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Cortical thickness abnormalities associated with dyslexia, independent of remediation status

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ABSTRACT

Abnormalities in cortical structure are commonly observed in children with dyslexia in key regions of the "reading network." Whether alteration in cortical features reflects pathology inherent to dyslexia or environmental influence (e.g., impoverished reading experience) remains unclear. To address this question, we compared MRI-derived metrics of cortical thickness (CT), surface area (SA), gray matter volume (GMV), and their lateralization across three different groups of children with a historical diagnosis of dyslexia, who varied in current reading level. We compared three dyslexia subgroups with: (1) persistent reading and spelling impairment; (2) remediated reading impairment (normal reading scores), and (3) remediated reading and spelling impairments (normal reading and spelling scores); and a control group of (4) typically developing children. All groups were matched for age, gender, handedness, and IQ. We hypothesized that the dyslexia group would show cortical abnormalities in regions of the reading network relative to controls, irrespective of remediation status. Such a finding would support that cortical abnormalities are inherent to dyslexia and are not a consequence of abnormal reading experience. Results revealed increased CT of the left fusiform gyrus in the dyslexia group relative to controls. Similarly, the dyslexia group showed CT increase of the right superior temporal gyrus, extending into the planum temporale, which resulted in a rightward CT asymmetry on lateralization indices. There were no group differences in SA, GMV, or their lateralization. These findings held true regardless of remediation status. Each reading level group showed the same "double hit" of atypically increased left fusiform CT and rightward superior temporal CT asymmetry. Thus, findings provide evidence that a developmental history of dyslexia is associated with CT abnormalities, independent of remediation status.

1. Introduction

Developmental dyslexia is a neurological condition characterized by difficulties in reading-related tasks such as word recognition and spelling in spite of normal intelligence, adequate education and motivation to read proficiently (Lyon et al., 2003). Structural MRI approaches [see Richlan et al. (2013) and Linkersdörfer et al. (2012) for meta-analyses] have identified abnormalities associated with dyslexia in regions within the reading network (Pugh et al., 2000a). Whether alteration in cortical structure reflects pathology inherent to dyslexia or environmental influence (e.g., impoverished reading experience or compensatory changes) remains unclear.

Prior studies have addressed this question using MRI measures of gray matter volume (GMV). Raschle et al. (2011) reported that pre-reading children with familial history of dyslexia have less GMV within the reading network, relative to control children without a familial history of dyslexia. This finding suggests that structural brain anomalies in dyslexia are present before reading experience rather than experience-dependent. In contrast, Krafnick et al. (2014) showed that GMV in multiple regions, including the left temporal cortex, is reduced in dyslexic children relative to age-matched controls, but not relative to reading-level-matched younger controls. The authors concluded that GMV differences in dyslexia are related to the level of current reading ability, which partially reflects the impoverished reading experience in dyslexics, rather than dyslexia per se.

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Alternative measurements of cortical gray matter to GMV include cortical thickness (CT) and surface area (SA). Both CT and SA are highly heritable (Joshi et al., 2011; Panizzon et al., 2009; Rimol et al., 2010) and can delineate genetic influences on brain structure with more precision than GMV (Winkler et al., 2010). Both can be potential markers for neurodevelopmental disorders (Hazlett et al., 2011; Narr et al., 2009). In addition, CT can be affected by life experience, such as training (Engvig et al., 2010; Lazar et al., 2005). Thus far, few studies have examined CT and SA variations associated with dyslexia (Altarelli et al., 2013; Altarelli et al., 2014; Frye et al., 2010; Kushch et al., 1993). Here, we examined CT, SA and GMV to identify structural abnormalities in subgroups of dyslexia with different levels of reading ability. We used an observational design and tested remediated (i.e., normalized reading ability) and non-remediated dyslexia subgroups, as well as an age-, gender-, handedness-, and IQ-matched typically developing comparison group. If structural abnormalities are present in all subgroups with a history of dyslexia, relative to controls, this would suggest persistent cortical abnormalities that characterize dyslexia, irrespective of current reading ability. Such findings could potentially serve as early and reliable cortical markers of dyslexia in children. By contrast, abnormal CT, SA or GMV only in the non-remediated group, but not in the remediated groups would reflect the effect of current reading impairments, and thus support environmental effects (e.g., impoverished reading experience, which may be normalized in the remediated groups).

Hypothesizing that cortical abnormalities are inherent to dyslexia (Galaburda et al., 1985; Raschle et al., 2011), we predicted that altered patterns of CT, SA and/or GMV, if present, could be found across all dyslexia subgroups, regardless of remediation status. We also addressed a long-lasting question regarding the absence of a leftward structural asymmetry in the dyslexia brain (Galaburda et al., 1985; Kushch et al., 1993; Larsen et al., 1990; Leonard et al., 2001). In addition, since CT is a measure genetically and phenotypically independent from SA and GMV (Dickerson et al., 2009; Lemaitre et al., 2012; Panizzon et al., 2009; Winkler et al., 2010), we expected that CT findings would generally diverge from other measures. Finally, we evaluated whether there was an additive effect of dyslexia and remediation on gray matter structure for each surface-based metric by testing for differential effects in each remediation subgroup (i.e., whether the largest gray matter abnormalities are found in the non-remediated subgroup).

2. Material and methods

2.1. Participants

Children with a history of dyslexia ("Dys") were identical to those published previously by Koyama et al. (2013), except for one participant excluded due to severe artifacts in the T1 image. They were native English speakers ($n = 32$), recruited through referrals from the clinical services at The Child Study Center at New York University Langone Medical Center and the New York International Dyslexia Association. Inclusion was based on parental report of prior diagnosis of reading disorder in accordance with DSM-IV or ICD-10, and prior written documentation. We also investigated history of previous or current DSM-IV-TR diagnoses other than dyslexia through informal interviews with parents and by reviewing prior clinical evaluations whenever available. Three out of the 32 children were diagnosed with ADHD.

Based on the current literacy competence level, measured by the Wechsler Individual Achievement Test—Second Edition (WIAT) (Wechsler, 2001), children with a history of dyslexia were sub-divided into three groups: (1) children with current deficits in both reading and spelling ("Dys-N": Dyslexia with no remediation, $n = 10$), (2) children with a previous diagnosis of dyslexia but exhibiting no current reading deficit ("Dys-R": Dyslexia with reading remediation, $n = 11$), and (3) children with a previous diagnosis of dyslexia but exhibiting no current deficits in either reading or spelling ("Dys-RS": Dyslexia with reading and spelling remediation, $n = 11$). A reading or spelling deficit was defined as a current standard score below 85 (i.e., one standard deviation below the norm) on the WIAT Word Reading or Spelling subscales. Information from parental report (and supporting documentation when available) confirmed that none of the children in the Dys-N group had a history of targeted dyslexia intervention training prior to the current study, while all children in the Dys-R and Dys-RS groups had been in one or more targeted programs (e.g., the Orton Gillingham approach, http://www.ortonacademy.org; Wilson Language Training, http://www.wilsonlanguage.com; or various school intervention efforts). Information from prior written documentation verified a history of literacy impairment in all children in the remediation groups (standard scores lower than 85 on any type of standardized literacy test prior to remediation), and provided evidence that the majority of these children had exhibited phonological deficits.

Typically developing children (TDC, $n = 32$), who were native speakers of English, were selected as controls from a larger pool of children participating in ongoing studies at NYU Child Study Center. All children in the TDC group exhibited intact reading and spelling skills with both WIAT Word Reading and Spelling scores above 85. No previous or current DSM-IV-TR diagnoses were found based on the Schedule for Affective Disorders and Schizophrenia for School-Age Children—Present and Lifetime Version (KSADS-PL) (Kaufman et al., 1996), which was administrated to parents and child participants separately.

The Dys and the TDC groups were group-matched on age (overall mean age = 12.1 ± 2.3 years: range = 7.7–16 years), gender, estimated full-scale IQ and handedness. Full-scale IQ was estimated with the Wechsler Abbreviated Scale of Intelligence (WASI) (Wechsler, 1999); all participants had full-scale IQ above 85. Subgroups within the Dys group were also matched on the same variables. Table 1 provides demographic and cognitive measures for the Dys and the TDC groups. Table 2 provides demographic and cognitive measures for the three subgroups within the Dys group.

2.2. MRI data acquisition

MRI data were collected on a Siemens Allegra 3 T scanner at the New York University Center for Brain Imaging. We acquired a high-resolution T1-weighted volume for each participant (TR = 2530 ms; TE = 3.25 ms; TI = 1100 ms; flip angle = 7°; 128 slices; field of view = 256 mm; voxel size = 1.3 × 1 × 1 mm).

2.3. Surface reconstruction and neuroanatomical measurements

FreeSurfer (5.1.0) software package (http://surfer.nmr.mgh.harvard.edu) was used to reconstruct cortical surfaces of each participant from the MRI scans. Main steps included (1) Talairach registration, (2) intensity normalization, (3) skull stripping, (4) white matter segmentation, (5) generation, refinement and tessellation of the white matter surface (i.e., the boundary between gray and white matter), (6) deformation of the white matter surface into the pial surface (i.e., the boundary between the gray matter and the cerebrospinal fluid) and (7) automatic correction of topological defects. Details of these steps are described elsewhere (Dale et al., 1999; Fischl et al., 1999, 2001). To ensure accuracy of the reconstruction, we also inspected and manually edited the reconstructed surfaces whenever necessary during the process. All inspection and editing were performed by one trained operator to avoid variability introduced by multiple raters.

CT at each vertex was measured as the average of the shortest distances from this vertex to the opposing surface, and to this vertex from the opposing surface (Fischl and Dale, 2000); SA at each vertex was measured as the average number of tessellation units surrounding it (Winkler et al., 2012). GMV at each vertex was the product of CT and SA. For group comparisons of CT, SA and GMV, cortical surfaces of each participant were registered based on folding patterns to a spherical coordinate system (Fischl et al., 1999). Individual CT, SA and GMV maps were smoothed with a Gaussian kernel (10 mm FWHM) before