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Aberrant functional activation in school age children at-risk for mathematical disability: A functional imaging study of simple arithmetic skill

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ABSTRACT

We used functional magnetic resonance imaging (fMRI) to explore the patterns of brain activation associated with different levels of performance in exact and approximate calculation tasks in well-defined cohorts of children with mathematical calculation difficulties (MD) and typically developing controls. Both groups of children activated the same network of brain regions; however, children in the MD group had significantly increased activation in parietal, frontal, and cingulate cortices during both calculation tasks. A majority of the differences occurred in anatomical brain regions associated with cognitive resources such as executive functioning and working memory that are known to support higher level arithmetic skill but are not specific to mathematical processing. We propose that these findings are evidence that children with MD use the same types of problem solving strategies as TD children, but their weak mathematical processing system causes them to employ a more developmentally immature and less efficient form of the strategies.

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Some children with normal intelligence have a disability in mathematics (MD) that makes the acquisition of grade-level mathematical competencies a challenge, despite adequate instruction (Barrouillet, Fayol, & Lathuliére, 1997; Fayol, Barrouillet, & Marinthe, 1998; Geary, 1990; Geary & Brown, 1991). Children with MD use the same types of strategies as their typically developing peers (Geary, 1990; Geary, Hamson, & Hoard, 2000; Geary, Hoard, & Hamson, 1999; Hanich, Jordan, Kaplan, & Dick, 2001; Jordan, Hanich, & Kaplan, 2003a,b). However, as early as first grade, children with MD use less mature strategies and make more calculation errors (Geary et al., 1999, 2000; Jordan & Montani, 1997; Jordan et al., 2003a). In particular, children with MD demonstrate a specific weakness in the ability to accurately and quickly retrieve mathematical facts to solve single digit arithmetic problems (Barrouillet et al., 1997; Garnett & Fleischner, 1983; Geary, 1990, 1993; Hanich et al., 2001; Jordan & Montani, 1997; Jordan et al., 2003a; Temple & Sherwood, 2002). Although there have been substantial gains in the understanding of cognitive risk factors for MD at a behavioral level, its neural bases in children remain to be explained.

Studies with adults provide evidence of the brain regions involved in mathematical disability (Dehaene & Cohen, 1991; Kahn & Whitaker, 1991; McCloskey, Harley, & Sokol, 1991). For example, lesion studies demonstrated that an individual with a left subcortical lesion exhibited an inability to retrieve and manipulate math facts; whereas, an individual with a left parietal lesion suffered from problems with subtraction while the ability to retrieve math facts via rote memory was unimpaired. Functional differences between disabled and control groups are evident in these areas in imaging studies investigating mathematical disorders in individuals with genetically based disorders such as Turner syndrome (Alexander & Money, 1966; Molko et al., 2003) and Fragile X (Burbaud et al., 1995; Menon, Rivera, White, Glover, & Reiss, 2000; Rickard et al., 2000). In particular, group differences that resembled the lesion studies' findings were found in the parietal cortex. Although these studies provide critical neurobiological information on brain regions involved in mathematical ability within the populations under investigation, the relevancy of these results to children with MD is uncertain. Brain trauma in the lesion studies typically encompasses large anatomical regions, limiting the specificity with which one can link a particular brain region to a deficient cognitive process. Additionally, the cognitive correlates

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underlying mathematical ability in adults with a genetically based mathematical disorder may differ from those that occur in MD.

According to these findings, children with poor mathematical skills ought to show functionally distinct profiles from children with good math skills in frontal and parietal regions during simple calculation tasks. A single functional imaging study investigating simple arithmetic skill has been published in which activation in children with MD was compared to activation in typically developing controls (Kucian et al., 2006). Using an ROI based approach, group differences were found in frontal and parietal regions during an approximate calculation task; children with MD had weaker activation. However, no group differences were found during an exact calculation task. The lack of group differences during the exact calculation task is inconsistent with the behavioral evidence that children with MD have a specific weakness in the ability to accurately retrieve math facts from long term memory (Barrouillet et al., 1997; Garnett & Fleischner, 1983; Geary, 1990, 1993; Hanich et al., 2001; Jordan & Montani, 1997; Jordan et al., 2003a; Temple & Sherwood, 2002). A possible explanation for this result is that the mixture of grade level in school in the Kucian et al. (2006) study may have diminished the power of the study to find group differences. Mathematical knowledge is significantly influenced by quantity and quality of instruction (Geary, Brown, & Samaranayake, 1991), and Kucian, von Aster, Loenneker, Dietrich, and Martin (2008) maintained that functional differences between adults and children during simple arithmetic tasks were associated with a specialization for mathematical skill that occurs with schooling.

For our purposes, the results of these studies suggest important directions for research on children with MD. The aim of the current study was to describe quantitatively the patterns of brain activation associated with different levels of performance in exact calculation and estimation tasks in well-defined cohorts of children with MD and normal controls (TD) in the same grade level in school. We hypothesized that we would find significant group differences in a largely left hemisphere network during fact retrieval and exact calculation and in frontal and parietal regions during an approximation task.

1. Materials and methods

1.1. Participants

Participants were 48 children in the third grade, ranging in age from 8 years and 1 month of age to 9 years and 1 month of age (mean age = 8.2, S.D. = 2.9). We focused on third grade because basic skills that support exact and approximate calculation tasks are taught in first and second grade, creating a range of skill development by third grade. Children were recruited over a period of 2 years from a larger study investigating the effects of types of intervention in mathematics. Behavioral scientists within the intervention study assumed responsibility for recruitment in the schools, excluding children with a brain injury, other physical disabilities, severe emotional problems, uncorrected sensory disorders, ADHD, or an IQ of less than 80. Within this larger study, children were identified as TD or MD. To be in the present imaging study, children in the TD group had to score at or above the 49th percentile on the calculation screening measure described below and had to receive all math instruction in a regular classroom. A high ability was used as a cut-off to ensure that participants identified as TD had good calculation skills (see Shaywitz et al., 2002). Difficulty in math was defined as a skill at or below the 25th percentile on the screening measure. This percentile was chosen because children who exhibit mathematics difficulties include those performing in the low average range (e.g., at or below the 25%). Imaging data were collected from January to July on 36 MD and 27 TD children. Twelve MD and 3 TD children were removed from analyses because of excessive movement artifacts or failure to complete the in-magnet tasks. High-resolution magnetic resonance scans indicated that none of the participants had any overt neuroanatomical abnormality. This study was approved by the Vanderbilt University Institutional Review Board. Written informed consent was obtained from the children's guardians. Written assent was obtained from the children.

1.2. Screening measure

As part of their screening process for inclusion in the larger study, trained examiners administered the calculation subtest of the Wide Range Achievement Test—Third Edition (WRAT-3, Wilkinson, 1993) to children during the first semester of their third-grade year. The WRAT-3 is a broadly used standardized measure of achievement. The calculation subtest involves the identification of numbers and computations that increase in difficulty. Means and standard deviations for the groups' performance on the screening measure are shown in Table 1.

1.3. Experimental design and procedure

1.3.1. Imaging stimuli and task

Children performed the imaging tasks on a computer outside of the MRI scanner to acclimate them to the structure and speed of the tasks. A subset of each task with novel equations was used for these practice sessions. Children were put in a mock scanner to simulate the in-magnet environment and to introduce them to the various noises made by the magnet. After completing the practice sessions, children performed the experimental tasks in the MRI scanner. During the scanning procedure, participants lay supine in the magnet, looking up at a mirror that reflected a screen on which computer-controlled stimuli were projected using E-Prime software (Psychology Software Tools, Inc.). At the beginning of each trial, participants saw a screen with written instructions, and the examiner read these instructions aloud to the participants. In a few cases, the child was unwilling or unable to complete a task. Data for those participants were not included in the present study.

The imaging paradigm was a standard block design. Each functional imaging run was 5 min in duration and consisted of three 40 s blocks of each experimental task (an exact and approximate calculation task), three 40 s blocks of the control task (Greek letter matching task) and three 20 s blocks of rest. The calculation tasks mirrored Dehaene, Spelke, Pinel, Stanescu, and Tsivkin (1999). All task items were presented vertically with three response choices shown horizontally at the bottom. Participants chose the correct answer by pressing a button (on a MRI compatible response pad) corresponding to the location (left, middle, right) of the correct response. The items and response choices remained on the screen until the participant responded or the block ended after 40 s. Numeric and control tasks were self-paced; therefore, the number of trials that participants completed within each block varied. Rogers, Anderson, Gatenby, Cannistraci, and Gore (2007) demonstrated that paced and self-paced versions of the same mathematical task place comparable demands on calculation-specific and comparison-specific brain regions. Task presentation was randomized across all participants, and items were randomized within each block. In all trials, when not actively engaged in a task, participants were instructed to fixate on a gray square on the screen.

A Philips 3 Tesla Achieva (Philips Healthcare Inc.) was used to acquire the MRI data. Anatomical scans were acquired for approximately 15 min prior to functional scans. The anatomical images were acquired with a T-1 weighted, 3D turbo field echo pulse sequence (170 slices, 1 mm^3 voxels). A high-resolution 2D T-1 anatomical series was also acquired at the same location and slice thickness as the functional data. All functional data were acquired using a gradient echo EPI sequence (FOV 220 mm, TE 35 ms, TR 2000 ms, flip angle of 79°, 80 × 80 acquisition matrix interpolated to 128 × 128 image matrix, 28 slices, 3.5 mm thick with a gap of 0.35 mm).

1.3.2. Data analysis

All functional data were analyzed using Brainvoyager QX (Brain Innovations Inc.). Each functional volume was motion corrected using 3D rigid body transformations to the first volume of the first functional run. Each subject's fMRI data sets were adjusted for slice timing differences and temporal drifts were removed with a linear trend removal. Individuals' functional data were coregistered to their own high-resolution 3D anatomic scan then normalized to Talairach standardized space (Talairach & Tournoux, 1988). The normalized volumes were smoothed with a 6 mm FWHM Gaussian kernel. Volumes where head motion exceeded 3 mm or 3° relative to the first volume were removed from the data set, with corresponding rows of the design matrix also removed prior to fitting. A general linear model was fit at each voxel in each subject to produce parametric maps of normalized signal change for each task condition. To investigate within-group activation, a second-level analysis was used to generate group-level statistical *t*-maps comparing each math task to its symbol-matching control task (for the MD and TD groups separately). MD and TD groups were compared directly in a two-way analysis of variance (ANOVA) with a between-subject effect of group (MD versus TD) and a within-subject effect of condition (math task versus symbol-matching control). A voxelwise statistical threshold of $p < 0.001$ was applied to the statistical maps, which were then additionally corrected for multiple comparisons at the cluster level ($p < 0.05$, corresponding to a cluster size of 432 mm^3). Talairach coordinates were derived from the local maxima of each cluster activated over the threshold. The Talairach Daemon (Lancaster et al., 2000) was used to identify the anatomical structures, considering those within 1 cm of the local maximum.

2. Results

2.1. Behavioral

Analysis with multivariate general linear model using SPSS 16.0 revealed no significant differences between children with versus without MD in accuracy levels on the exact calculation