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What difference does a year of schooling make?: Maturation of brain response and connectivity between 2nd and 3rd grades during arithmetic problem solving

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Abstract

Early elementary schooling in 2nd and 3rd grades (ages 7-9) is an important period for the acquisition and mastery of basic mathematical skills. Yet, we know very little about neurodevelopmental changes that might occur over a year of schooling. Here we examine behavioral and neurodevelopmental changes underlying arithmetic problem solving in a well-matched group of 2nd ($n = 45$) and 3rd ($n = 45$) grade children. Although 2nd and 3rd graders did not differ on IQ or grade- and age-normed measures of math, reading and working memory, 3rd graders had higher raw math scores (effect sizes = 1.46-1.49) and were more accurate than 2nd graders in an fMRI task involving verification of simple and complex two-operand addition problems (effect size = 0.43). In both 2nd and 3rd graders, arithmetic complexity was associated with increased responses in right inferior frontal sulcus and anterior insula, regions implicated in domain-general cognitive control, and in left intraparietal sulcus (IPS) and superior parietal lobule (SPL) regions important for numerical and arithmetic processing. Compared to 2nd graders, 3rd graders showed greater activity in dorsal stream parietal areas right SPL, IPS and angular gyrus (AG) as well as ventral visual stream areas bilateral lingual gyrus (LG), right lateral occipital cortex (LOC) and right parahippocampal gyrus (PHG). Significant differences were also observed in the prefrontal cortex (PFC), with 3rd graders showing greater activation in left dorsal lateral PFC (dlPFC) and greater deactivation in the ventral medial PFC (vmPFC). Third graders also showed greater functional connectivity between the left dlPFC and multiple posterior brain areas, with larger differences in dorsal stream parietal areas SPL and AG, compared to ventral stream visual areas LG, LOC and PHG. No such between-grade differences were observed in functional connectivity between the vmPFC and posterior brain regions. These results suggest that even the narrow one-year interval spanning grades 2 and 3 is characterized by significant arithmetic task-related changes in brain response and connectivity, and argue that pooling data across wide age

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ranges and grades can miss important neurodevelopmental changes. Our findings have important implications for understanding brain mechanisms mediating early maturation of mathematical skills and, more generally, for educational neuroscience.

Keywords

arithmetic; children; intraparietal sulcus; dorsal lateral prefrontal cortex; fMRI

How much difference does a year of schooling make in children's arithmetic problem solving abilities? This question is of great interest to psychologists and educators alike (Case, 1978). Previous behavioral and classroom-based research studies have shown that arithmetic proficiency undergoes significant improvement in elementary school; however, surprisingly little is known about its neurodevelopmental underpinnings. Here we examine the neural correlates of the maturation of arithmetic problem solving skills over a narrow developmental window spanning a one year interval between 2nd and 3rd grades.

Early elementary school represents an important period for the acquisition and mastery of arithmetic fact knowledge. Behavioral research has characterized a progression of increasingly sophisticated calculation procedures leading to the greater use of direct retrieval over time (Siegler & Shrager, 1984). By 2nd grade, children are typically able to answer single-digit addition problems, although rapid fact retrieval is still not mature in most children (N. C. Jordan, Hanich, & Kaplan, 2003a). Between 2nd and 3rd grades, problem solving abilities generally progress from effortful counting strategies to more automatic retrieval strategies, although the extent and magnitude of skill maturation and the sources of individual variability are less well understood. In a school-based study of typically developing children, growth curve modeling revealed that from the beginning of 2nd grade to the end of 3rd grade there was only a modest increase in the number of correctly answered problems (less than one item); however there was a large decrease in the use of finger counting and an increase in the number of correctly retrieved items (N. C. Jordan, et al., 2003a).

Although most of the school-based studies in this age group have focused on accuracy (Fuchs et al., 2006; J. A. Jordan, Mulhern, & Wylie, 2009; N. C. Jordan, Glutting, & Ramineni, 2010; N. C. Jordan, et al., 2003a; N. C. Jordan, Hanich, & Kaplan, 2003b), the few studies that have examined response times have suggested developmental improvements in reaction times of 1-4 seconds on average between 1st, 2nd and 3rd grades (Ashcraft, 1982; Geary, Hamson, & Hoard, 2000). Besides procedural improvements, significant increases in conceptual knowledge occur in this period (see Prather & Alibali, 2009, for a review). For example, understanding the commutative property of addition enables the use of more sophisticated strategies such as the *min* strategy, (i.e. counting up from the largest addend, regardless of presentation order (Geary, Brown, & Samaranayake, 1991)). Taken together, these findings suggest that both procedural and conceptual knowledge of arithmetic mature during early elementary schooling between grades 2 and 3, resulting in increased accuracy and faster reaction times. We currently know nothing about the neurocognitive basis of this change.

Normative functional neuroimaging studies in children and adults have consistently implicated the intraparietal sulcus (IPS) within the posterior parietal cortex (PPC) as a region specifically involved in the representation and manipulation of numerical quantity (Dehaene, Piazza, Pinel, & Cohen, 2003). With experience and learning, the IPS builds an increasingly amodal, language-independent semantic representation of numerical quantity (Ansari, 2008; Bruandet, Molko, Cohen, & Dehaene, 2004; Cantlon, Brannon, Carter, &

Pelphrey, 2006; Cantlon et al., 2009). In addition to the IPS, mathematical information processing also critically involves activation and deactivation in a more distributed network of regions within the dorsal visual stream encompassing the superior parietal lobule (SPL), the angular gyrus (AG) and the supramarginal gyrus regions of the PPC (Delazer et al., 2003; Grabner et al., 2009; Ischebeck et al., 2006; Menon, Rivera, White, Glover, & Reiss, 2000; Rickard et al., 2000; Wu et al., 2009; Zago et al., 2001).

Previous developmental brain imaging studies have focused on maturation of numerical and arithmetic skills over a large age range, spanning one or more decades. Kawashima and colleagues found that, compared to 40-49 year old adults, 9-14 year old children had reduced activation in the left and right IPS during multiplication and subtraction, but equal engagement of prefrontal cortex (PFC) for both groups (Kawashima et al., 2004). Kucian and colleagues (Kucian, von Aster, Loenneker, Dietrich, & Martin, 2008) found greater left IPS activity in 22-32 year old adults and greater right anterior cingulate cortex activity in 9- and 12-year old children during approximate addition. Rivera and colleagues (Rivera, Reiss, Eckert, & Menon, 2005) used a cross-sectional design in children and adults spanning ages 8-19 years to investigate changes in brain response during the solution of mixed addition and subtraction problems. They found that activity in the bilateral superior and middle frontal gyri and the left inferior frontal gyrus decreased with age whereas activity in left supramarginal gyrus and the adjoining IPS showed an opposite profile of increased responses with age. The authors argued that the development of arithmetic problem solving skills between childhood and adulthood is characterized by decreased engagement of the PFC and increased engagement and functional specialization of the PPC.

A similar pattern of developmental shifts from the PFC to the PPC have been reported in other numerical tasks involving symbolic and non-symbolic magnitude comparisons. In a non-symbolic magnitude discrimination task Cantlon and colleagues (Cantlon, et al., 2009) found that while 6-7 year old children engaged the bilateral inferior frontal gyrus and adjoining insular cortex, these PFC areas were not significantly activated in 24 year old adults. In contrast, both groups showed activation of the left IPS, although the spatial extent of activity was greater in adults. Further, numerical distance effects (greater activity for comparisons involving smaller ratios) were correlated with left IPS activity in adults (Pinel, Dehaene, Riviere, & LeBihan, 2001), whereas children displayed this effect in frontal areas (Ansari & Dhital, 2006; Ansari, Garcia, Lucas, Hamon, & Dhital, 2005). In a non-symbolic comparison task, Ansari and Dhital (Ansari & Dhital, 2006) found that only 9-11 year old children displayed a distance effect in the right dorsal lateral PFC, whereas 19-21 year old adults had stronger distance effect in the left anterior IPS. Similarly, in a symbolic number comparison task using the same age groups, Ansari and colleagues (Ansari, et al., 2005) found that adults showed sensitivity to numerical distance bilaterally in the IPS; whereas in children, the right precentral gyrus and right inferior frontal gyrus were sensitive to numerical distance. Thus, although the precise neural locus of development varies with cognitive process and stimulus, a consistent profile of decreased reliance on the PFC and increased reliance on the PPC has been found in a wide range of studies of numerical cognition involving comparisons of children and adults.

Most previous studies of numerical cognition have focused on dorsal stream areas, considerably less attention has been paid to ventral visual stream areas such as the parahippocampal gyrus (PHG), the lateral occipital cortex (LOC), the fusiform gyrus (FG) and the lingual gyrus (LG) which are often co-activated with the PPC during arithmetic processing (Keller & Menon, 2009; Rickard, et al., 2000; Rosenberg-Lee, Tsang, & Menon, 2009; Wu, et al., 2009; Zago, et al., 2001). These ventral areas are thought to play an important role in recognition and discrimination of visual objects and number-letter strings (Allison, Puce, Spencer, & McCarthy, 1999; Milner & Goodale, 2008), rather than semantic

processing of quantity and numerosity. Crucially, the involvement of ventral visual areas in arithmetic problem solving also undergoes significant developmental changes; specifically, the LOC showed increased activation with age, and the PHG showed reduced response with age (Rivera et al., 2005). Despite rapid progress in charting development across broadly defined age groups (e.g. children versus adults) over the past decade, almost nothing is known about neurodevelopmental changes that can occur in a narrow window of schooling in mathematics, reading or any other cognitive domain relevant for academic success. The present study addresses this important gap in our current understanding of cognitive skill development by investigating how the neural correlates of mathematical information processing change over a one year interval.

In the current study, we focus on developmental changes in math problem solving abilities in 7 to 9 year old children in the 2nd and 3rd grades of elementary school. We used functional magnetic resonance imaging (fMRI) and well-matched experimental tasks which manipulate arithmetic complexity. In adults, previous imaging studies have manipulated complexity by varying the number of operations in a problem (Menon, Rivera, et al., 2000) or the number of digits in the operands (Gruber, Indefrey, Steinmetz, & Kleinschmidt, 2001; Rosenberg-Lee, Lovett, & Anderson, 2009; Zago, et al., 2001). Behavioral research using single-digit problems in adults and children has consistently reported longer reaction times and more errors for problems with larger operands (Barrouillet & Lepine, 2005; Campbell & Metcalfe, 2007; Zbrodoff & Logan, 2005). In adults, imaging studies of single-digit problems have found increased fronto-parietal activation with increased complexity (Jost, Khader, Burke, Bien, & Rosler, 2009; Kiefer & Dehaene, 1997; Stanescu-Cosson et al., 2000). Based on these findings, we used single-digit addition problems in which we contrasted 'Complex' problems (neither of the addends were '1') with 'Simple' problems (one of the addends was '1'). This allowed us to simultaneously control for basic number and symbol processing, as well as decision making and sensorimotor response with both 'Complex' and 'Simple' problems presented in exactly the same format.

We used a cross-sectional design to characterize the effects of one year of schooling by comparing forty-five 2nd and forty-five 3rd grade children. We hypothesized that 3rd grade children would show significantly better behavioral performance than 2nd grade children. We predicted 3rd graders would show reduced reliance on PFC and greater reliance on PPC and LOC when compared to 2nd graders. Structural and functional brain imaging studies have suggested that development is characterized by protracted maturation of long range connectivity from childhood to adulthood (Supekar et al., 2010; Uddin, Supekar, & Menon, 2010). In particular, maturation of PFC connectivity with posterior association cortex is thought to play a prominent role in cognitive development (Menon, Boyett-Anderson, & Reiss, 2005; Stevens, 2009). We therefore predicted that functional maturation of arithmetic skills in 3rd grade children would be characterized by increased task-related temporal coupling of the PFC with posterior brain regions. Within posterior brain regions we distinguish between dorsal and ventral visual stream areas as both sets of areas have shown enhanced activation with development (Rivera et al (2005) allowing us to examine whether developmental changes in PFC connectivity are specific to the parietal cortex or extend to ventral visual areas as well.

Methods

Participants

Participants were recruited from a wide range of schools in the San Francisco Bay Area using mailings to schools, postings at libraries and community groups. Prior to inclusion in the study, parents completed a questionnaire which screened for handedness, history of psychiatric illness and medication use. If the child was right-handed and had no history of

psychiatric illness or medication use, they continued to a neuropsychological assessment session. One child failed to meet the inclusion criteria of having both performance and verbal IQ above 80, as measured using the Wechsler Abbreviated Scales of Intelligence (Wechsler, 1999). All participants were scanned in the summer following completion of either 2nd or 3rd grade. From a group of 62 2nd graders and 56 3rd graders we selected 90 typically developing participants based on their Wechsler Individual Achievement Test – Second Edition (WIAT-II, Wechsler, 2001) scores. Following Murphy and colleagues (Murphy, Mazzocco, Hanich, & Early, 2007), we chose participants who had Mathematical Reasoning scores between the 25th and 98th percentile. Mathematical Reasoning scores were the most discrepant measure between the grades, and using this criterion automatically allowed us to match the 2nd and 3rd graders on all the other cognitive measures including Numerical Operations, Word Reading and Reading Comprehension subtests of the WIAT-II. The final sample included 45 children in 2nd grade (15 girls, 30 boys) between the ages of 7.03 to 8.40 ($M = 7.67$ years; $SD = 0.40$), and 45 children in 3rd grade (24 girls, 21 boys) between the ages of 7.90 and 9.40 ($M = 8.67$ years; $SD = 0.40$). A chi-square test revealed that there was no significant difference in the distribution of genders between the grades ($\chi^2(1) = 3.66, p = .06$).

Standardized measures of cognitive abilities

Mathematical abilities—Mathematical abilities were assessed using the WIAT-II (Wechsler, 2001). This achievement battery includes nationally standardized measures of academic skills and problem-solving abilities which are normed by grade and time of the academic year (Fall, Spring, or Summer). The Numerical Operations subtest is a paper-and-pencil test that measures number writing and identification, rote counting, number production, and simple addition, subtraction, multiplication, and division calculations. For example, $4 - 2 = \underline{\quad}$ and $37 + 54$ (presented vertically) are two problems in the 2nd and 3rd grade range. The Mathematical Reasoning subtest is a verbal problem-solving test that measures counting, geometric shape identification, and single- and multi-step word problem-solving involving time, money, and measurement with both verbal and visual prompts. The child is required to solve problems with whole numbers, fractions or decimals, interpret graphs, identify mathematical patterns, and solve problems of statistics and probability. For example, a dime is presented and the child is asked: “How many pennies does it take to equal the value of one dime?” A probability problem asks: “If you flipped a coin ten times, how many times would the coin be most likely to land on heads?”

Reading abilities—The WIAT-II was also used to assess reading abilities. The Word Reading subtest involves reading individual words presented visually to the child, whereas the Reading Comprehension subtest requires them to match words to pictures and answer questions about sentences and passages they have read.

Working memory—Four subtests of the Working Memory Test Battery for Children (WMTB-C, Pickering & Gathercole, 2001) were used to assess the three components of working memory. The Central Executive was assessed by the Counting Recall and Backwards Digit Recall subtests. Phonological capacity was assessed by the Digit Recall subtest and visuo-spatial sketch capacity was assessed by the Block Recall subtest, as described elsewhere (Meyer, Salimpoor, Wu, Geary, & Menon, 2010).

Brain Imaging

Experimental procedures—The fMRI experiment consisted of four task conditions: (1) Complex addition, (2) Simple addition, (3) Number identification and (4) Passive fixation. In the Complex addition task, participants were presented with an equation involving two addends and asked to indicate, via a button box, whether the answer shown was correct or

incorrect (e.g. “3 + 4 = 8”). One operand ranged from 2 to 9, the other from 2 to 5 (tie problems, such as “5 + 5 = 10”, were excluded), and answers were correct in 50% of the trials. Incorrect answers deviated by ± 1 or ± 2 from the correct sum (Ashcraft & Battaglia, 1978). The Simple addition task was identical except that one of the addends was ‘1’ (e.g. “3 + 1 = 4”). Behavioral research in adults suggests that $N + 1$ addition is solved by incremental counting (Campbell & Metcalfe, 2007). Our use of this task was based on pilot studies which suggested that children are consistently faster on these problems compared to the Complex addition problems. Moreover, because stimuli in the Simple task have the same format as the Complex task, it provides a high-level control for sensory and number processing, as well as decision making and response selection. A verification, rather than verbal production, task format was used in the scanner because overt verbal responses can result in significant head movement and unusable fMRI data. In the number identification task, arithmetic symbols were replaced by alternative keyboard symbols (e.g. “4 o 5 @ 7”) and participants were asked to assess if “5” was among the presented digits. This task was intended to control for basic visual number processing and motor response. Finally, in the Passive fixation task, the symbol “*” appeared at the center of the screen and participants were asked to focus their attention on it. To aid children’s performance, specific task instructions appeared below each problem. During the Complex and Simple addition tasks, the word “Solve” appeared below the problem. In the number identification task, the word “Find” appeared on the screen, and during the passive fixation trials, the word “Look” appeared on the screen.

Stimuli were presented in a block fMRI design in order to optimize signal detection and task-related functional connectivity analysis (Friston, Zarahn, Josephs, Henson, & Dale, 1999). In each task, stimuli were displayed for 5 seconds with an inter-trial interval of 500 milliseconds. There were 18 trials of each task condition, broken up into 4 blocks of 4 or 5 trials, thus each block lasted either 22 or 27.5 seconds. The order of the blocks was randomized across participants with the following constraints: in every set of 4 blocks, all of the conditions were presented and the Complex and Simple addition task blocks were always separated by either a “Find 5” or a Passive fixation block. All orders of addition and non-addition task conditions were equally likely. The total length of the experimental run was 6 minutes and 36 seconds.

fMRI data acquisition—Images were acquired on a 3T GE Signa scanner (General Electric, Milwaukee, WI) using a custom-built head coil at the Stanford University Lucas Center. Head movement was minimized during the scan by a comfortable custom-built restraint. A total of 29 axial slices (4.0 mm thickness, 0.5 mm skip) parallel to the AC-PC line and covering the whole brain were imaged with a temporal resolution of 2 seconds using a T2* weighted gradient echo spiral in-out pulse sequence (Glover & Lai, 1998) with the following parameters: TR = 2 s, TE = 30 msec, flip angle = 80°, 1 interleave. The field of view was 20 cm, and the matrix size was 64 × 64, providing an in-plane spatial resolution of 3.125 mm. To reduce blurring and signal loss from field inhomogeneity, an automated high-order shimming method based on spiral acquisitions was used before acquiring functional MRI scans (Kim, Adalsteinsson, Glover, & Spielman, 2002).

fMRI preprocessing—fMRI data were analyzed using SPM8 (<http://www.fil.ion.ucl.ac.uk/spm/>). The first 5 volumes were not analyzed to allow for T1 equilibration. A linear shim correction was applied separately for each slice during reconstruction (Glover & Lai, 1998). ArtRepair software was used to correct for excessive participant movement (Mazaika et.al, 2009). Images were realigned in ArtRepair to correct for movement, smoothed with a 4 mm full width half maximum (FWHM) Gaussian kernel and motion adjusted. Deviant volumes resulting from sharp movement or spikes in the global signal were then interpolated using the two adjacent scans. No more than 20% of the

volumes were interpolated. Finally, images were corrected for errors in slice-timing, spatially normalized to standard MNI space, resampled to 2 mm isotropic voxels, and smoothed with a 4.5 mm FWHM Gaussian kernel. The two step sequence of first smoothing with a 4 mm FWHM Gaussian kernel and later with 4.5 mm FWHM Gaussian kernel approximates a total smoothing of 6 mm, because total smoothing is equivalent to the square root of the sum of the squares of the individual smoothing steps. The number of volumes interpolated did not differ between the 2nd and 3rd graders (11.41% vs. 12.31%, $p = .56$), nor did movement differ between the grades in any direction of translation ($x = 0.71$ vs. 0.83 , $y = 1.47$ vs. 1.67 or $z = 2.46$ vs. 2.64 ; all values in mm, all $ps > .5$) or rotation ($pitch = 0.047$ vs. 0.066 , $roll = 0.023$ vs. 0.024 , $yaw = 0.016$ vs. 0.024 ; all values in radians, all $ps > .18$).

Individual subject and group analyses—Task-related brain activation was identified using the general linear model implemented in SPM8. In the individual subject analyses, interpolated volumes flagged at the preprocessing stage were de-weighted. For the mathematical cognition task, brain activity related to each task condition was modeled using boxcar functions corresponding to the block length and convolved with a canonical hemodynamic response function and a temporal dispersion derivative to account for voxel-wise latency differences in hemodynamic response. Low-frequency drifts at each voxel were removed using a high-pass filter (0.5 cycle/min). Serial correlations were accounted for by modeling the fMRI time series as a first-degree autoregressive process. Voxel-wise t -statistics maps contrasting Complex and Simple addition problems were generated for each participant.

For group analysis, contrast images corresponding to the Complex – Simple addition tasks were analyzed using a random effects analysis. Two group-level analyses were conducted: (i) one-way t -tests on pooled data from all 2nd and 3rd graders ($n = 90$), were first used to identify areas of significant activation (Complex – Simple) and deactivation (Simple – Complex), and (ii) between-group t -tests were used to directly compare activation between 2nd and 3rd graders. Significant activation clusters were determined using a height threshold of $p < .01$, with family-wise error (FWE) correction for multiple comparisons at $p < .01$ determined using Monte Carlo simulations.

Monte Carlo simulations were implemented in MatLab using methods similar to AFNI's AlphaSim program (Forman et al., 1995; Ward, 2000). In each iteration of the Monte Carlo procedure, a 3-D image with the same resolution and dimensions as the fMRI scan was randomly generated and smoothed with a 6mm FWHM Gaussian kernel. For consistency with the inclusive mask used to report the results of the general linear model analysis, a gray matter mask was then applied to this image. The maximum cluster size at a given height threshold was recorded for each interaction, and 10,000 iterations were performed. The distribution of maximum cluster size across these 10,000 iterations was used to determine the FWE corrected extent threshold. At a height threshold of $p < .01$, less than 1% of the iterations had *maximum* cluster size greater than 128 voxels.

Additional analyses were conducted to examine differences in brain activation independent of any behavioral differences between 2nd and 3rd graders. This analysis was similar to group analysis described above, except that individual behavioral measures (accuracy or RT) were used as covariates of no interest.

Functional Connectivity Analysis—Functional connectivity assesses the similarity between the time series of two regions. Functional connectivity analyses were conducted by computing the cross-correlation between time courses, within task blocks, between specific pairs of ROIs. In each participant, fMRI time series were averaged across voxels within these ROIs after removing the mean global signal and linear drift over time in the fMRI

signal. The first two TRs of each block were removed from the resulting time series and inter-regional cross-correlation was computed separately for the two main task conditions (Complex and Simple addition). The correlation coefficients between regions i and j , $r_{i,j}$, were transformed to a normal distribution using Fisher's r -to- z transformation: $z_{i,j} = 0.5 \ln((1 + r_{i,j})/(1 - r_{i,j}))$. Grade- and task-related changes in functional connectivity were then examined using ANOVA on the resulting Z-scores. Note that because functional connectivity is computed within each task block after removing the first four seconds of transient changes in each block, our analysis captures temporal correlations within the Complex and Simple task blocks and it does not reflect transitions between high and low levels of activation across task blocks.

Regions of interest (ROI) used in the functional connectivity analysis were based on brain regions that showed activation differences between 2nd and 3rd graders. Two ROIs were identified in the prefrontal cortex: a vmPFC ROI based on the peak voxel where 2nd graders had greater activation than 3rd graders and a dlPFC ROI based on the peak voxel where 3rd graders had greater activation than 2nd graders. In posterior cortex, since 2nd graders did not show greater activation than 3rd graders, ROI peaks were based solely on brain regions that showed greater activation in 3rd graders. We considered the peak activity in two right side clusters. However, one of the clusters was very large spanning several anatomical regions, thus we also examined 3 subpeaks of this cluster which were separated by 32mm or more. ROIs were constructed using a sphere of radius 6mm centered at each peak. These 7 ROIs were used in the between group beta value plots.

Results

Standardized cognitive measures

Table 1 summarizes performance on standardized cognitive measures in our sample of 2nd and 3rd grade children. IQ, assessed using the Wechsler Abbreviated Scales of Intelligence, was not significantly different between 2nd and 3rd graders. On grade-normed scores, 2nd and 3rd graders did not differ in math and reading ability (assessed using the WIAT-II). They also did not differ on age-normed working memory measures of the central executive, phonological capacity and visuo-spatial capacity (assessed using the WMTB-C). However, 3rd graders had significantly higher raw scores on the Numerical Operations (14.2 vs. 19.4, $t(88) = 7.046$, $p < .001$), and Mathematical Reasoning (31.6 vs. 37.5, $t(88) = 6.915$, $p < .001$) subtests of the WIAT-II. Effect sizes for Numerical Operations and Mathematical Reasoning scores were 1.49 and 1.46 respectively. Thus, although the two groups were well-matched on grade- and age-normed cognitive measures, overall math abilities were significantly higher in 3rd grade.

Brain Imaging

Behavioral differences between 2nd and 3rd graders—We compared accuracy and reaction time during fMRI task performance on the Simple and Complex addition problems (Figure 1). A repeated measures ANOVA with between-subject factor Grade (2nd, 3rd) and within-subject factor Problem Type (Complex, Simple) was used to analyze differences in accuracy. The interaction between Grade and Problem Type was not significant ($F(1,88) = .066$, $p = .798$). However, the main effects of Grade and Problem Type were both significant. Accuracy on Complex addition (73.5%) problems was lower than Simple addition (81.7%) problems ($F(1,88) = 29.089$, $p < .001$) and 3rd graders (80.9%) were more accurate than 2nd graders (72.7%) ($F(1,88) = 4.080$, $p = .046$).

A similar analysis was conducted using reaction time as the independent variable. In this case, there was a trend towards a significant interaction of Grade and Problem Type ($F(1,88)$

= 3.654, $p = .059$). Post-hoc t -tests revealed this trend was driven by 3rd graders being marginally faster than 2nd graders on Simple addition problems (2.33 vs. 2.57 seconds; $t(88) = 1.979$, $p = .051$), but not on Complex addition problems (2.79 vs. 2.87 seconds; $t(88) = .590$, $p = .557$). There was also a significant main effect of Problem Type ($F(1,88) = 76.270$, $p < .001$) with Simple addition problems being faster than Complex addition problems (2.45 vs. 2.83 seconds).

Brain activation in 2nd and 3rd graders—To examine the overall pattern of brain activation in the combined group, we pooled data from all 90 2nd and 3rd graders. Compared to Simple problems, Complex addition problems elicited significant activation of the bilateral occipital cortex, the bilateral insula, medial pre-supplementary motor area, and the cerebellum. Activation was also detected in the right inferior frontal sulcus, right caudate, left IPS and supramarginal gyrus at $p < 0.05$, FWE-corrected threshold. These activations did not meet the stringent $p < 0.01$ FWE-corrected threshold but are presented for display purposes. Complex addition problems also evoked significant deactivation relative to Simple problems in the medial PFC, posterior cingulate cortex, left lateral occipital cortex, AG, and anterior temporal pole (Figure 2, Table 2).

Differences in brain activation between 2nd and 3rd graders—We next examined differences in brain responses between 2nd and 3rd graders by contrasting responses to Complex versus Simple addition problems (Table 3, Figures 3-5). 2nd graders showed greater activity in the ventral medial prefrontal cortex (vmPFC); whereas 3rd graders had greater activity in the left dorsal lateral prefrontal cortex (dlPFC) encompassing the middle frontal gyrus. These ventral medial and dorsal lateral PFC regions showed a contrasting pattern of task-related responses in 2nd and 3rd graders. In the vmPFC, 2nd graders showed positive values on the contrast of Complex – Simple whereas 3rd graders showed an opposite pattern with greater responses to Simple, compared to Complex, addition problems. In the dlPFC, 3rd graders showed greater responses to Complex addition problems whereas 2nd graders showed greater responses to Simple addition problems (Figure 3, Table 3). These differences remained after controlling for any differences in accuracy and reaction time between the groups (See Supplementary Figures S1 and S2).

As depicted in Figures 4-5 and Table 3, 3rd graders also showed significantly greater activity in the dorsal stream parietal and ventral visual stream areas, – right SPL extending to IPS, right AG (Figure 4), right LOC and PHG and bilateral LG (Figure 5). In these regions, 3rd graders showed greater responses to Complex relative to Simple addition problems, whereas 2nd graders showed either minimal differences (PHG and LG) or greater responses to Simple addition problems (SPL, AG, and LOC). All of the differences depicted in Figures 4 and 5 remained significant after controlling for accuracy (Figure S1) and reaction time (Figure S2).

Functional connectivity differences between 2nd and 3rd graders—We next examined whether PFC connectivity with posterior brain areas also differed significantly between 2nd and 3rd grades. We focused on the functional connectivity of two PFC areas, the left dlPFC and the right vmPFC (Figure 3, Table 4) which showed differential activation in the two groups, with right posterior brain areas (Figures 4 and 5, Table 4). A three-way repeated measures ANOVA of dlPFC connectivity was conducted using Grade (2nd, 3rd) as a between-subjects factor and Problem Type (Complex, Simple) and ROI (SPL, AG, LOC, LG, PHG) as within-subjects factors. There were no significant interactions ($p > .05$), but the main effects of Grade and ROI were both significant. Functional connectivity was significantly greater in 3rd graders than 2nd graders ($F(1,88) = 12.561$, $p < .001$) (Figure 6). ROI was the only other factor that showed a significant main effect ($F(4,352) = 6.631$, $p < .001$). To further characterize the anatomical profile of functional connectivity changes, we

grouped the posterior brain areas into dorsal stream (SPL, AG) and ventral stream (LOC, LG, PHG) ROIs. We found that functional connectivity differences between 2nd and 3rd grades was significantly higher in dorsal than ventral stream ROIs ($F(1,88) = 4.753, p = .032$), suggesting a differential pattern of change in functional coupling of the left dlPFC with dorsal and ventral visual stream areas between 2nd and 3rd grades. For the right vmPFC there was no difference between the grades ($F(1,88) = .283, p = .596$), nor any other significant interactions ($p > .05$). There was a main effect of arithmetic difficulty ($F(1,88) = 4.314, p = .041$), with more Complex problems having greater connectivity than Simple problems. These results indicate that functional coupling between the left dlPFC and posterior brain areas is significantly greater in 3rd graders, but that this difference does not generalize to other PFC areas which show differences in activation level between the two grades.

Discussion

In this study we examined neurodevelopmental changes during arithmetic problem solving over the one year interval spanning grades 2 and 3. To our knowledge, the ninety 7-9 year old children used in our study constitute the largest neuroimaging sample of mathematical reasoning and problem solving to date. In comparison, a recent meta-analysis by Houde and colleagues (2010) included a total of 88 participants from 7 studies. This large group allowed us to sample typically developing 2nd and 3rd graders with a wide range of abilities on several cognitive measures including IQ, reading and working memory. We show that despite being matched on these cognitive measures, 2nd and 3rd graders differed significantly in brain response and connectivity during arithmetic problem solving. Because of the closely matched arithmetic control task used in our study, our findings provide more precise information about the development of brain responses in relation to arithmetic complexity, independent of number processing, decision making and motor response. Based on the developmental literature (Ansari & Dhital, 2006; Ansari, et al., 2005; Cantlon, et al., 2009; Kucian, et al., 2008; Rivera, et al., 2005), we predicted that 3rd graders would have greater activation in posterior dorsal and ventral stream areas, whereas 2nd graders would have greater activation in the PFC. Consistent with our prediction, we found that 3rd graders had greater activity in right PPC and inferior occipitotemporal cortex. Surprisingly, 3rd graders had greater dlPFC responses than 2nd graders. Furthermore, functional connectivity of the left dlPFC with dorsal and ventral visual stream areas was also significantly greater in 3rd graders. We discuss these results below, emphasizing their implications for academic skill development.

Behavioral differences between 2nd and 3rd graders

The two groups were matched on grade-normed standardized measures of math ability, as assessed using the WIAT-II. However, 3rd graders had better overall abilities, as assessed using raw scores for both the Numerical Operations and Mathematical Reasoning, suggesting significant developmental changes in basic computation and verbal math problem solving skills over one year of schooling (effect size = 1.46-1.49). In contrast to this large effect size for general math abilities, effect sizes for in-scanner fMRI task performance were more modest. 3rd graders were more accurate than 2nd graders with about a 10% difference in accuracy on both Simple (effect size = .37) and Complex (effect size = .40) addition problems. Reaction times were marginally faster in 3rd graders for Simple addition problems (effect size = .42) but not on Complex addition problems (effect size = .12). Most previous behavioral studies of arithmetic abilities of children in this age group have used untimed trials (Fuchs, et al., 2006; N. C. Jordan, et al., 2010; N. C. Jordan, et al., 2003a, 2003b) so it is not possible to directly compare them with our in-scanner results. Nevertheless, the gains are comparable to the modest improvements in accuracy reported in

related studies (Geary, et al., 2000; N. C. Jordan, et al., 2003a). Our findings suggest that changes in timed arithmetic problem solving represent just one aspect of the overall improvement in math skills between 2nd and 3rd grades.

Arithmetic complexity modulates PFC responses differently in 2nd and 3rd graders

Previous studies have suggested that the development of numerical and mathematical skills between childhood and adulthood is characterized by decreased reliance on the PFC (Ansari & Dhital, 2006; Ansari, et al., 2005; Cantlon, et al., 2009; Rivera, et al., 2005). We examined whether 7-9 year old children would demonstrate a similar pattern of change over a one year interval. A direct comparison of the two groups, revealed differences in the vmPFC and left dlPFC. Interestingly, the right inferior frontal cortex and bilateral anterior insula areas that showed common activation in both groups did not show significant differences between 2nd and 3rd graders. These results suggest that core regions involved in cognitive control (Brass, Derrfuss, Forstmann, & von Cramon, 2005; Bunge, Ochsner, Desmond, Glover, & Gabrieli, 2001; Houde, et al., 2010; Menon & Uddin, 2010; Nelson et al., 2010; Sridharan, Levitin, Chafe, Berger, & Menon, 2007) play an obligatory role in both grades and reductions in activity in these PFC regions likely occur only after the 3rd grade.

Interestingly, compared to 3rd graders, 2nd graders had greater activity in the medial, but not the lateral, PFC. Analysis of the magnitude and direction of signal change revealed that these vmPFC differences arose from activation in 2nd graders and deactivation in 3rd graders. The vmPFC is a key node of the default mode network which typically shows decreased activation during more difficult cognitive tasks (Greicius, Krasnow, Reiss, & Menon, 2003; Raichle et al., 2001). While 3rd graders showed the expected pattern of deactivation in the vmPFC, 2nd graders showed an opposite pattern with greater activation during Complex, compared to Simple, problems. To our knowledge, no previous studies have reported such developmental differences in deactivation of the vmPFC during arithmetic or related problem solving tasks in young children (see also Kucian et al. (2008) for developmental differences between children and adults in other nodes of the default mode network). Our findings suggest that task-appropriate suppression of the default mode network shows significant maturational changes between 2nd and 3rd grades.

Contrary to our prediction of a complete reduction in PFC activity between 2nd and 3rd grades, we found that the left dlPFC showed greater activity in 3rd grade children. One possibility is that this region plays a greater role in retrieval of arithmetic facts in 3rd grade children. However, this region is dorsal to the left inferior frontal gyrus regions which have most consistently been implicated in domain-general controlled memory retrieval (Badre & Wagner, 2007) and in domain-specific retrieval of arithmetic facts (Kucian, et al., 2008; Rosenberg-Lee, Lovett, et al., 2009; Stocco & Anderson, 2008). An alternative possibility is that this region may be involved in more precise manipulation of the contents of working memory for Complex addition problems in 3rd graders. These results suggest that frontal executive processes undergo significant maturation between 2nd and 3rd grades during arithmetic problem solving. It is interesting to contrast these findings with those of Rivera and colleagues (2005) who observed linear decreases in left dlPFC response from childhood to adulthood. Our data suggest that such analyses can miss important developmental changes that occur during key stages of learning and skill acquisition. One way to reconcile these findings is to note that the oldest children in our study were the youngest age in that study. Thus, decreases in PFC engagement during arithmetic problem solving may only show age-related reductions after 3rd grade.

Arithmetic complexity related PPC maturation between 2nd and 3rd grades

Consistent with our prediction, 3rd graders showed greater activity in multiple PPC regions including the right SPL extending to IPS and the right AG. No PPC regions showed greater activation in 2nd graders. These developmental changes are more right lateralized than those reported by Rivera et al. (2005), wherein linear increases between childhood and adulthood were limited to the left supramarginal gyrus and adjoining IPS. Based on recently published cytoarchitectonic maps (Choi et al., 2006; Scheperjans et al., 2008), the PPC differences observed here were localized to lateral superior parietal lobule region SPL 7P (posterior) and posterior angular gyrus region PGp. Dorsal PPC regions such as SPL 7P are known to play an important and obligatory role in visuo-spatial attentional processes associated with numerical problem solving (Andres, Pelgrims, Michaux, Olivier, & Pesenti, 2010; Wu, et al., 2009). These findings indicate that maturation of multiple PPC regions involved in numerical reasoning starts early during the formal learning process.

No differences were observed in the left AG, which is surprising because this area that has been proposed to be involved in verbally mediated retrieval of arithmetic facts (Dehaene, et al., 2003) and the use of verbal retrieval increases in this age range (N. C. Jordan, et al., 2003a). Furthermore, the left AG was deactivated in both 2nd and 3rd graders and the level of deactivation did not differ between the two grades. In contrast, the right AG showed deactivation in 2nd graders and activation in 3rd graders. These findings are consistent with the emerging view that the right AG contributes to increased task proficiency (Andres, et al., 2010; Grabner, et al., 2009; Wu, et al., 2009). Disentangling the precise role of left and right AG deactivation in light of these developmental changes and the maturation of procedural and retrieval strategies remains an important question for future research. Taken together, our findings suggest that the PPC undergoes extensive and heterogeneous developmental changes during a period important for arithmetic skill acquisition.

Arithmetic complexity related maturation of ventral visual areas in 3rd graders

Although the PPC has been the most direct focus of most studies of numerical skill development, changes between childhood and adulthood in ventral visual stream activity have also been reported. Rivera et al (2005) found that left LOC responses increased with age. Cantlon et al (2009) found bilateral LOC activity for adults during both symbolic and non-symbolic number comparison tasks, but children did not display this amodal processing in the LOC. We found that 3rd graders had greater responses in the LG and the LOC, extending anteriorly into parahippocampal regions. Furthermore, these developmental changes are load-dependent and characterized by differential activity related to problem complexity. These results suggest that the development of numerical skills is characterized not just by a shift to dorsal PPC areas involved in visuo-spatial attention, but also to ventral visual areas that are involved in higher-order visual processing (Menon, White, Eliez, Glover, & Reiss, 2000). We suggest that ventral visual areas contribute to arithmetic skill development by building improved perceptual and mnemonic representations for numerical problems.

Maturation of functional connectivity between dIPFC and posterior brain regions

Analysis of developmental changes in connectivity between 2nd and 3rd graders provided additional insights into the maturation of functional circuits involved in arithmetic problem solving. Our goals in conducting this analysis were to address two questions: (1) did key brain regions that differ in activity level between the two grades also differ in inter-regional temporal coupling during arithmetic processing? and (2) were there between-grade differences in PFC connectivity to parietal compared to ventral visual areas? We focused on the functional connectivity of two PFC regions with posterior brain regions that showed significant activation differences between 2nd and 3rd graders. Posterior brain regions

consisted of two parietal areas (SPL and AG) and three ventral visual areas (LG, LOC and PHG). We found that functional connectivity between the left dlPFC and posterior areas was significantly greater in 3rd graders. Interestingly, we also found that between-grade differences in connectivity were larger between the dlPFC and parietal areas, compared to differences between the dlPFC and ventral visual areas. In contrast, functional connectivity between the vmPFC and posterior brain regions did not differ between the grades, suggesting that changes in task-related temporal coupling are not global and do not generalize to other PFC areas which show differences in activation level between the two grades. Our results provide novel evidence that increased reliance on posterior brain areas is also accompanied by increased connectivity of the dlPFC between 2nd and 3rd grades.

One potential concern here is the non-independence of ROIs used in the functional connectivity analysis since they were based on PFC and posterior areas that showed group differences in activation (Kriegeskorte, Simmons, Bellgowan, & Baker, 2009). An alternative approach would have been to select ROIs on the basis of areas that showed significant activation in the combined group of 2nd and 3rd graders. However, we were specifically interested in understanding connectivity in regions which showed developmental changes in activation between the two groups. In this context, we acknowledge the non-independence as a legitimate concern but point to important aspects of our analysis which minimize the potential for bias. There is general consensus that when statistical effects tested are independent of the ROI selection process (such as main effects and interactions) the results are valid and meaningful (Kriegeskorte, Lindquist, Nichols, Poldrack, & Vul, 2010). This was indeed the case in our study because we examined developmental changes in dlPFC connectivity with ventral and dorsal posterior areas using ROIs that were defined on the basis of activation differences between grades. Furthermore, because functional connectivity in our study is computed within each task block, our analysis is not influenced by transitions between high and low levels of activation across task blocks. Thus, for example, the ventral visual area LOC had stronger activation differences between the grades than the parietal cortex, but the latter had stronger differences in dlPFC functional connectivity between the grades. The methods used in our study therefore minimize potential bias arising from our ROI selection procedure. Taken together, our results suggest that increased dlPFC connectivity with the parietal cortex contributes to the early maturation of problem solving skills. Further studies, using independently defined PFC and parietal ROIs, are needed to examine the role of multiple fronto-parietal circuits in mathematical skill acquisition.

Implications for academic skill development and educational neuroscience

Our participants were drawn from a broad range of classrooms, schools and school districts which are likely to differ in the delivery of academic mathematics instruction. Despite this, we found that a single year of schooling has a major impact on brain function and connectivity. It is also noteworthy that 2nd and 3rd graders show reliable and consistent patterns of brain activity during mathematical problem solving in the bilateral anterior insula regions of the PFC. Importantly, these same PFC have also been implicated in reading and executive control tasks in young children spanning multiple grades (Houde, et al., 2010). The profile of anatomical overlap suggests a common mechanism by which maturation of basic cognitive control can influence skill development in multiple cognitive and academic domains.

Importantly, our findings also suggest that pooling data from a wide age-range in children and comparing them with adults can miss major developmental changes that occur during the early stages of academic learning. For example, several previous studies of number and arithmetic processing have highlighted a consistent shift from the PFC to posterior brain areas between childhood and adulthood (Ansari & Dhital, 2006; Ansari, et al., 2005;

Cantlon, et al., 2009; Rivera, et al., 2005). In contrast, we found that dIPFC responses increased in the narrow time window between 2nd and 3rd grades. Our data provides new evidence that the initial stages of learning may be accompanied by increases, rather than decreases, in PFC response. There are several possible reasons for this. One possibility is that learning may reduce variability in PFC response. A second possibility is that PFC responses may become more focal with learning and functional maturation (Durstun et al., 2004). In either case, our findings suggest a nonlinear trajectory of developmental changes characterized by an initial increase in dIPFC engagement during the early stages of learning, followed by more protracted decreases in response between childhood and adulthood (Rivera, et al., 2005). Precise knowledge of this trajectory is important not only for understanding the effects of various types of instruction in typically developing children but also for assessing and remediating abnormal developmental patterns in children with dyscalculia and math learning disabilities at an early age (Geary, Bailey, & Hoard, 2009; Geary et al., 2009; Rykhlevskaia, Uddin, Kondos, & Menon, 2009).

Previous neurodevelopmental studies have mainly focused on localization of age-related changes, but it is becoming increasingly clear that cognition depends on interactions within and between large-scale brain networks (Bressler & Menon, 2010). Our study is the first to highlight the significant and specific changes in frontal-posterior functional connectivity that take place during a time period important for arithmetic skill development. We suggest that a systems neuroscience approach, with its emphasis on networks and connectivity, rather than pure localization, is better-suited to educational neuroscience. Academic skill acquisition and mastery requires the integration of multiple cognitive processes, which in turn relies on the dynamic engagement of distal brain areas subserved by long-range connections that undergo significant changes with development (Fair et al., 2008; Supekar, et al., 2010). Our findings demonstrate that an exclusive focus on activity levels in a small set of brain regions identified in highly skilled adults can miss important changes in functional organization that accompany learning and development associated with schooling.

In this study we asked: what difference does a year of schooling make? We found robust cortical differences between children differing in a single grade. We have used “schooling” as proxy for all the things which go on in the classroom over a one year interval, including domain specific instruction and practice, as well as domain general learning. All of these factors, as well as brain maturation, are likely to contribute to the changes observed in our study. Further studies are required to disentangle the differential impact of these variables on academic learning.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations used

fMRI	functional magnetic resonance imaging
PFC	prefrontal cortex
PPC	posterior parietal cortex
IPS	intraparietal sulcus
SPL	superior parietal lobule
AG	angular gyrus
PHG	parahippocampal gyrus
LG	lingual gyrus
LOC	lateral occipital cortex
dlPFC	dorsal lateral prefrontal cortex
vmPFC	ventral medial prefrontal cortex
WIAT-II	Wechsler Individual Achievement Test – Second Edition
WMTB-C	Working Memory Test Battery for Children
ROI	region of interest
FWHM	full width half maximum

Highlights

- fMRI response compared in 90 2nd and 3rd graders while solving addition problems
- Prefrontal, parietal and ventral visual cortex activity greater in 3rd graders
- Fronto-parietal functional connectivity greater in 3rd graders
- Significant changes in brain response and connectivity observed over 1 year
- Pooling data across wide age ranges can miss important neurodevelopmental changes

Figure 1. Behavioral performance in 2nd and 3rd grade children on Simple and Complex addition problems

Children in the 3rd grade were more accurate ($p = 0.046$) than 2nd grade children on Complex and Simple addition problems and there was a trend ($p = .051$) towards 3rd grade children being faster than 2nd grade children on Simple addition problems. Both groups showed strong effects of problem type, with Simple problems being faster and more accurate than Complex problems ($p < 0.001$). * $p < .05$, *** $p < .001$.

Figure 2. Arithmetic complexity effects in combined data from 2nd and 3rd grade children
 Brain response related to arithmetic complexity obtained by contrasting Complex and Simple addition problems. Surface renderings and slices show significant activation (Complex > Simple, orange scale) in the pre-supplementary motor Area (preSMA), bilateral anterior insula cortex (AIC), and the visual cortex (VC). Significant deactivation (Simple > Complex, light-blue scale) was detected in the medial prefrontal cortex (mPFC), posterior cingulate cortex (PCC), left anterior temporal pole and left angular gyrus (AG). Differences in the AG arise from differences below “rest” baseline (negative beta values, left inset), whereas AIC differences arise from differences above “rest” baseline (positive beta values, right inset). For display purposes we have also included activity significant at the height threshold of $p < .05$ and cluster extent of $p < .05$ FWE corrected., which highlights additional activations in the right inferior frontal sulcus (IFS) and left intraparietal sulcus (IPS), and deactivation in the middle temporal gyrus. ** $p < .01$, *** $p < .001$.

Figure 3. Comparison of prefrontal cortex responses in 2nd and 3rd grade children
 Between-grade differences in prefrontal cortex response related to arithmetic complexity. (a) 2nd grade children showed greater activation in the ventral medial prefrontal cortex (vmPFC), compared to 3rd grade children (orange scale). The graph on the right shows average beta-values, contrasting the Complex and Simple addition tasks, in each group. (b) 3rd grade children showed greater activation in the left dorsolateral prefrontal cortex (dlPFC) compared to 2nd grade children (blue scale). In the bar graphs 2nd and 3rd graders are shown in red and blue, respectively. ** $p < .01$, *** $p < .001$.

Figure 4. Comparison of dorsal stream parietal cortex responses in 2nd and 3rd grade children Between-grade differences in parietal cortex response related to arithmetic complexity. Children in the 3rd grade (blue) showed greater activity than 2nd grade children (red) in the left and right intraparietal sulcus (IPS), right angular gyrus (AG) and left and right superior parietal lobule (SPL). ** $p < .01$. Other details as in Figure 3.

Figure 5. Comparison of ventral visual stream responses in 2nd and 3rd grade children
 Between-grade differences in ventral visual stream response related to arithmetic complexity. Children in the 3rd grade (blue) showed greater activity than 2nd grade children (red) in the left and right parahippocampal gyrus (PHG), left and right lingual gyrus (LG) and right lateral occipital cortex (LOC). ** $p < .01$. Other details as in Figure 3.

Figure 6. Functional connectivity of prefrontal cortex ROIs with posterior brain regions in 2nd and 3rd graders

(a) Compared to 2nd graders, 3rd graders had greater functional connectivity between the dorsal lateral prefrontal cortex (dlPFC) and the posterior brain regions. (b) In contrast, functional connectivity between the ventral medial prefrontal cortex (vmPFC) and the posterior regions did not differ between the two grades. The anatomical locations of dlPFC, vmPFC, dorsal and ventral stream regions of interest are as shown in Figures 3, 4 and 5, respectively and Table 4. SPL = Superior Parietal Lobule; AG = Angular Gyrus, PHG = Parahippocampal Gyrus, LOC = Lateral Occipital Cortex, LG = Lingual Gyrus. ** $p < .01$.

Table 1
Standardized scores on IQ, math and reading achievement and working memory for 2nd and 3rd grade children.

Measure	Grade					
	2 nd (N = 45)		3 rd (N = 45)		t	p
	M	SD	M	SD		
<i>Males/Females</i>						
	30/15		21/24			
<i>Age (years)</i>	7.67	0.40	8.67	0.40	-12.134	<0.001
<i>WASI</i>						
Verbal IQ	111.07	14.22	109.89	10.06	0.454	0.651
Performance IQ	110.04	12.83	108.53	11.97	0.578	0.565
Full Scale IQ	111.82	10.96	110.58	9.29	0.581	0.563
<i>WIAT-II</i>						
Word Reading	109.84	12.99	107.91	10.51	0.776	0.440
Reading Comprehension	106.49	11.13	106.78	10.10	-0.129	0.898
Numerical Operations	102.56	14.42	103.93	13.75	-0.464	0.644
Mathematical Reasoning	109.24	9.33	108.53	10.07	0.348	0.729
<i>WMTB-C</i>						
Digit Recall	107.38	19.63	106.07	21.49	0.302	0.763
Block Recall	93.49	15.11	94.58	11.68	-0.382	0.703
Counting Recall	92.18	15.86	88.69	23.87	0.817	0.416
Backward Digit Recall	94.56	16.19	98.89	15.44	-1.299	0.197

WASI = Wechsler Abbreviated Scales of Intelligence, WIAT-II = Wechsler Individual Achievement Test – Second Edition, WMTB-C = Working Memory Test Battery for Children.

Brain areas that showed significant activation and deactivation in combined data from 2nd and 3rd grade children related to arithmetic complexity, obtained by contrasting Complex and Simple problems ($p < 0.01$, with $p < 0.01$ FWE corrections for multiple comparisons).

Table 2

Region	# of Voxels	Peak Z-score	Peak MNI Coordinates x y z
<i>Complex > Simple</i>			
Brain Stem, Cerebellum	1322	4.48	0 -36 -10
Visual Cortex	2934	3.97	26 -94 -6
R Insula	248	3.60	32 24 0
SMA, Premotor Cortex	632	3.25	0 16 52
L Insula	229	3.19	-32 20 2
<i>Simple > Complex</i>			
Dorsal Medial Prefrontal Cortex	262	3.85	-10 54 40
Dorsal Medial Prefrontal Cortex	923	3.83	-6 62 8
Lateral Occipital Cortex, Angular Gyrus	367	3.62	-58 -68 8
Temporal Pole	153	3.40	-50 8 -20
Posterior Cingulate Cortex	392	3.18	8 -48 32

SMA = Supplementary Motor Area,

Brain areas that showed differential activity between 2nd and 3rd graders for Complex, compared to Simple, problems ($p < 0.01$, with $p < 0.01$ FWE corrections for multiple comparisons).

Table 3

Region	# of Voxels	Peak Z-score	Peak MNI Coordinates		
			x	y	z
<i>2nd Grade > 3rd Grade</i>					
R Medial Prefrontal Cortex	133	3.75	22	48	2
<i>3rd Grade > 2nd Grade</i>					
L Dorsolateral Prefrontal Cortex	193	3.95	-48	30	34
R Lateral Occipital Cortex	2619	3.67	38	-86	-8
R Sup Parietal Cortex *		3.46	18	-76	58
R Angular Gyrus *		3.08	52	-70	20
R Lingual Gyrus *		2.69	2	-72	10
R Parahippocampal Gyrus	246	3.23	36	-34	-4
L Cerebellum	191	3.01	-10	-74	-26
L Lingual Gyrus	365	2.86	-16	-86	-2

* subpeaks separated by 32mm or more.

Table 4

Peak coordinates of prefrontal and posterior regions of interest (ROI) used in the functional connectivity analysis. These regions were also used for beta values in Figures 3, 4, 5, S1 and S2.

ROI	Peak Coordinates		
	x	y	z
<i>Prefrontal</i>			
Dorsal Lateral Prefrontal Cortex (dlPFC)	-48	30	34
Ventral Medial Prefrontal Cortex (vmPFC)	22	48	2
<i>Dorsal Stream Parietal Regions</i>			
Superior Parietal Lobule (SPL)	18	-76	58
Angular Gyrus (AG)	52	-70	20
<i>Ventral Stream Visual Areas</i>			
Lingual Gyrus (LG)	2	-72	10
Parahippocampal Gyrus (PHG)	36	-34	-4
Lateral Occipital Cortex (LOC)	38	-86	-8