four words were presented rapidly and sequentially with a duration of 250 ms per word and with an ISI of 200 ms between words. Although not analyzed here, participants were also presented with stimuli in three other conditions: spoken words, vocoded speech (i.e.,
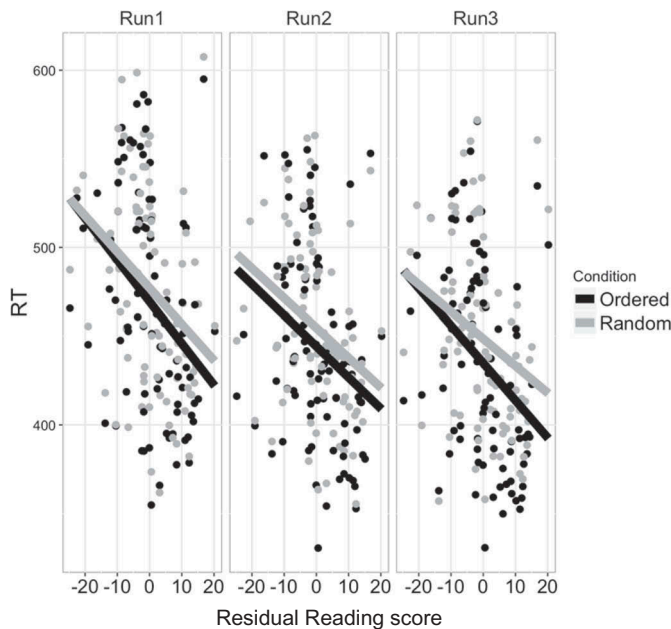

Figure 2. Reaction times (RTs) in the ordered condition and random condition across the three runs of the serial reaction time task as a function of residual reading score (regressing out the variance of Performance IQ). *Note*. The RT difference between the random and ordered condition in the third run significantly correlated with reading score.

unintelligible noise), and false font. Between trials, there was a jittered intertrial interval of 4–7 s. There were two runs with twelve trials in each of the four conditions per run, for a total of 24 trials per condition.

Acquisition of MRI data

SRT task

Anatomical and functional imaging data were acquired using a Siemens 3.0T Trio Tim whole-body MRI System (Siemens Medical Solutions, Erlangen, Germany) with a 12-channel head coil located at the Yale University School of Medicine. T2*-weighted functional images were acquired for 32 axial-oblique slices prescribed parallel to the intercommissural line using single-shot, gradient echo, echo planar imaging with the following parameters: flip angle (FA) = 80º; echo time = 30 ms; repetition time = 2000 ms; field-of-view = 220; 4 mm slice thickness, no gap; matrix size = 64 × 64; voxel size = 3.438 mm × 3.438 mm × 4 mm.There were 156 volumes in each run. A high-resolution structural scan was acquired in the same orientation as the functional slices using an MPRAGE sequence with the following parameters: FA = 7°; echo time = 3.66; repetition time = 2530 ms; field-of-view = 256; 1 mm slice thickness, no gap; matrix size = 256 × 256; voxel size 1 mm isotropic.

Word reading task

Acquisition parameters were identical to those for the SRT task, except that there were 151 volumes acquired per run.

Analysis of MRI data

SRT task

Data analysis was performed using Analysis of Functional NeuroImages (AFNI; Cox, 1996). Anatomic images were skull stripped and warped to Talairach space using a nonlinear transform. For functional runs, the first six volumes in each run were removed to allow for stabilization of the magnetic field. Functional images were corrected for slice acquisition time, corrected for motion, coregistered with anatomical images, warped to Talairach space using a nonlinear transform, and smoothed using an 8-mm FWHM Gaussian kernel. All trials were included regardless of whether responses were correct; however, any volumes with greater than 10% outlier voxels or more than 0.3-mm point-to-point movement were removed from further analyses (2.0%). Single-subject data were entered into a standard generalized linear model analysis with two variables of interest (run and condition) as well as nuisance regressors for the six motion parameters (three rotation and three translation parameters) and third-order polynomial drift terms. Six activation maps for each subject were used in group analyses: the ordered condition and the random condition for each of the three runs.

Word reading task

Preprocessing was identical to the SRT task, and 1.9% of volumes were removed due to outliers and/ or head motion. Single-subject data were entered into a standard generalized linear model analysis with regressors for the four stimulus conditions and nuisance regressors for the six motion parameters and second-order polynomial drift terms. Only the activation map of the visual word condition for each subject was used in group analyses (i.e., the spoken word and nonlinguistic conditions were not included for further analysis).

Conjunction analysis

An activation map for the SRT task was created by averaging across the six conditions (i.e., ordered and random trials in each of the three runs) for each subject and then a groupwise map was generated using the AFNI program *3dttest++* (whole-brain FDR corrected at $p < .05$). The random

condition, though it does not tap into sequential processing, requires learning to map between visual information and motor responses. The latter process is also involved in reading. Hence, both conditions in the SRT task were included to allow us to extract the common processes between the SRT and the word reading task. A groupwise activation map for the word reading task was created for the visual word condition in the same way as the SRT task. The conjunction map was created using a step function in the AFNI program *3dcalc* on the groupwise activation maps of the SRT task and the word reading task. Brain regions identified in the conjunction map were further constrained using the CA-N27-ML and Talairach Daemon atlases in AFNI.

Results

Behavioral results in the SRT task

Any trials with incorrect responses (11.05% of the data) were excluded from further analyses. Afterward, RTs that were either shorter than 250 ms or more than 3 *SD*s above or below each participant's respective condition-wise mean (1.24% of the data) were excluded from further analyses. The learning score of the sequence was defined by the RT difference (dRT) between the random and ordered condition, which was calculated separately for each of the three runs (Table 2). Woodcock–Johnson III Tests of Achievement Basic Reading scores were regressed on Wechsler Abbreviated Scale of Intelligence II Performance IQ so that any observed effects could be specifically attributed to individual differences in reading skill. Learning scores were entered into a linear mixed effects model based on maximum likelihood methods using the *lme4* package in R (Barr et al., 2013). The model included run (categorical within-participants factor), reading score (continuous between-participants factor), and the interaction between run and reading score as fixed effects, and random by-participant intercepts as well as random by-subject slopes for all of the fixed effects (i.e., the maximal random effect structure; see Barr, 2013). Results showed that the effect of run and the effect of reading score were not significant, $\chi^2(1) = 5.73$, $p = .057$; $\chi^2(1) = 3.17$, $p = .075$. However, the interaction between run and reading score was significant, $\chi^2(2) = 7.8$, $p = .02$ (Figure 2). Post oc comparisons showed that dRTs significantly correlated with reading score in the third run ($r = .33$, $p = .001$) but not in the other runs ($ps > .1$). No effects were detected for mean error rates ($ps > .5$).

Neuroimaging results

The conjunction analysis revealed brain regions that were commonly activated in the SRT task and the word reading task including the cerebellum, fusiform gyrus, the anterior and posterior STG (aSTG and pSTG), inferior parietal lobule, the insula, the IFG *pars triangularis* (IFGpTr) and the IFG *pars opercularis* (IFGpOp), the putamen, the precentral gyrus, and the SMA, in both hemispheres (Figure 3).

For the brain regions that were commonly activated across the SRT and word reading tasks, we tested whether the extent of engagement of these regions for each task was related to reading ability. For the SRT task, similar to the behavioral data analysis, we calculated the difference in beta values between the ordered and random conditions in the 22 common brain regions identified by the conjunction analysis, and used these values as the dependent variable in a linear mixed effects model with Run and Reading score and their interaction as fixed effects and participants as a random effect. A significant

Table 2. Grand Averaged Reaction Times Across Participants in the Ordered Condition and Random Condition in the Three Runs of the Serial Reaction Time Task.

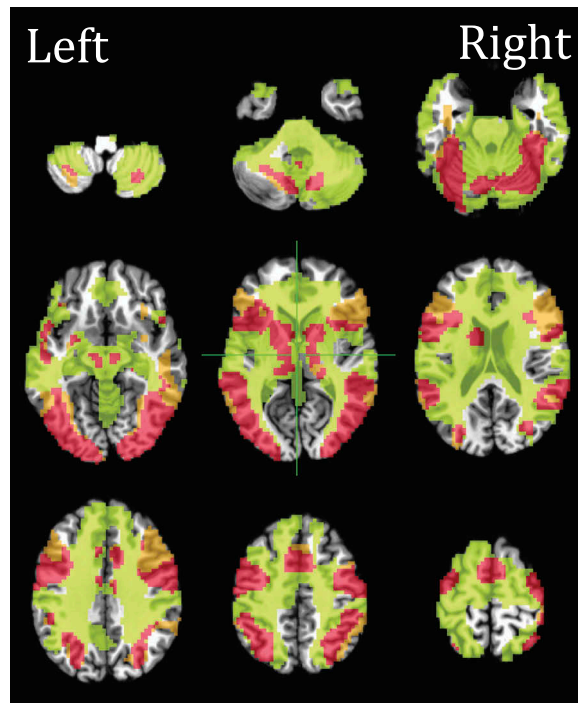| Condition	Run		
	1	2	3
Ordered	469.46	444.24	434.89
Random	477.11	454.65	448.6

Figure 3. Green areas indicate brain regions that were significantly active in the serial reaction time task at the group level. *Note.* Orange areas indicate brain regions that were significantly active in the word reading task at the group level. Red areas indicate brain regions that were commonly activated in both tasks.

interaction between reading score and run was observed in the right insula, $\chi^2(2) = 8.28$, $p = .016$, and the right IFGpTr, $\chi^2(2) = 6.06$, $p = .048$. A follow-up correlation analysis showed that in the right insula, the difference in beta values between the ordered and random conditions in the second run significantly correlated with reading score ($r = .26$), $t(87) = 2.48$, $p = .015$. In the right IFGpTr, there was a marginal correlation between reading score and the difference in beta values between the ordered and random conditions in the second run ($r = .21$), $t(87) = 1.97$, $p = .052$ (Figure 4a).

For the word reading task, we performed a simple correlation analysis between reading scores and beta values in the visual word condition. Reading scores were significantly correlated with beta values in the left fusiform ($r = .29$), $t(87) = 2.81$, $p = .006$; the right insula ($r = .29$), $t(87) = 2.87$, $p = .005$; the left pSTG ($r = .26$), $t(87) = 2.47$, $p = .015$; and the right IFGpTr ($r = .35$), $t(87) = 3.51$, $p = .001$ (Figure 4b).

Discussion

The current study had two aims. First, we identified shared brain circuits for the SRT task and reading; second, we examined whether brain regions that were commonly engaged during sequence learning and word reading were also related to individual differences in reading ability (given the observed correlation between sequence learning and reading). Behaviorally, the correlation between learning in the SRT task and reading skill was replicated in the current study: more skilled readers showed a greater difference in their reaction times between the ordered and random conditions compared to less skilled readers.

At the neural level, we identified a network of regions common to both the SRT and word reading tasks. Specifically, the fusiform gyrus, the precentral area and the SMA might reflect visual (symbols, letters) and motoric (button press, covert speech) processing common to the SRT task and the word
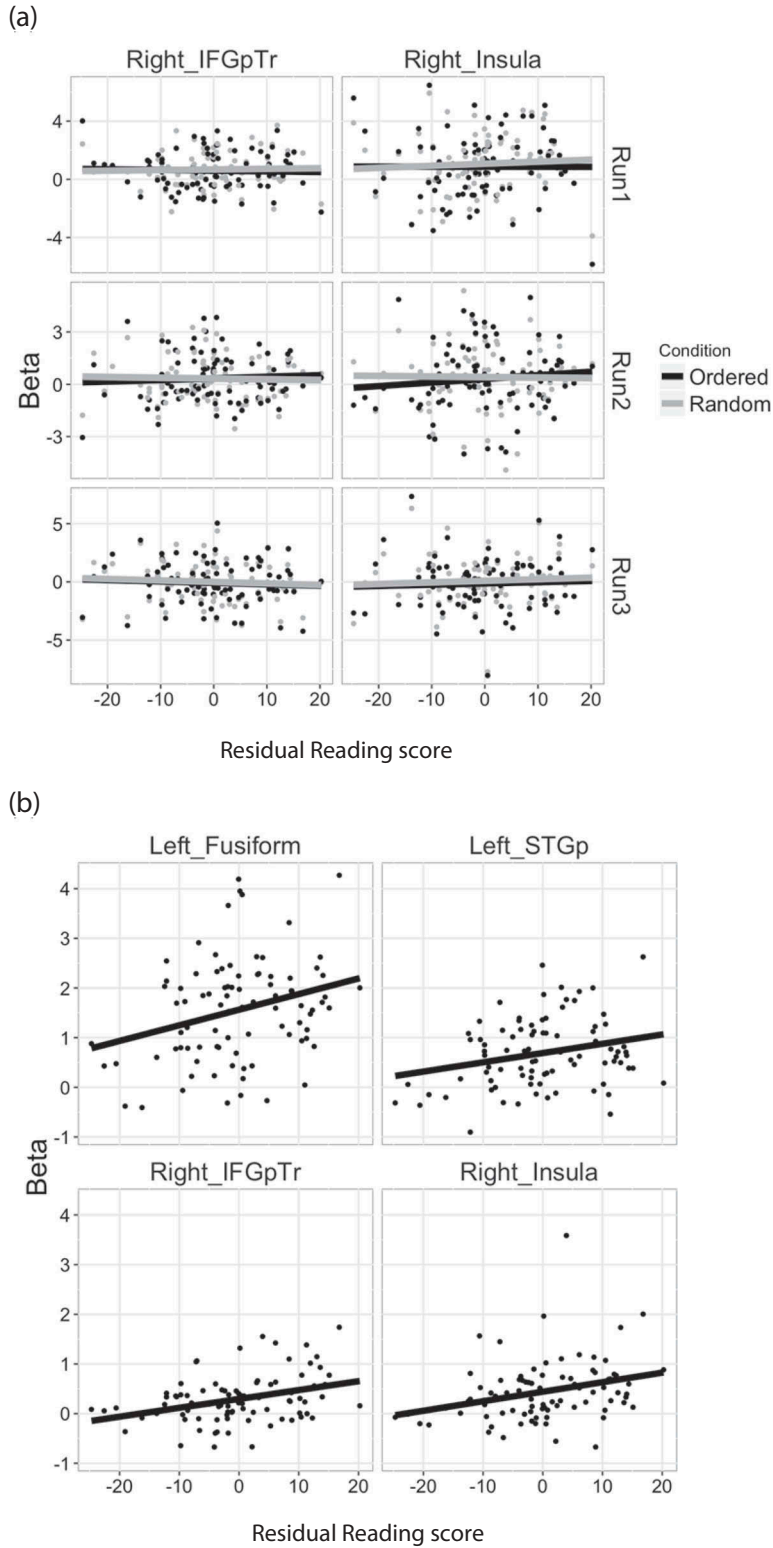
Figure 4. Brain regions that showed sensitivity to individual differences in reading skill in the serial reaction time (SRT) and word reading tasks. *Note*. Beta weights for (a) the SRT task and (b) the word reading task are plotted as a function of residual reading score. IFGpTR = inferior frontal gyrus pars triangularis; STGp = posterior superior temporal gyrus.

reading task. The aSTG and pSTG likely reflect the need for cross-modal association in the SRT task, and similarly, print–speech conversion during the word reading task (Friederici, 2011; Price, 2012). The IFGpTr, IFGpOp, and insula are involved in sequence coding and sequential binding, which are required for both tasks (Friederici, 2011; Witt, Laird, & Meyerand, 2008). Finally, the putamen and cerebellum have been associated with consolidation and automatic performance of learned skills, which are known to be important to both reading and sequence learning (Doyon, 2008; Kotz, Schwartze, & Schmidt-Kassow, 2009; Nicolson & Fawcett, 2007; Ullman, 2004). The shared neural network suggests that bimodal mapping, sequential binding, and storage were commonly involved in sequence learning and reading.

The brain–behavior correlations observed for the SRT task show that more skilled readers exhibit greater activation in the right insula and the right IFGpTr for ordered relative to random trials. Reading ability was also positively associated with activation of the left fusiform area, the left pSTG, the right IFGpTr, and the right insula during the word reading task, findings that are consistent with previous neuroimaging studies of individual differences in reading (Paulesu et al., 2014; Pugh et al., 2013; Richlan et al., 2011). The current results indicate that shared variance between sequence learning and reading skill may arise from common engagement of the right insula and the right IFGpTr for these tasks.

In the nonlinguistic domain, the right insula and the right IFG are often associated with visuomotor synchrony and sequential processing (Cross, Stadler, Parkinson, Schütz-Bosbach, & Prinz, 2013; Rieckmann, Fischer, & Bäckman, 2010; Witt et al., 2008). In the linguistic domain, the insula is involved in phonological processing (McDermott, Petersen, Watson, & Ojemann, 2003; Mechelli et al., 2007) and is sensitive to the complexity of speech sequences (Bohland & Guenther, 2006); furthermore, it is has been shown to be more active in successful learners of speech sounds than it is in less successful learners (Segawa, Tourville, Beal, & Guenther, 2015; Wong, Perrachione, & Parrish, 2007). The right IFGpTr associates number word combination (Hung et al., 2015). With respect to studies of good and poor readers, DD adults failed to activate the left insula in a rhyming judgment task compared to TD adults (Paulesu et al., 1996). Nicolson et al. (1999) observed that those with DD overactivated the left insula in the contrast of newly learned versus well-practiced sequences. The group difference in activation patterns and lateralization in Nicolson et al.'s study were different from our findings, which may be ascribed to the differences between explicit and implicit learning. In addition, Nicolson et al.'s results were based on the contrast between TDs and DDs, whereas the current study focused on the effect of individual differences in decoding skills on sequential learning. The current findings suggest that sequential processing is commonly involved and predicts individual differences in motor learning in the SRT task and word retrieval in the word reading task. In the word reading task, we speculate that the skilled readers engaged these areas more than less skilled readers because they were more likely to retrieve the serial phonological patterns and covertly or overtly read the visual words.

There have been claims, albeit somewhat controversial, that dyslexia is caused by impaired phonological processing (Castles & Coltheart, 2004; Melby-Lervag et al., 2012; Morais & Kolinsky, 1994). However, because phonological processing is supported by phonemic sequencing and acquisition of grapheme-to-phoneme conversion rules, deficits in learning regularities, serial-order, and rules may also contribute to reading problems (Morrison & Manis, 1982). Consistent with this hypothesis, the current findings and previous research from our lab has demonstrated that sequential processing of motoric action (the current article) and temporal order (Pugh et al., 2013) both covary with reading ability in adults and beginning readers. However, brain regions mediating the covariance between the two abilities differed across the two studies: here, effects are observed in the insula and IFGpTr, whereas for temporal order (Pugh et al., 2013), associations were observed in the STG and the thalamus. Future studies should consider whether such differences can be attributed to either age differences (15–25 vs. 5–9) or task differences.

It is worth noting that the brain–behavior correlation for the SRT task was observed in the second run, whereas the correlation between decoding ability and learning scores for the SRT was observed

only in the third run. Whereas we cannot be sure it reflects a meaningful pattern, an interesting speculation is that this mismatch could be attributed to brain signals and behavioral performance reflecting different stages of the cognitive processing under investigation. Brain signals during the SRT task reflect visual-motor association and sequential encoding (Eversheim & Bock, 2001; Hikosaka et al., 1999; Müller, Kleinhans, Pierce, Kemmotsu, & Courchesne, 2002), whereas the external behavior (i.e., the learning outcome based on the reaction time measure) is presumably the consequence of all preceding neural activity. As a second note, some limitations of the current study should be considered. First, the SRT task and the word reading task may tap into other common cognitive process, such as attention or inhibition (Aron et al., 2014; Corbetta & Shulman, 2002), other than the sequential processing on which we focused. The SRT task demands overt motor responses and taps into sequential learning. The word reading task requires covert naming and does not tap into learning processes. Besides, sequential decoding is not necessarily involved in reading, especially for the familiar words like those used in the current study. Future studies should elicit online sequential learning for both linguistic and nonlinguistic motor stimuli to verify the locus of the correlation between motor sequence learning and reading ability (e.g., Francois & Schön, 2011). Second, the results of region of interest analyses were not corrected for multiple comparisons in the current exploratory study. Hence, the neuroimaging results should be interpreted with caution due to the risk of type I error as well as the need for future replications.

To our knowledge, the present study provides the first evidence for a common neural network for nonlinguistic sequence learning and word reading in the same individuals, as well as associated relations to sequence learning and reading. A neural network of visual motor association (the precentral area and the SMA), sequential, orthographic and linguistic processing (STG, insula, the fusiform gyrus, and IFG), learning, and memory (the putamen and the cerebellum) was commonly recruited during both nonlinguistic sequence learning and reading. Activation of the right insula and the right IFGpTr was associated with individual differences in reading skill in both tasks, suggesting that sequential processing is commonly involved across motor sequence learning and retrieving graphemic/phonemic sequences in reading.

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