Year: 2018

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DOI: https://doi.org/10.1016/j.dcn.2018.07.001

Originally published at:
Zuk, Jennifer; Perdue, Meaghan V; Becker, Bryce; Yu, Xi; Chang, Michelle; Raschle, Nora Maria; Gaab, Nadine (2018). Neural correlates of phonological processing: Disrupted in children with dyslexia and enhanced in musically trained children. Developmental Cognitive Neuroscience, 34:82-91.
DOI: https://doi.org/10.1016/j.dcn.2018.07.001

Developmental Cognitive Neuroscience 34 (2018) 82–91

Contents lists available at ScienceDirect

Developmental Cognitive Neuroscience

journal homepage: www.elsevier.com/locate/dcn

Neural correlates of phonological processing: Disrupted in children with dyslexia and enhanced in musically trained children

Jennifer Zuk[a,b], Meaghan V. Perdue[a,e], Bryce Becker[a], Xi Yu[a,b], Michelle Chang[a], Nora Maria Raschle[a,c], Nadine Gaab[a,b,d,*]

[a] *Laboratories of Cognitive Neuroscience, Division of Developmental Medicine, Department of Medicine, Boston Children's Hospital, Boston, MA 02115, USA*
[b] *Harvard Medical School, Boston, MA 02115, USA*
[c] *Department of Child and Adolescent Psychiatry, University of Basel, Psychiatric University Hospital, Basel, Switzerland*
[d] *Harvard Graduate School of Education, Cambridge, MA 02138, USA*
[e] *Department of Psychological Sciences, University of Connecticut, Storrs, CT 06268, USA*

ARTICLE INFO

Keywords:
Music training
fMRI
Children
Dyslexia
Phonological processing

ABSTRACT

Phonological processing has been postulated as a core area of deficit among children with dyslexia. Reduced brain activation during phonological processing in children with dyslexia has been observed in left-hemispheric temporoparietal regions. Musical training has shown positive associations with phonological processing abilities, but the neural mechanisms underlying this relationship remain unspecified. The present research aims to distinguish neural correlates of phonological processing in school-age typically developing musically trained children, musically untrained children, and musically untrained children with dyslexia utilizing fMRI. A whole-brain ANCOVA, accounting for gender and nonverbal cognitive abilities, identified a main effect of group in bilateral temporoparietal regions. Subsequent region-of-interest analyses replicated temporoparietal hypoactivation in children with dyslexia relative to typically developing children. By contrast, musically trained children showed greater bilateral activation in temporoparietal regions when compared to each musically untrained group. Therefore, musical training shows associations with enhanced bilateral activation of left-hemispheric regions known to be important for reading. Findings suggest that engagement of these regions through musical training may underlie the putative positive effects of music on reading development. This supports the hypothesis that musical training may facilitate the development of a bilateral compensatory neural network, which aids children with atypical function in left-hemispheric temporoparietal regions.

1. Introduction

Prior research has repeatedly demonstrated the importance of phonological awareness for learning to read (Snowling, 2000; Ramus, 2001; Lyon et al., 2003; Ramus, 2004). Phonological awareness, the ability to manipulate speech sounds within orally presented words, has been shown to be a critical predictor of later reading ability in preschool and school-age children (Nation and Hulme, 1997; Scarborough, 1998; Pennington and Lefly, 2001; Snowling et al., 2003; Flax et al., 2009). Phonological awareness is also one of the core risk-factors for developmental dyslexia, a specific learning disorder characterized by difficulties with decoding, speed, and accuracy of word reading (dyslexia; Pennington, 2006; van Bergen et al., 2014; Ozernov-Palchik et al., 2016). Functional magnetic resonance imaging (fMRI) studies have revealed atypical neural correlates of phonological processing in individuals with dyslexia. Specifically, children and adults with dyslexia compared to those without show hypoactivation within posterior brain areas, including left-hemispheric temporoparietal and occipitotemporal regions (for a review, see Richlan et al., 2009). Moreover, these neural alterations have been observed even prior to reading onset in pre-school age children with familial risk for dyslexia compared to children with no familial risk (Raschle et al., 2012a, b). Among school-age children with dyslexia, greater right-hemispheric activation during a reading task has been associated with better reading outcomes over time, which suggests a possible neural mechanism associated with compensating for reading difficulties (Hoeft et al., 2011). Thus, neural activation during phonological processing in children and adults with dyslexia has been characterized by hypoactivation in left-hemispheric temporoparietal

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[*] Corresponding author at: 1 Autumn Street #643, Laboratories of Cognitive Neuroscience, Department of Medicine, Division of Developmental Medicine, Boston Children's Hospital/Harvard Medical School, Boston, MA, 02115, USA.

E-mail address: Nadine.gaab@childrens.harvard.edu (N. Gaab).

https://doi.org/10.1016/j.dcn.2018.07.001
Received 23 December 2017; Received in revised form 27 June 2018; Accepted 13 July 2018

and occipitotemporal brain regions, with some evidence of right-hemispheric activation that may reflect compensatory processing strategies for reading.

As phonological processing skills require perception of individual speech sounds, which requires discerning basic auditory components that distinguish speech sounds, atypical neural responses to basic auditory stimuli have also been observed in struggling readers (Gaab et al., 2007a; Stefanics et al., 2011; Kovelman et al., 2015). Moreover, basic auditory training has demonstrated changes to these neural responses along with improvements in reading achievement among children with dyslexia (Temple et al., 2003; Gaab et al., 2007a). Accordingly, it has been suggested that general auditory processing difficulties may underlie phonological processing weaknesses in those with dyslexia (as reviewed in Goswami, 2011; Hamalainen et al., 2013; Goswami, 2015). However, not all children with dyslexia show deficits in auditory processing (Nittrouer, 1999; Marshall et al., 2001; Ramus, 2003; Rosen, 2003; Grube et al., 2014; Steinbrink et al., 2014; Christmann et al., 2015). Therefore, a multiple deficit view of dyslexia, in which deficits in basic auditory processing may be one of several factors that give rise to difficulties with learning to read, offers a promising perspective that accounts for the complex nature of reading acquisition (Pennington, 2006).

Considering auditory-related training that may facilitate neural activation in regions important for phonological awareness, musical training has been viewed as one approach to training-induced or experience-dependent brain plasticity (Jäncke, 2009; Herholz and Zatorre, 2012). Longitudinal studies employing MRI with school-age children have demonstrated neural changes following instrumental musical training (Hyde et al., 2009; Seither-Preisler et al., 2014; Habibi et al., 2017; Sachs et al., 2017). Specifically, six-year old children who received approximately one-to-two years of instrumental musical training demonstrated structural changes in several brain regions, particularly right-hemispheric primary auditory and pre-motor cortices, and the corpus callosum (Hyde et al., 2009; Habibi et al., 2017). Enhanced functional responses to auditory stimuli have also been observed over the course of musical training (Seither-Preisler et al., 2014), and significantly greater cortical auditory evoked potentials have been found relative to children in sports training and children with no specific training (Habibi et al., 2016). Overall, these longitudinal studies have demonstrated structural and functional changes following musical training, primarily within auditory and motor-related regions as well as the corpus callosum. These findings suggest that musical training induces neuroplasticity in brain regions that are not only important for music but also for non-musical cognitive/perceptual skills that may play a role in reading.

A growing body of evidence suggests that musical skill is directly associated with phonological awareness and reading achievement (Lamb and Gregory, 1993; Fisher and McDonald, 2001; Corrigall and Trainor, 2011; Goswami et al., 2012; Moritz et al., 2012; Zuk et al., 2013; Williams et al., 2015). Phonological awareness and musical ability (as indicated by either musical training experience or music perception task performance) have shown a significant positive correlation across studies (Standley and Hughes, 1997; Fisher and McDonald, 2001; Anvari et al., 2002; Forgeard et al., 2008; Loui et al., 2011; Moritz et al., 2012; Zuk et al., 2013). Music-based interventions have further shown improved phonological awareness skills in typically developing school-aged children and children with dyslexia (Hurwitz et al., 1975; Atterbury, 1985; Farmer et al., 1995; Overy, 2003; Santos et al., 2007; Dege and Schwarzer, 2011; Bhide et al., 2013; Thomson et al., 2013; Flaugnacco et al., 2015; Habib et al., 2016). Moreover, children with dyslexia have demonstrated improvements in reading following music-based interventions (Thomson et al., 2013; Flaugnacco et al., 2015; Rautenberg, 2015; Habib et al., 2016). Another investigation focused on low-income children observed that one year of musical training led to age-appropriate reading achievement, whereas age-matched peers without musical training showed below average reading scores (Slater et al., 2014). Thus, converging evidence suggests positive associations between music and reading abilities.

While behavioral links between music and reading have been observed, the neural mechanisms underlying this relationship have yet to be investigated. The evidence implicating specialized brain structure and function within auditory regions in musicians (Schneider et al., 2002; Gaser and Schlaug, 2003b, 2003a; Gaab et al., 2005) calls into question whether musicians may also exhibit specialized neural activation during reading-related processes due to training-induced plasticity or basic auditory training that may be advantageous for reading. Reading ability has been shown to positively correlate with gray matter structure within right-hemispheric primary auditory regions of children with musical training who practice frequently (Seither-Preisler et al., 2014). However, no study to date has investigated the functional neural correlates of reading-related processing in trained musicians. In fact, scarcely any studies have investigated functional activation during language-related processing in musicians compared to non-musicians utilizing fMRI. One study employed resting state functional connectivity in adult musicians compared to nonmusicians and observed enhanced connectivity in musicians between the left superior temporal gyrus and multiple language-related regions, including bilateral temporoparietal regions (Fauvel et al., 2014). Similarly, functional activation in bilateral temporoparietal regions has been shown in adults for a pitch memory task, and musicians showed greater right temporoparietal activation during this task when compared to nonmusicians (Gaab and Schlaug, 2003). Moreover, temporoparietal activation during music processing has shown a positive relationship with total number of hours of practice among children and adults with musical training (Ellis et al., 2013). Collectively, these studies provide initial evidence of a specialized pattern of activation in musicians within brain regions shown to be important for language and reading, particularly involving the right-hemisphere. In addition, greater interhemispheric white matter connectivity between left and right temporal regions has been shown in adult musicians compared to nonmusicians, which may be associated with bilateral functional integration of these regions (Elmer et al., 2016). However, this has yet to be investigated directly in relation to reading-related processes. Thus, it remains unclear whether the neural correlates of reading-related processes, altered among children and adults with dyslexia, may be specialized in musicians.

The present study seeks to identify a missing link in the literature by investigating the neural correlates of phonological processing in musically trained children as compared to musically untrained typically developing controls as well as children with dyslexia. Since phonological processing is considered a prominent deficit associated with dyslexia (Nation and Hulme, 1997; Scarborough, 1998), the present study builds on the collective behavioral evidence linking musical training with enhanced phonological processing to investigate the functional neural activation underlying these associations. Based on the previous literature implicating enhanced bilateral activation and connectivity related to auditory processing in adult musicians (Gaab and Schlaug, 2003; Fauvel et al., 2014; Elmer et al., 2016), we hypothesize that this functional specialization associated with musical training will be evident during phonological processing in musically trained children as well. In addition, longitudinal evidence in school-age children demonstrating neuroplasticity following musical training within auditory regions as well as the corpus callosum suggests that musically trained children may be characterized by less lateralization (Hyde et al., 2009; Seither-Preisler et al., 2014; Habibi et al., 2017). Based on these findings, we hypothesize that musically trained children will show greater bilateral activation in posterior temporal regions also known to be important for phonological processing relative to musically untrained groups. Moreover, we hypothesize that we will replicate previous findings of hypoactivation within these regions in children with dyslexia relative to the typically developing groups, particularly in the left hemisphere (Richlan et al., 2009). Thus, we further hypothesize that direct comparison between these three groups will reveal that the neural correlates of phonological processing show hyperactivation in musically trained children and hypoactivation in children with dyslexia. This study will be the first to specify the neural correlates that may underlie the positive effects of musical training on phonological processing during typical and atypical reading development. In addition, this study serves as a starting point to explore whether musical training may facilitate the development of a compensatory neural network that may be advantageous for literacy development.

2. Material and methods

2.1. Participants

40 healthy monolingual English-speaking children participated in the present study (age range: 6–13 yrs; mean: 9.81 yrs, SD: 1.85 yrs). These children were categorized into three groups as follows: 16 musically trained (8 male, 8 female) and 13 musically untrained (3 male, 10 female) typically developing children, as well as 11 musically untrained children with dyslexia (7 male, 4 female). Children with dyslexia were identified by reports of a formal diagnosis of dyslexia and/or characterization of literacy abilities based on psychometric assessment (described further below). Children were classified as musically trained if they had completed a minimum of two years in private instrumental music lessons at the time of study participation. On average, musically trained children had been studying their instrument for four years (mean: 4.22 yrs, SD: 1.96 yrs), and had started musical training at age five (mean 5.72 yrs, SD: 1.34 yrs). Among these musically trained children, 10 of them reportedly played more than one instrument (refer to Table 1 for further detail regarding musical training experience). Musically untrained children had not participated in any musical training outside of the general school music curriculum. Participants were screened to ensure no history of neurological/psychological disorder or head injury, and no vision or hearing impairments. The majority of children were right-handed per parent report; however, one child with dyslexia was reportedly left-handed and two were ambidextrous (one child with dyslexia, one musically untrained typically developing child). This research was approved by the Boston Children's Hospital Institutional Review Board (IRB). Written assent and informed consent were obtained from each child participant and guardian, respectively. These participants were part of a larger investigation of the neural mechanisms associated with (a) musical training (Zuk et al., 2014) and (b) early risk factors associated with dyslexia (Raschle et al., 2012a).

2.2. Group demographics

Participants were characterized by group with two approaches: (a) group assignment was established based on a reported diagnosis of dyslexia and the extent of musical training, as indicated via questionnaires completed by parents, and (b) group assignment was then verified through performance on a subset of standardized measures of reading, completed by all participants as part of the larger investigation. This set of literacy assessments included the subtests from the Test of Word Reading Efficiency (TOWRE; Sight Word Efficiency, SWE, and Phonemic Decoding Efficiency PDE; Torgesen et al., 1999) and the Test of Silent Word Reading Fluency (TOSWRF; Mather et al., 2004). Children were assigned to the dyslexia group if they had a formal diagnosis of dyslexia and/or demonstrated a standard score below 90 on at least one subtest of the TOWRE assessment. General demographics by group were characterized as follows (see Table 2 for an overview):

Table 1
Characteristics of musical training experience among musically trained children.

	Musicians (n = 16)
Group characteristics	**Mean ± SD**
Age at musical training onset (years)	5.69 ± 1.41
Duration of musical training (years)	4.25 ± 1.96
Intensity of practice time (hrs/wk)[a]	3.62 ± 2.38
Primary musical instrument	**Number of children**
Piano	9
Strings	1
Woodwinds	1
Guitar	2
Percussion	3

[a] n = 15 (Information not reported for one child).

Nonverbal cognitive abilities: The nonverbal intelligence subtest of the Kaufman Brief Intelligence Test was administered to measure nonverbal cognitive abilities (KBIT; Kaufman and Kaufman, 1997). All participants demonstrated nonverbal cognitive abilities within or above the Average range, with standard scores greater than or equal to 89. To check for group differences in nonverbal cognitive abilities, a one-way ANOVA by group was employed (outlined in Table 2). Subsequent post-hoc tests with Bonferroni adjustment for multiple comparisons revealed no significant difference between musically trained and untrained children. However, musically trained children exhibited significantly higher scores relative to children with dyslexia ($p = 0.035$).

Socioeconomic Status: Guardians of participants completed an evaluation of current socioeconomic status (adapted from the MacArthur Research Network: http://www.macses.ucsf.edu/Default.htm). Two parents (of one musically untrained child and another with dyslexia) did not provide complete documentation of socioeconomic status. Kruskal Wallis tests confirmed no significant differences between groups in highest level of parent education or total family income.

Age: An ANOVA was employed to confirm no significant group differences in age ($p > 0.1$).

Accordingly, group comparisons of reading measures were then evaluated through one-way ANCOVAs accounting for nonverbal cognitive abilities and gender as covariates due to group differences observed for these factors. Post-hoc pairwise comparisons were then performed using the Bonferroni adjusted significance levels for multiple comparisons.

2.3. Neuroimaging

2.3.1. Neuroimaging procedures

Children were first introduced to the MR scanner setting and fMRI task with a mock scanner training, which allowed them to acclimate to the MR environment and learn the tasks thoroughly (for a full description of our child-friendly imaging protocol, see Raschle et al., 2009, 2012b). The task presently described is one component of a larger 90-minute neuroimaging protocol, including breaks as individually requested. The fMRI task was divided into two pseudo-randomized runs of 5–6 minutes each, in order to minimize potential for movement artifacts and fatigue. Intensive quality control was conducted as follows: (i) during data acquisition, a researcher stayed in the MR room with the child to monitor engagement and limit motion, and (ii) visual inspection of data quality was conducted throughout processing, including the screening of auditory activation relative to the rest condition during first-level analysis. Behavioral and neuroimaging sessions were completed in either one or two days, according to parent and child preference. Sessions that occurred on two different days were less than 6 months apart.

2.3.2. fMRI phonological processing task

The phonological processing fMRI task has been previously employed and described in detail (see Raschle et al., 2012b, a; Raschle et al., 2014b; Yu et al., 2018a). In this task, children were orally presented with two common-object words, in a male or female voice, as a corresponding picture appeared on the screen. In the experimental condition (first sound matching), children were asked to determine whether the two words began with the same first sound or different first

Table 2
Participant demographics by group [Significance indicated by *$p \leq 0.05$].

	Musically trained	**Musically untrained**	**Dyslexia**	
n	16	13	11	
	Mean ± SD	Mean ± SD	Mean ± SD	F (max df = 2,37)
Age (months)	10.27 ± 1.97	9.54 ± 1.89	9.45 ± 1.46	.821
KBIT (nonverbal cognitive abilities)	113.88 ± 8.43	110.77 ± 11.16	103.72 ± 8.29	3.585*[a]
Socioeconomic status	Mean rank	Mean rank	Mean rank	Asymp. sig.
Parent education level[b]	18.50	17.29	16.06	.842
Total family income[c]	15.71	15.50	22.72	.156

[a] Post-hoc tests on one-way ANOVA by group with Bonferroni adjustment for multiple comparisons indicate significant differences between musically trained children and children with dyslexia; musically untrained children did not significantly differ from either group.

[b] Parental education scores were calculated according to the seven-point Hollingshead Index Educational Factor Scale, summed for husband and wife and divided by two (Hollingshead, 2011). Information not reported for one child with dyslexia.

[c] Total Family Income determined by a scale where 1 = \$0–\$5000; 2 = \$5000–\$11,999; 3 = \$12,000–\$15,999; 4 = \$16,000–\$24,999; 5 = \$25,000–\$34,999; 6 = \$35,000–\$49,900; 7 = \$50,000–\$74,999; 8 = \$75,000–\$99,999; 9 = \$100,000+; 10 = Don't know; 11 = No response. Information not reported for one child in the musically untrained group.

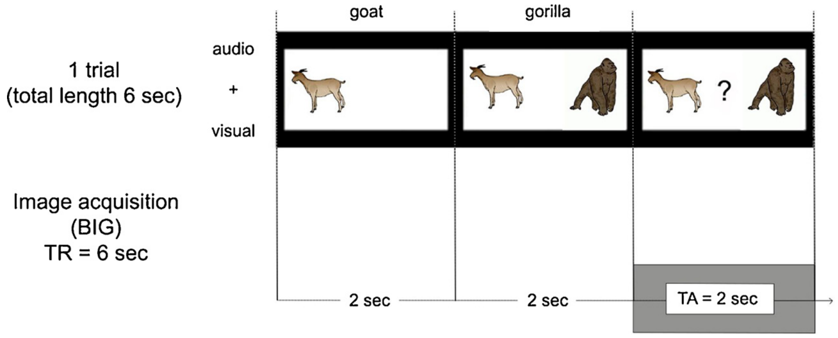

Fig. 1. Phonological processing fMRI task design, implementing a behavioral interleaved gradient (BIG) technique.

sounds. During the control condition (voice matching), children determined whether the two words were spoken by the same voice (same gender) or not. The experimental and control conditions were divided into separate runs, with matched fixation-cross rest conditions included in each run. In both conditions, each word was presented for two seconds followed by presentation of a question mark for two seconds to represent the answering period, for a total of six seconds per trial. A behavioral interleaved gradient (BIG) design was used to allow for presentation of the auditory stimuli without scanner noise interference (Hall et al., 1999; Gaab et al., 2007b, 2008), as is depicted in Fig. 1 for one trial. The tasks were presented in a block design with seven blocks per condition and four trials per block (with a total of 28 trials per condition).

2.3.3. *In-scanner task performance*

In-scanner performance was collected for participants for both the experimental and control tasks, which included tracking button presses for accuracy and reaction time for each trial. Accuracy was determined by the total number of correct trials. For the task of interest, first sound matching, each group averaged above 75% accuracy (as indicated by the number of correct trials). Three children have not been included in these group-level averages of in-scanner performance due to technical difficulties with the button press acquisition (two musically untrained children, one with dyslexia). However, these children were deemed eligible for imaging analyses based on accurate task performance during training prior to the scan.

2.3.4. *fMRI acquisition and analyses*

During the phonological processing task, 60 whole-brain images were collected per run. Images were acquired on a Siemens 3 T Trio MR scanner with a TR of 6000 ms; TA of 1995 ms; TE of 30 ms; flip angle of 90°; field of view of 194 mm^2; voxel size of $3 \times 3 \times 4\ \text{mm}^3$; and slice thickness of 4 mm. A 32-slice echo planar imaging interleaved sequence was used. All processing and general linear modeling analyses were conducted in SPM5 (www.fil.ion.ucl.ac.uk/spm) using MATLAB (Mathworks, Natick, MA, USA). During acquisition, extra functional images were obtained preceding the first block of each run and then discarded during pre-processing in order to account for T1 equilibration. Following the drop, all remaining images were realigned using a least-squares approach referencing the first image. This accounted for movement artifacts within the fMRI time series. Then, all images underwent spatial normalization into standard space with the MNI152 T1 template (Ashburner and Friston, 2005). Finally, all images were smoothed with an 8-mm full-width-at-half-maximum isotropic Gaussian kernel, which removed noise and effects arising from lasting differences in functional and structural anatomy during inter-subject averaging (www.fil.ion.ucl.ac.uk/spm/doc/spm5_manual.pdf). A stringent process of artifact detection was then followed, using the art-imaging toolbox (http://www.nitrc.org/projects/artifact_detect), particularly because the child population is prone to greater movement during imaging (Raschle et al., 2012b). Using the toolbox, motion was visualized, potential movement artifacts were plotted, and individual analysis masks were visually inspected. Differences in motion between consecutive images were also plotted, and artifactual time points were reviewed, identifying any images that exceeded a movement threshold of 3 mm and rotation threshold of 0.05 degrees. Every image that exceeded these thresholds was visually inspected, and any that contained artifacts (e.g., missing voxels, stripes, ghosting, or intensity differences) were removed from analysis. The number of omitted scans per group did not significantly differ between groups ($p > 0.05$). After excluding artifactual time points, explicit masks were created and movement regressors were saved. Fixed-effects within each subject was first estimated using the general linear model (GLM). Experimental conditions were modeled in a block-design fashion and entered into a GLM with motion regressors. Explicit masks generated by the art-imaging toolbox were also applied to confine analyses to the brain area only. After model estimation, the contrast map for the experimental > control conditions (i.e., FSM-VM) were built and computed for every subject.

Group differences were then evaluated through a one-way ANCOVA model for the main contrast of interest ($FSM > VM$), with nonverbal cognitive abilities and gender as covariates. Effects were initially evaluated at the threshold utilized in previous publications that employed this phonological processing fMRI task (Raschle et al., 2012a, a; Raschle et al., 2014b), at a voxel level significance of $p < 0.005$, $k > 50$ voxels, which corresponds to uncorrected cluster-level thresholds of $p \leq 0.1$ (specific thresholds for each cluster are provided in Table 4). To further examine results with correction for multiple comparisons, the Monte-Carlo method was employed utilizing the REST toolbox (http://restfmri.net/forum/index.php). Monte-Carlo correction for multiple comparisons revealed that a voxel level significance of $p < 0.005$ and cluster level significance at $p < 0.05$ corresponded to a cluster size of 93 voxels. To further investigate the main effects of group, regions of interest (ROI) analyses were employed to evaluate activation differences between each pair, including musically trained vs. untrained, between untrained vs. dyslexia, and musically trained vs. dyslexia. Specifically, for each region derived from the ANCOVA analyses of the three groups, weighted parameter estimates were extracted from each participant's first-level result for $FSM > VM$ with MarsBar (http://marsbar.sourceforge.net/). Pairwise comparisons between each pair (musically trained vs. musically untrained, musically trained vs. dyslexia, musically untrained vs. dyslexia) were then conducted in SPSS with Bonferroni adjusted significance levels for multiple comparisons.

3. Results

3.1. Behavioral group characteristics

One-way ANCOVAs investigating group differences on reading measures, while accounting for nonverbal cognitive abilities and gender revealed significant group differences for all standardized reading measures employed (see Table 3 for an overview). Pairwise comparisons with Bonferroni adjustment for multiple comparisons revealed that children with dyslexia had significantly lower scores on measures of sight word reading and decoding relative to both musically trained and untrained children. Children with dyslexia also showed significantly lower reading fluency scores relative to musically trained children; musically untrained children did not significantly differ from either group. Musically trained children did not differ significantly from musically untrained children on any of the behavioral measures employed.

3.2. Neuroimaging results

3.2.1. In-scanner performance

For the fMRI task, in-scanner performance by group was evaluated by employing one-way ANCOVAs while accounting for nonverbal cognitive abilities and gender. In-scanner performance was charactersized by accuracy (number of correct trials). ANCOVAs revealed significant group differences in accuracy for the experimental condition, first sound matching (FSM; outlined in Table 3). Pairwise comparisons with Bonferroni adjustment for multiple comparisons showed significantly lower accuracy in children with dyslexia as compared to both musically trained and untrained children, and no significant differences were observed between musically trained and untrained children. For the control condition, voice matching (VM), no significant differences were found between groups for in-scanner performance.

3.2.2. fMRI whole brain results

An ANCOVA was then employed to examine differences in brain activation during phonological processing ($FSM > VM$) between all three groups, accounting for nonverbal cognitive abilities and gender as covariates. ANCOVA comparison for the main effect of group, Monte-Carlo cluster-level corrected for multiple comparisons, revealed significant group differences in a left-hemispheric temporoparietal cluster (located in the angular gyrus). In addition, group effects were observed within bilateral temporoparietal regions, including the angular gyrus (AG), supramarginal gyrus (SMG), and superior temporal gyrus (STG; shown in Fig. 2 and summarized in Table 4). Furthermore, to rule out handedness effects, an ANCOVA comparison was employed excluding the three participants who were not right-handed (one non-musician, two children with dyslexia), which resulted in an effect of neuronal activation during $FSM > VM$ in the same bilateral temporoparietal regions observed with the whole sample, with Monte-Carlo cluster-level corrected significant differences in the same left-hemispheric temporoparietal cluster.

3.2.3. Region of interest results

To further illustrate specific differences between groups within brain regions identified in the ANCOVA, region-of-interest (ROI) analysis was employed. Subsequent pairwise comparisons via ROI analysis revealed that musically trained children significantly differed from musically untrained children in bilateral temporoparietal regions, specifically the left SMG ($p < 0.05$) and right AG ($p < 0.001$), Bonferroni correction for multiple comparisons. Musically trained

Table 3

Group characteristics as outlined by standardized measures of phonological processing and reading [Significance indicated by *$p \leq 0.05$, **$p \leq 0.01$, ***$p \leq 0.001$]. Standard scores are reported for all psychometric measures. Raw scores are reported for in-scanner performance, maximum correct = 28.

	Musically urained	**Musically untrained**	**Dyslexia**	
n	16	13	11	
	Mean ± SD	Mean ± SD	Mean ± SD	F (max df = 4,37)
Reading measures				
TOWRE SWE[c]	112.07 ± 10.20	106.2 3 ± 10.48	85.6 ± 10.01	21.772***[a]
TOWRE PDE[c]	111.27 ± 13.19	110.31 ± 12.15	88.20 ± 5.64	12.741***[a]
TOSWRF[d]	109.93 ± 9.78	106.00 ± 9.76	92.78 ± 10.10	6.05**[b]
In-scanner performance accuracy				
First sound matching[e]	27 ± 1.41	26.09 ± 1.62	23.50 ± 2.73	7.58**[a]
Voice matching[e]	25.81 ± 1.81	26.18 ± 2.82	22.90 ± 5.75	1.534

[a] Pairwise comparisons of one-way ANCOVA with Bonferroni adjustment for multiple comparisons indicate that children with dyslexia significantly differ from both musically trained and untrained children. No significant differences were observed between musically trained and untrained children.

[b] Pairwise comparisons of one-way ANCOVA with Bonferroni adjustment for multiple comparisons indicate significant differences between musically trained children and children with dyslexia; musically untrained children did not significantly differ from either group.

[c] One musically trained and one child with dyslexia did not complete all testing.

[d] One musically trained and two children with dyslexia did not complete all testing.

[e] Button-presses not collected for one musically untrained and two children with dyslexia.

Table 4
ANCOVA comparison between musically trained children, musically untrained children, and children with dyslexia during phonological processing *(FSM > VM)*. In this comparison, one left temporoparietal region survived cluster-level $p < 0.05$, Monte-Carlo corrected for multiple comparisons (indicated in bold).

ANCOVA									
Voxels	Maximum (Z)	Cluster-level p-value	Peak-level p-value	Coordinates			Cerebrum	BA	Region
				x	y	z			
104	**3.48**	**0.029**	**< 0.001**	**−34**	**−52**	**28**	**L**	**39**	**Angular gyrus**
56	3.63	0.095	< 0.001	−54	−36	34	L	40	Supramarginal gyrus
54	3.05	0.101	0.001	64	−22	14	R	40	Superior temporal gyrus/ Supramarginal gyrus
50	3.34	0.113	< 0.001	48	−64	20	R	39	Angular gyrus

children also significantly differed from children with dyslexia in all bilateral ROIs: the left AG ($p < 0.001$), left SMG ($p < 0.001$), right AG ($p < 0.005$), and right STG ($p < 0.005$). Moreover, musically untrained children also significantly differed from children with dyslexia in the left AG ($p < 0.05$) and right STG ($p < 0.01$). An overview of functional activation by group within each ROI is provided in Fig. 3.

4. Discussion

The present study demonstrates that the functional activation in left-hemispheric temporoparietal brain regions associated with phonological processing is disrupted in children with dyslexia and enhanced bilaterally in musically trained children. Specifically, comparison between musically trained children, musically untrained children, and those with dyslexia revealed group differences in temporoparietal regions (e.g., bilateral angular gyrus, left supramarginal gyrus, right posterior superior temporal gyrus), thereby identifying regions which have been previously implicated in phonological processing and reading-related tasks in the left hemisphere (Turkeltaub et al., 2003). Subsequent region-of-interest analyses within these temporoparietal regions revealed that children with dyslexia show the previously established hypoactivation relative to typically developing children (as reviewed in Richlan et al., 2009). Moreover, musically trained children showed significantly greater activation in these temporoparietal regions relative to children with dyslexia as well as musically untrained children. These findings provide initial evidence with a relatively small sample size to link the putative positive effects of music and reading with enhanced bilateral neural activation in reading-related brain regions.

This study provides the first fMRI evidence to directly link musical training with reading-related processes. In line with longitudinal studies in school-age children demonstrating functional and structural changes in auditory regions following one-to-two years of musical training (Hyde et al., 2009; Seither-Preisler et al., 2014; Habibi et al., 2016, 2017), it is conceivable that the neuroplasticity induced by musical training may explain the enhanced temporoparietal activation identified in the present findings. Functional responses to auditory stimuli have been shown to increase after one year of musical training in school-age children (Seither-Preisler et al., 2014), and significantly greater cortical auditory evoked potentials have been shown over and above children in sports training and children with no specific training (Habibi et al., 2016). In addition, enhanced temporoparietal activation in the right hemisphere has been shown in adult musicians compared to nonmusicians during a pitch-memory task (Gaab and Schlaug, 2003), and temporoparietal activation during music processing has shown positive associations with the total number of hours of practice among children and adults with musical training (Ellis et al., 2013). Training studies in school-age children have also observed alterations in the corpus callosum following musical training (Hyde et al., 2009; Habibi et al., 2017). These training effects suggest that musical training leads to less lateralization, which is directly in line with the enhanced bilateral activation observed in musically trained children compared to the other groups in the present region-of-interest analysis. These findings are further supported by evidence in adults, as adult musicians have demonstrated greater functional resting state connectivity between the left superior temporal gyrus and bilateral temporoparietal regions compared to nonmusicians (Fauvel et al., 2014). Such potential for enhanced bilateral connectivity in adult musicians has been further corroborated by findings of greater interhemispheric white matter connectivity between left and right temporoparietal regions (Elmer et al., 2016). Taken together, these findings bring forth a pattern of neural activation that may underlie the behavioral relationships previously found between musical training and phonological awareness skills (Standley and Hughes, 1997; Fisher and McDonald, 2001; Anvari et al., 2002; Forgeard et al., 2008; Loui et al., 2011; Moritz et al., 2012; Zuk et al., 2013). Therefore, by characterizing the neural correlates of phonological processing in musically trained children, the present findings bring forth functional neuroimaging evidence with a modest sample size that support the previously reported behavioral links between music and reading-related abilities.

The present findings call into question the extent to which the significant differences observed may reflect an effect of musical training,

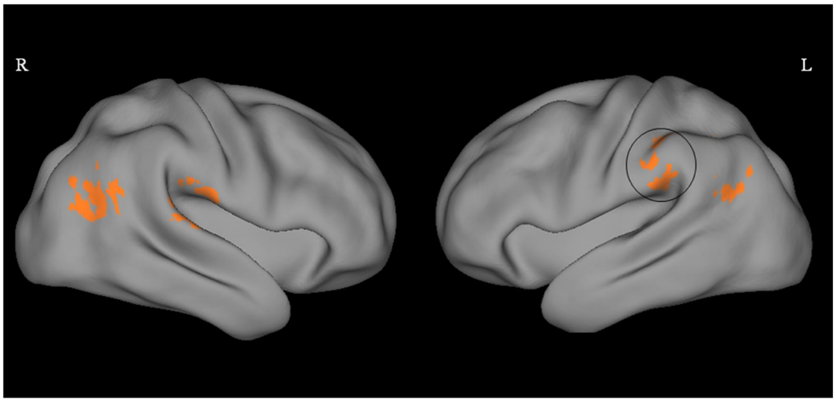

Fig. 2. Statistical parametric map from the ANCOVA displaying significant group differences in bilateral temporoparietal regions ($p_{voxel} < 0.005$, $k > 50$) during phonological processing (*FSM > VM*). Among these regions, one left-hemispheric temporoparietal cluster (marked with circle) survived cluster-level $p < 0.05$, Monte-Carlo corrected for multiple comparisons.

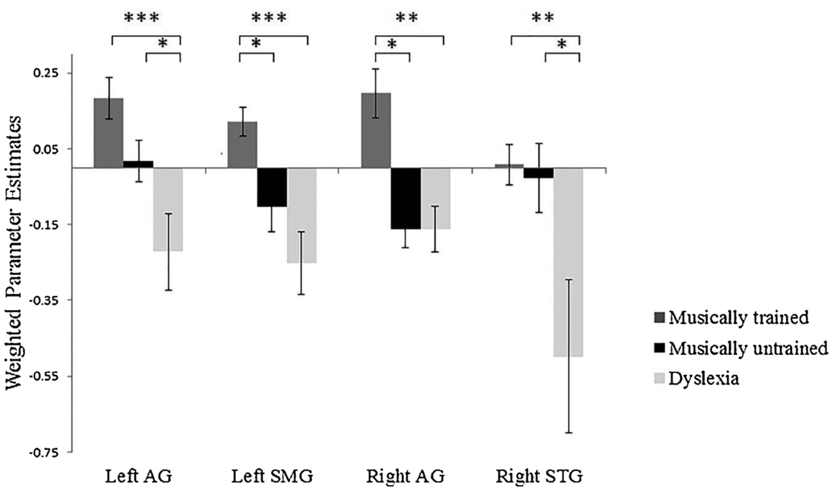

Fig. 3. Mean brain activation (weighted parameter estimates) during phonological processing (*FSM* > *VM*) in bilateral temporoparietal regions of interest (left AG, SMG and right SMG/STG and AG) for musically trained children (gray), untrained children (black), and children with dyslexia (light gray). Error bars represent standard error of the mean (SEM) [Significant pairwise group differences from ANCOVA, controlling for nonverbal cognitive abilities and gender and corrected for multiple comparisons, are indicated by $^{*}p \leq 0.05$, $^{**}p \leq 0.01$, $^{***}p \leq 0.001$].

or an effect of dyslexia. Since the whole brain analysis only indicated regions that significantly differ between all three groups (musically trained, untrained, and those with dyslexia), the subsequent region-of-interest analyses allowed for further specification of pairwise differences and directionality of the activation differences between the groups. Musically trained children significantly differed from children with dyslexia in all four bilateral regions of interest, which leads to a question of which group may be driving the overall effects identified in the whole-brain ANOVA. Musically trained children significantly differed from untrained children in bilateral temporoparietal regions, suggesting a musician-specific effect. In addition, typically developing musically untrained children also significantly differed from children with dyslexia, which is in line with the previously reported hypoactivation among individuals with dyslexia (Richlan et al., 2009). Interestingly, musically trained children demonstrated positive parameter-weighted estimates in all regions, whereas children with dyslexia showed negative parameter estimates during phonological processing (first sound matching > voice matching). The directionality of activation observed in typically developing untrained children aligns with the typical pattern of activation expected for this age, as previous longitudinal work has established that activation associated with this phonological processing task decreases in left-hemispheric temporoparietal regions as reading abilities emerge in school-age children who develop typical word reading abilities (Yu et al., 2018a). As for children with dyslexia, an abundance of previous literature has revealed atypical brain structure and function within these regions in children and adults with dyslexia (as recently reviewed in Ozernov-Palchik et al., 2016; Yu et al., 2018b), characterized by hypoactivation patterns during phonological processing and reading-related tasks (Richlan et al., 2009). Therefore, the observation of negative parameter estimates among children with dyslexia aligns with previous findings, and further suggests that among children with dyslexia, the neural correlates of reading-related tasks, such as phonological processing, fundamentally differs from that of typical development. That said, auditory training has been shown to increase temporoparietal activation in children with dyslexia (Temple et al., 2003), which is also in line with the present findings of hypoactivation patterns in children with dyslexia and enhanced activation by comparison among children with musical training.

Although the cross-sectional design employed only provides findings based on one time point in a relatively small sample, it is intriguing to consider how the enhanced bilateral temporoparietal activation identified among musically trained children may be advantageous for reading development. While hypoactivation in left-hemispheric temporoparietal regions are characteristic of children and adults with dyslexia (as reviewed in Richlan et al., 2009), it has been suggested that this can lead to a 'detour' in the right hemisphere that, if successful and efficient, can lead to improved reading abilities. Specifically, greater right-hemispheric activation in school-age children with dyslexia during a reading task has shown associations with better reading outcomes over time (Hoeft et al., 2011). Similarly, preschool age children with familial risk for dyslexia who subsequently developed into good readers have shown greater white matter development in right-hemispheric language tracts as compared to those who went on to develop reading difficulties (Wang et al., 2017). Additional studies suggest that these differences in hemispheric specialization for language and reading may be shaped by certain environmental experiences. For example, two different instructional approaches to word reading acquisition in an artificial language have shown distinct lateralization preferences such that instruction with a grapheme-phoneme focus led to left-lateralization, whereas a whole-word focus led to less lateralization during subsequent reading (Yoncheva et al., 2015). In another study, right-hemispheric activation during phonological processing has been positively linked with home literacy environment in children with familial risk for dyslexia more so than those without risk, suggesting that home literacy support may facilitate emerging compensatory networks in children at risk for dyslexia (Powers et al., 2016). This finding suggests that environmental factors may facilitate less lateralization. Moreover, the specificity of this finding among children with a family history of dyslexia supports the notion that engagement of right-hemispheric brain regions may be more likely to occur in children who do not have an established left-hemispheric network and engage an alternate pathway that may support their reading development. Although left-hemispheric specialization is typically associated with reading achievement, right-hemispheric activation may be beneficial among individuals who exhibit atypical patterns of neural activation during reading in the left hemispheric reading network and may be engaged through environmental experiences such as musical training.

Converging evidence suggests a working hypothesis that musical training facilitates bilateral temporoparietal activation that, in-turn, establishes an alternate neural pathway for reading that can promote right-hemispheric compensatory neural mechanisms in struggling readers. Specifically, training studies have demonstrated that musical training is one form of dedicated training in the auditory domain that leads to training-induced plasticity in bilateral networks in school-age children, as evidenced in particular by alterations in the corpus callosum (Hyde et al., 2009; Habibi et al., 2017). The neuroplasticity induced by musical training may then lead to less lateralization in brain regions that are not only important for music but also for other non-musical skills, as observed during phonological processing within bilateral temporoparietal regions in the present study. For children with dyslexia, in which hypoactivation has been characteristically identified in left-hemispheric temporoparietal regions, engagement of the right hemisphere may serve as an alternate neural pathway to support their reading development (Hoeft et al., 2011; Powers et al., 2016). Accordingly, engagement of a bilateral network during musical training may build the foundation for improvements in reading skills over time that have been shown behaviorally (Thomson et al., 2013; Flaugnacco et al., 2015; Rautenberg, 2015; Habib et al., 2016), and in-turn facilitate right-hemispheric compensatory neural mechanisms in children with dyslexia.

Future investigations of the neural links between musical training and reading-related processes are needed to further examine the causal mechanisms that underlie this relationship. Since the present study only captured the neural correlates of phonological processing at one time point in development, this design precludes determination of whether musical training directly led to the enhanced pattern of activation during phonological processing observed, and how this may appear in children with dyslexia who have received musical training. However, longitudinal studies demonstrating neural changes in temporal regions following musical training support the notion of a causal link (Hyde et al., 2009; Seither-Preisler et al., 2014; Habibi et al., 2016, 2017). Nonetheless, future work is needed to determine the extent to which musical training may uniquely impact reading development (Thomson et al., 2013), and to further reveal the potential of a concurrent music and literacy-based approach to instruction (Habib et al., 2016). In addition, future research will be necessary to uncover the neural correlates of phonological processing among those with dyslexia who also have extensive musical training, as this group has only been characterized by behavioral measures to date (Bishop-Liebler et al., 2014; Weiss et al., 2014; Zuk et al., 2017). In addition, the age of onset of musical training is an important consideration for future work, given that musicians who started training earlier than age seven have shown significantly larger gray matter cortices in right-hemispheric regions as compared to those who started training later in development (Bailey et al., 2014). Longitudinal neuroimaging investigation is needed to identify whether the neural correlates of phonological processing observed in musically trained children manifest as a direct result of training, or whether these children show predispositions that may be advantageous for both music and reading-related processes. In order to distinguish training effects from potential predispositions, studies are needed that track development from prior to the onset of both formal reading instruction and musical training (Zuk and Gaab, 2018). Taken together, future studies are needed to investigate the precise role and developmental age in which music may have the most positive impact on the trajectories of typical and atypical reading development.

This study sets the foundation for delineating how musical training is associated with the neural correlates of reading-related processes; yet, important additional limitations are to be recognized. The present sample size was constrained by the challenges of recruiting and acquiring quality functional neuroimaging data with pediatric musically trained and atypical populations. Therefore, the present findings need to be interpreted with caution, and replications in future studies with larger sample sizes are necessary. Furthermore, a Behavioral Interleaved Gradient (BIG) design was applied in this study (Eden et al., 1999). While this design ensures that the auditory presentation of the stimuli and the scanner background noise do not overlap, the relatively short TR (6 s) does not allow a compete separation between the hemodynamic response function (HRF) induced by the auditory stimulation from the HRF induced by the scanner background noise, as achieved by a sparse temporal sampling design (Gaab et al., 2007b). However, given the fact that participants in this study were children, the BIG design was chosen in order to ensure task compliance. A sparse temporal sampling designs usually takes a very long time (see Gaab et al., 2003; Gaab and Schlaug, 2003) and further requires the participants to lay still without any task/stimulation for a relative long period of time, which is difficult to achieve in children. This is a particularly significant concern for fMRI investigation with pediatric and special populations, in which recruitment and acquisition of usable data is such a challenge. Limitations also pertain to the corresponding threshold of the whole brain results reported. Although Monte-Carlo cluster-level correction for multiple comparisons was achieved for one left-hemispheric temporoparietal cluster, the other effects reported were established based on uncorrected thresholds and should therefore be interpreted with great caution. We decided to report these results since a) the reported activation of temporoparietal brain regions during phonological processing closely aligns with a substantial body of evidence that has shown disruptions in these regions among children with reading difficulties (as reviewed in Richlan et al., 2009) and b) previous studies which utilized the same thresholds have reported activations in these regions for the identical task (Raschle et al., 2012a, a). It is further important to note that pediatric populations often show lower signal-to-noise ratios and greater interindividual variance (Thomason et al., 2005). As for behavioral measurements, hearing screening was conducted but more formal evaluation would be necessary to determine whether sub-clinical deficiencies in sound processing or hearing may be evident. Moreover, standardized assessments of word reading and fluency abilities were acquired, but only included timed measures for the purposes of verifying appropriate group assignment in the present study. It will be of interest in future work to further consider brain-behavioral relationships in this context through measurements of specific components of phonological awareness, or reading comprehension, for instance. Future studies are needed to affirm the implications of the present findings with more substantial sample sizes, conservative functional neuroimaging thresholds, and a more extensive battery of standardized assessments to further examine corresponding behavior in the areas of phonological awareness and reading.

5. Conclusions

Overall, the present study has identified neural correlates of phonological processing in temporoparietal regions that are disrupted in children with dyslexia and enhanced in musically trained children relative to musically untrained children. This study provides neural evidence of specialization in musically trained children that may underlie the putative positive effects of musical training on phonological processing during typical and atypical reading development. These findings suggest that musical training may facilitate neural activation that can potentially serve as a compensatory mechanism to support children with dyslexia. This line of work has implications for the importance of music education programs in the general school curriculum as one training option that may be advantageous for supporting reading development in addition to providing musical instruction.

Declarations of interest

None.

Acknowledgements

We thank all former lab members for their contributions to parts of the data collection and analysis, particularly Christopher Benjamin, Sarah Meissner, Monica Vakil-Dewer, and Maria Chang. We also thank all participants and their families for dedicating their time to this study. This research was supported by the GRAMMY Foundation, the Eunice Kennedy Shriver National Institute of Child Health and Human Development, the National Institute of Health Institutional National Research Service Award (NIH T32 DC000038-22 and F31 DC015919-01 to Zuk), the American Speech-Language-Hearing Foundation (to Zuk), the Sackler Scholar Programme in Psychobiology (to Zuk), and the National Science Foundation (IGERT grant DGE-1144399 and GRFP grant DGE-1747453 to Perdue).

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