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Neural dysfunction in ADHD with Reading Disability during a word rhyming Continuous Performance Task

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ABSTRACT

Background: Attention-Deficit/Hyperactivity Disorder (ADHD) is a heterogeneous, neurodevelopmental disorder which co-occurs often with Reading Disability (RD). ADHD with and without RD consistently have higher inattentive ratings compared with typically developing controls, with co-occurring ADHD and RD also demonstrating impaired phonological processing. Accordingly, inattention has been associated with greater phonological impairment, though the neural correlates of the association are poorly understood from a functional neuroimaging perspective. It was postulated that only the co-occurring subgroup would demonstrate hypoactivation of posterior, left hemispheric, reading-related areas and, to a lesser extent, alterations in right hemispheric, attention areas compared with controls.

Methods: A novel word rhyming Continuous Performance Task assesses functional activation differences in phonology- and attention-related areas between three groups: ten boys with ADHD and RD, fourteen boys with ADHD without RD, and fourteen typically developing controls. Subjects respond to words that rhyme with a target word as mono- and disyllabic, English words are visually presented over 90 s blocks.

Results: Behavioral performance was not different between groups. Some hypoactivation of left hemispheric, reading-related areas was apparent in ADHD and RD, but not ADHD without RD, compared with controls. Right hemispheric, attention areas showed alterations in both ADHD subgroups relative to controls; however, the differences for each subgroup were dissimilar.

Conclusions: The dorsal decoding subnetwork may not be grossly compromised in ADHD with Reading Disability. The role of cognitive impairments, including the level of inattention, on phonology requires clarification from a neuroimaging perspective.

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1. Introduction

Attention-Deficit/Hyperactivity Disorder (ADHD) and Reading Disability (RD) are common childhood, neuropsychiatric disorders, each occurring in about 5–10% of the population (American Psychiatric Association, 2000; Polanczyk, Willcutt, Salum, Kieling, & Rohde, 2014). Approximately 45% of those originally diagnosed with ADHD qualify for a co-occurring RD diagnosis (ADHD/+RD; DuPaul, Gormley, & Laracy, 2012; Yoshimasu et al., 2010). Poor attention and impulse control typifies ADHD (Barkley, 1997; Willcutt, Pennington, Olson, Chhabildas, & Hulslander, 2005); whereas, individuals with ADHD/+RD also show impaired phonological processing (Pugh et al., 2001; Shaywitz & Shaywitz, 2008; Snowling, 2001). There is evidence of increased academic problems from an early age in ADHD/+RD that result in increased societal and economic burden (Fried et al., 2013). Interestingly, little is understood about cognitive

impairments in ADHD children with a co-occurring RD diagnosis from the perspective of neural dysfunctions.

RD is characterized by impairments in a specific phonological process called decoding, which refers to the mental process of grapheme-to-phoneme conversion (for review, Carreiras, Armstrong, Perea, & Frost, 2014). The primary neural subnetwork for decoding includes the left hemispheric, posterior superior temporal gyrus (pSTG; BA 22), inferior parietal lobe (iPL; BA 39/40), and inferior frontal gyrus (IFG; BA 44/45; for review, Jobard, Crivello, & Tzourio-Mazoyer, 2003) and will be referred to as the dorsal decoding subnetwork. In accordance with impaired decoding skills, hypoactivations in the pSTG (BA 22) and iPL (BA 39/40) are frequently reported in RD neuroimaging studies (Hoeft et al., 2007; Temple et al., 2001). Though ADHD/+RD show considerable phonological impairments relative to ADHD/−RD or typically developing controls (TDC) on standardized tests (e.g., Willcutt et al., 2010), it is currently unknown whether the phonological impairments in ADHD/+RD are related to similar, neural dysfunctions as those reported for RD alone. Thus, the primary goal of this study was to investigate potential activation differences in the dorsal decoding subnetwork between ADHD/+RD and ADHD/−RD and typically developing controls (TDC) during a novel, phonologically-based task.

Current neuropsychological evidence supports the multiple deficit hypothesis of ADHD/+RD (McGrath et al., 2011; Willcutt et al., 2010), in which impairments related to the individual disorders co-occur in the same person (Sexton, Gelhorn, Bell, & Classi, 2012) and may also be greater in ADHD/+RD (de Jong et al., 2009; Willcutt et al., 2005). Evidence suggests greater attention impairments predicts poorer phonological ability in ADHD/+RD (c.f., de Jong et al., 2009) and RD (Rogers, Hwang, Toplak, Weiss, & Tannock, 2011; Willcutt & Pennington, 2000). Additionally, those with worse inattentive symptomatology or the inattentive subtype have a greater likelihood of being diagnosed with ADHD/+RD (Levy, Young, Bennett, Martin, & Hay, 2013; Mayes & Calhoun, 2007). Some neuroimaging studies have implicated right hemispheric frontostriatal and frontoparietal attention networks in ADHD (Banich et al., 2009; Durston et al., 2003; Epstein et al., 2007). However, in our previous study (Mohl et al., 2013), we reported no activation differences along attention-related areas in ADHD/+RD compared to TDC in response to the fMRI task of sustained attention with digits as stimuli (i.e., a non-linguistic Continuous Performance Task). Therefore, a second objective of the current study is to identify to what extent ADHD/+RD and ADHD/−RD share attention network alterations during the novel, phonologically-based task that is attentionally demanding.

The novel paradigm, called the word rhyming Continuous Performance Task (wr-CPT), introduced in this study combines the phonological skills necessary to rhyme a target word and simple words with orthographically similar (e.g., "day-play") and dissimilar ending rimes (e.g., "too-true"; Booth, Mehdiratta, Burman, & Bitan, 2008) with a sustained attention load similar to a conventional CPT (i.e., with a much longer block length than typical rhyming tasks; Langner & Eickhoff, 2013). We postulated that those with ADHD/+RD, but not ADHD/−RD, would show extensive hypoactivation in the left pSTG (BA 22) and left iPL (BA 40) compared with TDC. We also posited that ADHD/+RD would evidence some alterations in right hemispheric attention areas relative to TDC. This is an important step in assessing the neural correlates of poor phonological processing and attention in ADHD/+RD and would be concordant with the multiple deficit hypothesis.

2. Methods

2.1. Subjects

Ten boys meeting criteria for DSM-IV co-occurring ADHD and RD (specified below), fourteen ADHD/-RD boys, and fourteen TDC boys from the Detroit (Michigan) and Windsor (Ontario) surrounding area with English as their first and primary language participated. Following a complete description of the study, assent from the child and written informed consent was obtained from the parents or guardians, as approved by the Wayne State University Institutional Review Board. Exclusion criteria for all subjects included history of head injury resulting in loss of consciousness, contraindications for MRI, Full Scale IQ (FSIQ) less than 80, a first-degree relative with a past or present diagnosis of a major DSM-IV disorder including schizophrenia, pervasive developmental disorders, tic disorders, eating disorders or mood disorders. Co-morbid oppositional defiant disorder (ODD), conduct disorder (CD), or obsessive–compulsive disorder (OCD) were allowed for ADHD subjects.

Clinical determination of ADHD status was based on a semi-structured interview given by clinical neuropsychologists using the Kiddie Schedule of Affective Disorders - Present and Lifetime (Kaufman et al., 1997). Each subject's parent/guardian and teacher completed the Disruptive Behavior Disorders Scale (DBD) and Iowa Conners Hyperactivity/Impulsivity Scale questionnaires to augment the diagnostic interview. The Wechsler Abbreviated Scale of Intelligence (WASI; PsychCorp, Pearson Education; San Antonio, TX) was administered to estimate FSIQ. Reading skills were assessed using the Wechsler Individual Achievement Test-III (WIAT-III) battery subtests of Word Reading, Pseudoword Decoding, and Spelling (PsychCorp, Pearson Education; San Antonio, TX). RD was defined as a significant discrepancy ($p = .01$) between the predicted and achieved scores, per the WIAT-III Aptitude Achievement Discrepancy tables, on at least two of the three subtests. Controls meeting RD criteria were excluded from the current study.

The ADHD/−RD group contained ten combined subtype; four inattentive. Two combined subtype had co-morbid CD. One combined subtype had a secondary diagnosis of OCD. Twelve of the fourteen ADHD/−RD subjects were currently on a stable dose of psychostimulants (maintained for at the current dose for six months). Six of the ADHD/+RD group were combined subtype, four were predominately inattentive. Two combined subtype and one inattentive subtype had co-morbid CD. Five of the ten ADHD/+RD subjects were receiving stable doses of psychostimulants. All subjects were free of psychostimulant medication for at least a 24-h period prior to the reading assessment and MR examination. Two controls, one ADHD/−RD, and three ADHD/+RD subjects were left-handed; however, left-hemispheric language dominance was confirmed for all subjects through inspection of first-level fMRI analyses.

2.2. Demographic and behavioral analysis

Age, FSIQ, and WIAT-III reading scores were compared using an ANOVA with diagnosis as the main effect. WIAT-III scores were reported with a Bonferroni correction for three tests ($p < .017$). wr-CPT performance (d', Mean Hit RT, and Variance of Hit RT) was assessed by ANCOVA with age as the covariate and are reported without correction to represent any effect of performance. Tukey's HSD *post hoc* analyses were performed for main effects reaching $p < .05$. One subject with ADHD/−RD did not have recorded responses, due to technical issues. All statistics were modeled using JMP version 11 (SAS; Cary, NC).

2.3. Imaging protocol

The structural and functional imaging data were collected on a 3 T Siemens MAGNETOM Verio system (Siemens, Erlangen, Germany) using a 12-channel receive-only volume head coil. Anatomical T_1-weighted images using the Magnetization Prepared

Rapid Gradient Echo (MPRAGE) sequence were collected with the following parameters: TR = 2.2 s, TE = 3 ms, TI = 799 ms, flip-angle = 13°, FOV = 256 × 256 mm^2, 256 axial slices, slice thickness = 1 mm, matrix = 176 × 256, and scan-time = 6 min:27 s. Blood oxygen level-dependent (BOLD) fMRI images were collected using a gradient echo planar imaging sequence with the following parameters: TR = 2.6 s, TE = 29 ms, FOV = 256 × 256 mm^2, matrix = 128 × 128, 36 axial slices, and pixel dimension = 2x2x3mm^3. Presentation® software (15.0, http://www.neurobs.com) was used to present stimuli in the scanner during the fMRI paradigm and log responses with reaction times. Tokens projected onto a screen were viewed through a mirror attached above the head coil. Responses were recorded with an MRI-compatible, two-button response box in the right hand.

2.4. Word rhyming Continuous Performance Task (wr-CPT)

The novel wr-CPT consisted of two 90 s. blocks of rhyming words and three, 30 s. passive fixation blocks (i.e., "###"; Fig. 1). Total scan time for the wr-CPT was 6 min:42 s, as a 90 s block of letter rhyming was excluded for the present study. Participants pressed a button each time a token (duration = 1 s; interstimulus interval = 1.5 s) rhymed with the target word, but did not respond to non-rhymes. Rhyming tokens were presented once for every four non-rhyming tokens and were not restricted to similar orthography (e.g., "flew" and "too"). All tokens were mono- or di-syllabic, familiar words (mean log HAL frequency = 10.9; all stimuli log HAL frequency > 7), three to five letters in length from the English Lexicon Project online database (Balota et al., 2007). All participants received verbal instructions and completed 1 min:30 s mock task training outside of the scanner; target words and tokens were different from those presented during the fMRI scan. Sensitivity (d′), mean Hit Reaction Time (RT), and variance of Hit RT were calculated offline and reported in Table 2. Sensitivity reflects an individual's accuracy-speed tradeoff (e.g., consistently responding to all stimuli results in a low d′ score). Hit RT refers to the time between presentation onset and response to a rhyming token.

2.5. Image processing and analyses

Each subject's structural T_1-weighted image underwent spatial adaptive non-local means Gaussian filtering (Manjón, Coupé, Martí-Bonmatí, Collins, & Robles, 2010). The resulting, anatomical images were corrected for field inhomogeneities, averaged, and segmented with tissue probability maps. Preprocessing of the fMRI data included discarding the first four volumes, realigning to the first image, unwarping (Andersson, Hutton, Ashburner, Turner, & Friston, 2001), co-registering to the subject's anatomical average, normalizing to MNI space using forward deformations,

and smoothing (6 mm FWHM). The Artifact Detection Toolkit (ART, http://www.nitrc.org/projects/artifact_detect/) was used to mark volumes exceeding 2.0 mm of translation or 0.2° of rotation or signal change greater than 3.0 standard deviations and model them as covariates as no interest. All scans had more than 75% of the volumes complying with these motion parameters (c.f., Kovelman et al., 2012). To model the neural response, references waveforms were created by convolving the canonical hemodynamic response function with a boxcar function. An autoregressive model (AR1) to account for serial correlations and detrending with a high pass filter (1/300 s) to remove signal due to scanner drift were used in the first-level analysis comparing activation during word rhyming blocks minus fixation blocks.

To minimize potential, confounding performance- or age-related effects in the interpretation of the fMRI results, d′ and age were entered as covariates in the second-level analyses. The primary regions of interest, including the inferior and middle frontal gyri, dorsal anterior cingulate, basal ganglia, thalamus, parietal lobe, middle and superior temporal lobe, and fusiform gyrus, were assessed using masks generated with Wake Forest PickAtlas (Maldjian, Laurienti, Kraft, & Burdette, 2003). Significant clusters were reported after multiple comparison correction to *alpha* < .05, based on 10^4 iterations of a Monte Carlo simulation within 3dClustSim (AFNI; Ward, 2000). Given the limited sample size, a value of *p* < .02 at the peak-level was chosen to generate the values necessary for cluster-level correction. For ADHD subjects, parameter estimates from within 5 mm of the right SMG peak were correlated with WIAT-III Pseudoword Decoding and age as a covariate.

3. Results

3.1. Demographics and symptoms

The three groups of boys, ADHD/+RD, ADHD/−RD, and TDC, did not differ in age ($F_{2,37}$ = .43; *p* = .65) or FSIQ ($F_{2,37}$ = .32; *p* = .73). Symptomatology did not differ between ADHD subgroups for Conners' Cognitive Problems/Inattention ($F_{1,23}$ = .49, *p* = .49) or Hyperactivity ($F_{1,23}$ = .70, *p* = .41) subscales. ADHD/+RD was significantly impaired on WIAT-III Word Reading, Pseudoword Decoding, and Spelling scores relative to either ADHD/-RD or TDC, even after implementing a Bonferroni correction (all *post hoc p*'s < .002). Sentence Span did not differ between groups ($F_{2,37}$ = 1.1; *p* = .34). Demographic and reading assessment results are available in Table 1.

3.2. wr-CPT behavioral performance

All three groups demonstrated compliance during the wr-CPT (Table 2). After covarying for age, there were no significant group
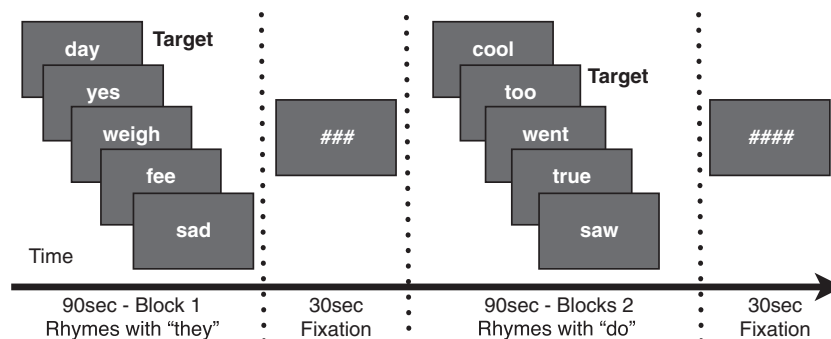

Fig. 1. A diagram of the visual, word rhyming-CPT (see Section 2). Subjects respond to visually presented words that rhyme with a target word. The first-level, directional contrast is rhyming > fixation.

Table 1
Demographics.

	TDC	ADHD/−RD	ADHD/+RD	p-Value	Tukey's HSD post hoc
n	14	14	10		
Age (years)	11.7 (1.6)	12.4 (2.0)	12.2 (1.7)	0.65	
FSIQ	112 (14)	107 (16)	110 (14)	0.73	
Conners' cognitive problems/inattention	–	57 (12)	60 (10)	0.49	
Conners' hyperactivity	–	65 (18)	71 (14)	0.41	
Word reading (WIAT-III)	103 (8)	105 (10)	90 (16)	0.01	a, $p = .044$; b, $p = .014$
Pseudoword decoding (WIAT-III)	106 (8)	109 (9)	87 (20)	<.001	a, $p = .002$; b, $p < .001$
Spelling (WIAT-III)	106 (11)	106 (12)	85 (15)	<.001	a, $p < .001$; b, $p < .001$
Sentence span – completed items	16.9 (1.9)	18.0 (2.9)	16.3 (3.1)	0.34	

Bracketed numbers are standard deviations. a = ADHD/+RD < TDC; b = ADHD/+RD < ADHD/−RD.

differences in the variance of Hit RT ($F_{3,36} = .17$, $p = .84$), percent correct ($F_{3,36} = 3.08$, $p = .059$), or d' scores ($F_{3,36} = 2.60$, $p = .089$). However, mean Hit RT differed significantly between groups ($F_{3,36} = 3.38$, $p = .046$) with ADHD/+RD responding slower than ADHD/−RD (Tukey's HSD, $p = .037$), but not TDC (Tukey's HSD, $p = .25$).

3.3. fMRI – activation differences in response to the wr-CPT

Following the dual route framework, hypoactivation in ADHD/+RD compared with TDC was evident in both reading subnetworks (Table 3), including the left pSTG (BA 22) and left MTG (BA 21). Compared with TDC, ADHD/−RD also demonstrated differences in reading-related areas, including hyperactivation along the left, posterior dPFC (BA 9) and hypoactivation in the left STG (BA 21) and left dPFC (BA 9). Details are provided in Table 3.

Group comparisons within right hemispheric regions associated with attention (Petersen & Posner, 2012) showed increases in the ADHD subgroups, generally. Hyperactivation of the right IFG (BA

44), right sPL (BA 7), and right pSTG (BA 22) were observed in ADHD/−RD compared with TDC (Fig. 4). Activation in the right supramarginal gyrus (SMG; BA 40) was also increased in both ADHD subgroups relative to TDC (Figs. 2a and 4a). Upon further inspection, the extracted parameter estimates for the right SMG (BA 40) showed a relatively higher mean functional activation in ADHD/+RD compared with ADHD/−RD or TDC (Fig. 3a). By contrast, the only hypoactivation in the right hemisphere for either ADHD subgroup compared with TDC was in the right angular gyrus (AG; BA 40), where ADHD/+RD showed significantly less functional activation relative to TDC (Figs. 2a and 3b).

Since differences in the right parietal lobe have also been reported in relation to reading tasks (McDermott, Petersen, Watson, & Ojemann, 2003; Pammer, Hansen, Holliday, & Cornelissen, 2006), we also investigated the potential association between activation and WIAT-III Pseudoword Decoding. Pseudoword Decoding scores did not correlate with extracted parameter estimates from the right AG (BA 39; $r^2 = .006$, $p = .73$), but did reveal a significant, inverse relationship with the right SMG (BA 40; $r^2 = .28$, $p = .0078$, Fig. 2b).

Table 2
wr-CPT behavioral performance.

	TDC	ADHD/−RD	ADHD/+RD	p-value	Tukey's HSD post hoc
Mean hit RT (ms)	683 (83)	636 (90)	743 (124)	0.046	a, $p = .037$
Variance of hit RT	25,784	24,696	27,250	0.84	
Percent correct	82 (5)	81 (5)	69 (5)	0.059	
Sensitivity (d')	2.7 (1.0)	2.6 (0.9)	2.0 (1.1)	0.089	

Bracketed numbers are standard deviations. a = ADHD/+RD > ADHD/−RD.

Table 3
Functional activation differences in response to word rhyming CPT.

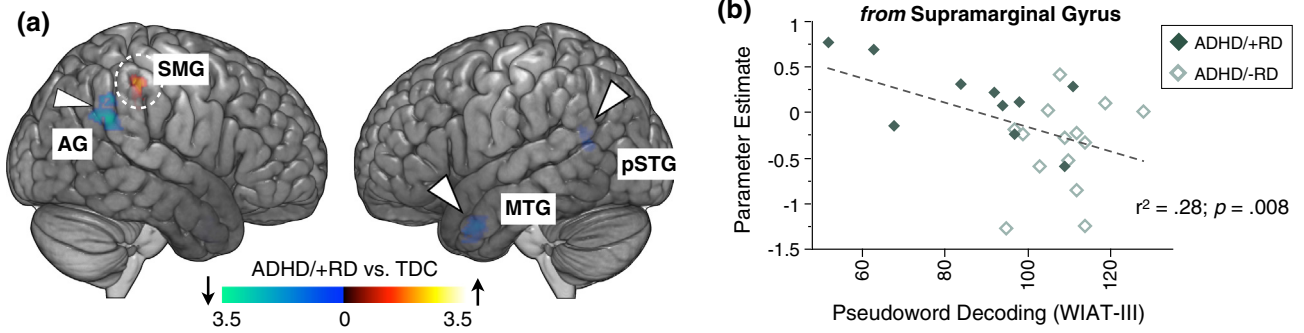| Hemisphere	Region	Brodmann Area	K_E	Peak t-score	MNI coordinates x	y	z
ADHD/+RD > TDC							
Right	SMG	BA 40	290	3.83	56	−31	46
ADHD/+RD < TDC							
Left	MTG	BA 21	225	3.01	−50	3	−32
	STG	BA 22	146	3.46	−42	−54	21
Right	AG	BA 40	350	4.14	56	−49	30
ADHD/−RD > TDC							
Left	IFG	BA 9	185	3.68	−46	6	28
Right	IFG	BA 44	647	3.94	51	18	19
	SMG	BA 40	168	3.32	39	−34	37
	pSTG	BA 22	145	3.94	64	−30	3
	sPL	BA 7	319	3.23	28	−69	52
ADHD/−RD < TDC							
Left	dPFC	BA 9	174	3.27	−42	29	42
	STG	BA 21	217	3.21	−38	−10	−8

Fig. 2. (a) In response to the wr-CPT, hypoactivation in left hemispheric, reading areas and the right AG along with hyperactivation of the right SMG were observed in ADHD/+RD compared with TDC. (b) Extracted parameter estimates show a significant, inverse relationship between activation of the right SMG and phonological ability.
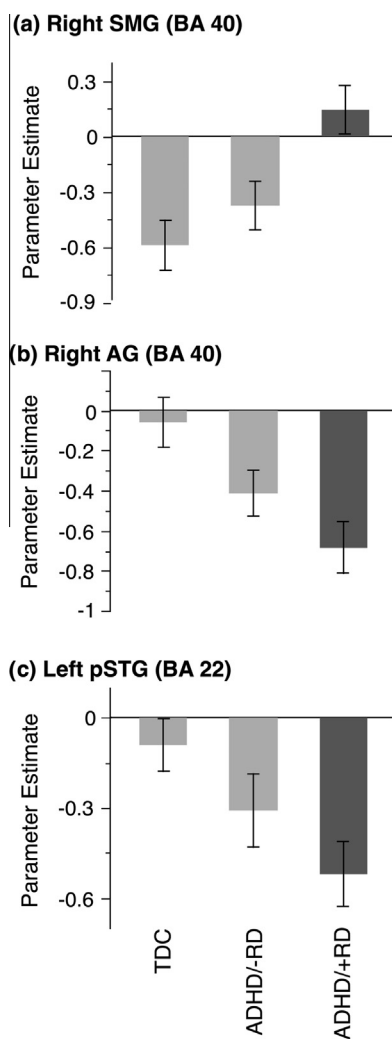

Fig. 3. (a) Activation in the right SMG is relatively greater in ADHD/+RD compared with ADHD/−RD. ADHD/−RD evidenced intermediate activation within the right AG (b) and left pSTG (c) relative to TDC and ADHD/+RD. Error bars represent SEM.

Fig. 4. (a) In response to the wr-CPT, ADHD/−RD showed hyperactivation of attention-related areas compared with TDC. (b) and (c) Extracted parameter estimates demonstrate relative differences between the ADHD subgroups in both the right sPL (BA 7; b) and right IFG (BA 44; c). Error bars represent SEM.

4. Discussion

In this study, we examined neural activation differences in decoding and attention areas for boys with ADHD/+RD compared with ADHD/−RD or typically developing controls (TDC) during a novel word rhyming task (wr-CPT). The wr-CPT leverages phonological 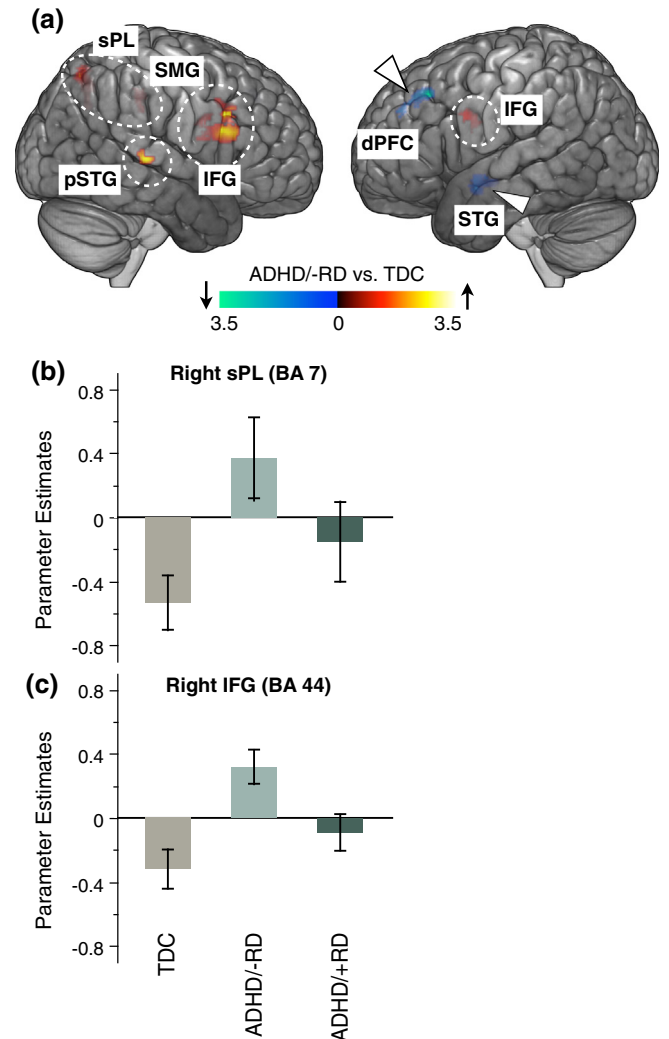demands of rhyming and attentional demand of a typical CPT (Rosvold, Mirsky, Sarason, Bransome, & Beck, 1956), as these two cognitive domains are often reported to be impaired in ADHD/+RD (Willcutt et al., 2010). Comparisons between ADHD/+RD, ADHD/−RD, and TDC, revealed significantly poorer WIAT-III reading scores for ADHD/+RD, but no differences in ADHD symptoms between the patient groups (Table 1).

Behavioral performance during the wr-CPT was also similar between groups except for a slower, average response in ADHD/+RD (Table 2). ADHD/+RD evidenced hypoactivations in left hemispheric areas associated with reading compared with TDC (Fig. 2a), though one may argue the extent is not striking considering the degree of phonologic impairment in ADHD/+RD. Both ADHD subgroups showed alterations in the right parietal lobe, but ADHD/−RD showed an additional, distinctive pattern of greater frontal and superior parietal activation versus TDC (Fig. 4). The data suggest ADHD/−RD exercised greater cognitive control or re-engagement (Weissman, Roberts, Visscher, & Woldorff, 2006) that was not observed in ADHD/+RD. Thus, continued investigation is needed to further address these distinctive patterns in the attention network between subgroups and its impact on reading ability.

As noted, behavioral performance during the wr-CPT reflected the abilities of each group (Table 2). ADHD/+RD was slower (Mean Hit RT; $p = .046$) and tended to be less accurate (Percent Correct; $p = .059$) relative to ADHD/−RD or TDC. The poorer performance is in line with decoding (Table 1) and processing speed impairments reported for ADHD/+RD (Christopher et al., 2012; McGrath et al., 2011). However, similar variance of mean Hit RT further suggests comparable levels of attentional engagement throughout the task (cf., Kofler et al., 2013; Miranda et al., 2012).

The functional hypoactivation in the left iPL evident in ADHD/+RD (Fig. 2a), but not ADHD/-RD (Fig. 4), compared with TDC is consistent with the dual route model of reading that associates the pSTG and iPL with decoding processes (Coltheart, Rastle, Perry, Langdon, & Ziegler, 2001; Ziegler et al., 2008). However, given the relative degree of phonological impairment in the ADHD/+RD group (Table 1) and extent of hypoactivation reported in numerous studies of RD alone compared with controls (Kovelman et al., 2012; Shaywitz et al., 2002; Temple et al., 2001; for review, Shaywitz & Shaywitz 2008), the magnitude and extent of the decoding-related differences in ADHD/+RD were somewhat underwhelming. Overall, the evidence suggests that neural substrates related to inattention, within the framework of the multiple deficit hypothesis, may play a particularly important role in the poor phonological performance exhibited by ADHD/+RD.

Despite similar inattentive symptomatology and attention-related performance on the wr-CPT, the two ADHD subgroups had distinct patterns of differences compared with TDC in the right hemispheric attention network areas. Differences in ADHD/+RD relative to TDC were limited to the right parietal lobe (Fig. 2a). By contrast, ADHD/−RD evidenced a greater extent of increased activation in frontoparietal attention-related areas, as well as the right temporal lobe, relative to TDC (Fig. 4a). To a certain extent, the increased activation in frontal areas of ADHD/−RD is similar to our previous result of increased frontal activation in ADHD/−RD, but not ADHD/+RD, in response to a CPT with numeric tokens (Mohl et al., 2013). However, it remains unclear whether attention network dysfunctions that appear to be divergent between the ADHD subpopulations influence the extent of phonological processing impairments.

The functional differences in the right iPL, part of the frontoparietal attention network (Petersen & Posner, 2012) frequently implicated in ADHD, were generally more exaggerated in ADHD/+RD than ADHD/−RD compared with TDC. Specifically, the right AG showed hypoactivation in ADHD/+RD (Fig. 2a) and was also hypoactive in ADHD/−RD compared with TDC, but to a lesser extent (Fig. 3b). The magnitude of extracted parameter estimates and extent of hyperactivation in the right SMG (BA 40) was nearly twice as large in ADHD/+RD than ADHD/−RD relative to TDC (Figs. 2a and 3a, and Table 3). These observations are in line with others showing attention can mediate relationships between certain executive functions and reading outcomes (Rogers et al., 2011). Additionally, the peak activation in the right SMG correlated inversely with WIAT-III Pseudoword Decoding scores (Fig. 2b), providing support for associations between executive control and left-hemispheric language network function (Hickok & Poeppel, 2004; Ziegler et al., 2008). An MEG study (Pammer et al., 2006) demonstrated an effect of attention on early word recognition processes in the left hemisphere through activation of the right ventral iPL, in a site near the peak in our study. Thus, further investigation is warranted to ascertain how attention, through neural substrates in the right iPL, may play a key role in phonological ability through modulation of left-hemispheric, reading network areas.

We do acknowledge that there are inherent limitations in this study, which may be viewed as being preliminary. This includes a small sample that is heterogeneous with respect to the number of boys with ADHD and a comorbid condition other than RD, as well as to the psychostimulant medication status difference between ADHD subgroups. However, in controlling for the acute effect of psychostimulant medication, all subjects on medication went through a washout period of at least 24 h prior to the fMRI. Also, not having a fourth group of boys with RD alone limits the extent of our understanding of neural deficits in response to this novel attention-demanding phonological processing task. Despite these limitations, there are a considerable number of interesting observations in this study that contributes to our understanding of the neural etiology of ADHD/+RD and warrants further investigation on larger samples.

5. Conclusion

Boys with ADHD/+RD demonstrated impaired phonological abilities compared to TDC and ADHD/−RD. However, corresponding neural evidence for dysfunction in the dorsal decoding subnetwork was not overwhelming, leading to the interpretation that other cognitive functions may contribute to poor phonology in ADHD/+RD. One of the chief constructs likely to influence phonological skill is attention (Levy et al., 2013; Mayes & Calhoun, 2007; Rogers et al., 2011; Willcutt & Pennington, 2000). Both ADHD subgroups evidenced altered function in the right iPL, which have been linked with dysregulation of left hemispheric reading areas (Pammer et al., 2006) and may be involved in phonological processing (Booth et al., 2008; McDermott et al., 2003). Specifically, the shared hyperactivation in the right SMG and corresponding correlation between parameter estimates and WIAT-III Pseudoword Decoding scores suggested that attention may influence phonological processing through neural mechanisms. Collectively, our findings indicate that instead of the dorsal decoding subnetwork being grossly compromised in ADHD/+RD, other cognitive impairments, including the level of inattention, may contribute to the development of RD within ADHD. Continued investigation of the roles for attention and other executive functions, which may lead to sub-optimal reading strategies, is warranted.

References

American Psychiatric Association (2000). *Diagnostic and statistical manual of mental disorders* (4th ed.).
Andersson, J. L., Hutton, C., Ashburner, J., Turner, R., & Friston, K. (2001). Modeling geometric deformations in EPI time series. *Neuroimage, 13*(5), 903–919.

Balota, D. A., Yap, M. J., Cortese, M. J., Hutchison, K. A., Kessler, B., Loftis, B., et al. (2007). The English lexicon project. *Behavior Research Methods, 39*(3), 445–459.

Banich, M. T., Burgess, G. C., Depue, B. E., Ruzic, L., Bidwell, L. C., Hitt-Laustsen, S., et al. (2009). The neural basis of sustained and transient attentional control in young adults with ADHD. *Neuropsychologia, 47*(14), 3095–3104. http://dx.doi.org/10.1016/j.neuropsychologia.2009.07.005.

Barkley, R. A. (1997). Behavioral inhibition, sustained attention, and executive functions: Constructing a unifying theory of ADHD. *Psychological Bulletin, 121*(1), 65–94.

Booth, J. R., Mehdiratta, N., Burman, D. D., & Bitan, T. (2008). Developmental increases in effective connectivity to brain regions involved in phonological processing during tasks with orthographic demands. *Brain Research, 1189*, 78–89.

Carreiras, M., Armstrong, B. C., Perea, M., & Frost, R. (2014). The what, when, where, and how of visual word recognition. *Trends in Cognitive Sciences, 18*(2), 90–98. http://dx.doi.org/10.1016/j.tics.2013.11.005. ISSN: 1364–6613.

Christopher, M. E., Miyake, A., Keenan, J. M., Pennington, B., DeFries, J. C., Wadsworth, S. J., et al. (2012). Predicting word reading and comprehension with executive function and speed measures across development: A latent variable analysis. *Journal of Experimental Psychology, 141*(3), 470–488.

Coltheart, M., Rastle, K., Perry, C., Langdon, R., & Ziegler, J. (2001). DRC: A dual route cascaded model of visual word recognition and reading aloud. *Psychological Review, 108*(1), 204–256.

de Jong, C. G. W., Van De Voorde, S., Roeyers, H., Raymaekers, R., Oosterlaan, J., & Sergeant, J. A. (2009). How distinctive are ADHD and RD? Results of a double dissociation study. *Journal of Abnormal Child Psychology, 37*(7), 1007–1017.

DuPaul, G. J., Gormley, M. J., & Laracy, S. D. (2012). Comorbidity of LD and ADHD: Implications of DSM-5 for assessment and treatment. *Journal of Learning Disabilities, 46*(1), 43–51.

Durston, S., Tottenham, N. T., Thomas, K. M., Davidson, M. C., Eigsti, I.-M., Yang, Y., et al. (2003). Differential patterns of striatal activation in young children with and without ADHD. *Biological Psychiatry, 53*(10), 871–878. http://dx.doi.org/10.1016/S0006-3223(02)01904-2.

Epstein, J. N., Casey, B. J., Tonev, S. T., Davidson, M. C., Reiss, A. L., Garrett, A., et al. (2007). ADHD- and medication-related brain activation effects in concordantly affected parent-child dyads with ADHD. *Journal of Child Psychology and Psychiatry, 48*(9), 899–913. http://dx.doi.org/10.1111/j.1469-7610.2007.01761.x.

Fried, R., Petty, C., Faraone, S. V., Hyder, L. L., Day, H., & Biederman, J. (2013). Is ADHD a risk factor for high school dropout? A controlled study. *Journal of Attention Disorders.* http://dx.doi.org/10.1177/1087054712473180).

Hickok, G., & Poeppel, D. (2004). Dorsal and ventral streams: A framework for understanding aspects of the functional anatomy of language. *Cognition, 92*(1–2), 67–99.

Hoeft, F., Meyler, A., Hernandez, A., Juel, C., Taylor-Hill, H., Martindale, J. L., et al. (2007). Functional and morphometric brain dissociation between dyslexia and reading ability. *Proceedings of the National Academy of Sciences of the United States of America, 104*(10), 4234–4239.

Jobard, G., Crivello, F., & Tzourio-Mazoyer, N. (2003). Evaluation of the dual route theory of reading: A metanalysis of 35 neuroimaging studies. *Neuroimage, 20*(2), 693–712.

Kaufman, J., Birmaher, B., Brent, D., Rao, U., Flynn, C., Moreci, P., et al. (1997). Schedule for affective disorders and schizophrenia for school-age children-present and lifetime version (K-SADS-PL): Initial reliability and validity data. *Journal of the American Academy of Child & Adolescent Psychiatry, 36*(7), 980–988.

Kofler, M. J., Rapport, M. D., Sarver, D. E., Raiker, J. S., Orban, S. A., Friedman, L. M., et al. (2013). Reaction time variability in ADHD: A meta-analytic review of 319 studies. *Clinical Psychology Review, 33*(6), 795–811.

Kovelman, I., Norton, E. S., Christodoulou, J. A., Gaab, N., Lieberman, D. A., Triantafyllou, C., et al. (2012). Brain basis of phonological awareness for spoken language in children and its disruption in dyslexia. *Cerebral Cortex, 22*(4), 754–764.

Langner, R., & Eickhoff, S. B. (2013). Sustaining attention to simple tasks: A meta-analytic review of the neural mechanisms of vigilant attention. *Psychological Bulletin, 139*(4), 870–900.

Levy, F., Young, D. J., Bennett, K. S., Martin, N. C., & Hay, D. A. (2013). Comorbid ADHD and mental health disorders: Are these children more likely to develop reading disorders? *Attention Deficit and Hyperactivity Disorders, 5*(1), 21–28.

Maldjian, J. A., Laurienti, P. J., Kraft, R. A., & Burdette, J. H. (2003). An automated method for neuroanatomic and cytoarchitectonic atlas-based interrogation of fMRI data sets. *Neuroimage, 19*(3), 1233–1239.

Manjón, J. V., Coupé, P., Martí-Bonmatí, L., Collins, D. L., & Robles, M. (2010). Adaptive non-local means denoising of MR images with spatially varying noise levels. *Journal of Magnetic Resonance Imaging, 31*(1), 192–203.

Mayes, S. D., & Calhoun, S. L. (2007). Learning, attention, writing, and processing speed in typical children and children with ADHD, autism, anxiety, depression, and oppositional-defiant disorder. *Child Neuropsychology, 13*(6), 469–493.

McDermott, K. B., Petersen, S. E., Watson, J. M., & Ojemann, J. G. (2003). A procedure for identifying regions preferentially activated by attention to semantic and phonological relations using functional magnetic resonance imaging. *Neuropsychologia, 41*(3), 293–303.

McGrath, L. M., Pennington, B. F., Shanahan, M. A., Santerre-Lemmon, L. E., Barnard, H. D., Willcutt, E. G., et al. (2011). A multiple deficit model of reading disability and attention-deficit/hyperactivity disorder: Searching for shared cognitive deficits. *Journal of Child Psychology and Psychiatry, 52*(5), 547–557.

Miranda, M. C., Barbosa, T., Muszkat, M., Rodrigues, C. C., Sinnes, E. G., Coelho, L. F. S., et al. (2012). Performance patterns in Conners' CPT among children with attention deficit hyperactivity disorder and dyslexia. *Arquivos De Neuro-Psiquiatria, 70*(2), 91–96.

Mohl, B., White, R., Goradia, D. D., Khatib, D., Dick, R. M., Zajac-Benitez, C., et al. (2013). Evidence of a reading disability effect on attention in ADHD children: A task-based fMRI study. *Organization for Human Brain Mapping* (pp. 1103). WA: Seattle.

Pammer, K., Hansen, P., Holliday, I., & Cornelissen, P. (2006). Attentional shifting and the role of the dorsal pathway in visual word recognition. *Neuropsychologia, 44*(14), 2926–2936.

Petersen, S. E., & Posner, M. I. (2012). The attention system of the human brain: 20 Years after. *Annual Review of Neuroscience, 35*(1), 73–89.

Polanczyk, G. V., Willcutt, E. G., Salum, G. A., Kieling, C., & Rohde, L. A. (2014). ADHD prevalence estimates across three decades: An updated systematic review and meta-regression analysis. *International Journal of Epidemiology, 43*(2), 434–442.

Pugh, K. R., Mencl, W. E., Jenner, A. R., Katz, L., Frost, S. J., Lee, J. R., et al. (2001). Neurobiological studies of reading and reading disability. *Journal of Communication Disorders, 34*(6), 479–492.

Rogers, M., Hwang, H., Toplak, M., Weiss, M., & Tannock, R. (2011). Inattention, working memory, and academic achievement in adolescents referred for attention deficit/hyperactivity disorder (ADHD). *Child Neuropsychology, 17*(5), 444–458.

Rosvold, H. E., Mirsky, A. F., Sarason, I., Bransome, E. D., Jr., & Beck, L. H. (1956). A continuous performance test of brain damage. *Journal of Consulting Psychology, 20*(5), 343.

Sexton, C. C., Gelhorn, H. L., Bell, J. A., & Classi, P. M. (2012). The co-occurrence of reading disorder and ADHD: Epidemiology, treatment, psychosocial impact, and economic burden. *Journal of Learning Disabilities, 45*(6), 538–564.

Shaywitz, S. E., & Shaywitz, B. A. (2008). Paying attention to reading: The neurobiology of reading and dyslexia. *Development and Psychopathology, 20*(04), 1329–1349.

Shaywitz, B. A., Shaywitz, S. E., Pugh, K. R., Mencl, W. E., Fulbright, R. K., Skudlarski, P., et al. (2002). Disruption of posterior brain systems for reading in children with developmental dyslexia. *Biological Psychiatry, 52*(2), 101–110.

Snowling, M. J. (2001). From language to reading and dyslexia. *Dyslexia, 7*(1), 37–46.

Temple, E., Poldrack, R. A., Salidis, J., Deutsch, G. K., Tallal, P., Merzenich, M. M., et al. (2001). Disrupted neural responses to phonological and orthographic processing in dyslexic children: An fMRI study. *NeuroReport, 12*(2), 299–307.

Ward, B. D. (2000). Simultaneous inference for fMRI data. *AFNI 3dDeconvolve Documentation, Medical College of Wisconsin.*

Weissman, D. H., Roberts, K. C., Visscher, K. M., & Woldorff, M. G. (2006). The neural bases of momentary lapses in attention. *Nature Neuroscience, 9*(7), 971–978.

Willcutt, E. G., Betjemann, R. S., McGrath, L. M., Chhabildas, N. A., Olson, R. K., DeFries, J. C., et al. (2010). Etiology and neuropsychology of comorbidity between RD and ADHD: The case for multiple-deficit models. *Cortex, 46*(10), 1345–1361.

Willcutt, E. G., & Pennington, B. F. (2000). Comorbidity of reading disability and attention-deficit/hyperactivity disorder: Differences by gender and subtype. *Journal of Learning Disabilities, 33*(2), 179–191.

Willcutt, E. G., Pennington, B. F., Olson, R. K., Chhabildas, N., & Hulslander, J. (2005). Neuropsychological analyses of comorbidity between reading disability and attention deficit hyperactivity disorder: In search of the common deficit. *Developmental Neuropsychology, 27*(1), 35–78.

Yoshimasu, K., Barbaresi, W. J., Colligan, R. C., Killian, J. M., Voigt, R. G., Weaver, A. L., et al. (2010). Gender, attention-deficit/hyperactivity disorder, and reading disability in a population-based birth cohort. *Pediatrics, 126*(4), e788–95.

Ziegler, J. C., Castel, C., Pech-Georgel, C., George, F., Alario, F.-X., & Perry, C. (2008). Developmental dyslexia and the dual route model of reading: Simulating individual differences and subtypes. *Cognition, 107*(1), 151–178.