The Neural Correlates of the Core Number Systems Contribute to Mathematical Ability in
Adolescence

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Highlights

Math skills relate to systems that process small (PI) and large quantities (ANS)

This study examined the link between these systems and math achievement in adolescence

The PI system and its neural underpinnings were associated with higher math achievement

The left hippocampus was related to higher number comparison and math skills

Greater connectivity between brain areas was related to low math performance

Abstract

There are two proposed systems for number processing: one that precisely represents small numerosities (<4), the Parallel Individuation (PI) system, and one that encodes approximate large quantities, the Approximate Number system (ANS). Research suggests that these systems contribute to math performance. Nevertheless, most studies have focused on one of the two systems, mostly on the ANS, and have only investigated them in childhood and adulthood. Adolescence is a critical period for developing the math skills required for adult life. We investigated how the ANS, and in particular the PI system, and their neural underpinnings relate to different levels of mathematical achievement during adolescence. We examined numerical comparison abilities of 42 adolescents (mean age=16.34 years) with a wide range of math performance levels (1st-99th percentile), ranging from mathematical learning difficulties to mathematical talent. Adolescents compared quantities in the range of the PI system and the ANS during fMRI. Results showed that adolescents with lower math ability were less accurate than their peers with higher math ability, especially when comparing small quantities. At the brain level, adolescents' math performance was associated with differences in task-related activity in a region involved in small quantity comparisons (right lateral occipital cortex) and in regions involved in comparisons across both quantity ranges (e.g., left hippocampus). Furthermore, low math ability was negatively associated with greater connectivity between these regions. These results suggest that mechanisms related to the PI system and general mechanisms associated with retrieval-based strategies are associated with different levels of mathematical achievement during adolescence.

Keywords: Adolescents, core number systems, fMRI, mathematical cognition, mathematical learning difficulties

How do we learn the meaning of the number words *one*, *two*, and *three*? How do we know there is *one more* candle on our birthday cake each year? How are we able to learn to add, subtract, and multiply? These numerical abilities are rooted in two evolutionary cognitive systems that allow us to non-verbally represent, manipulate, and compare numerical quantities: the Parallel Individuation (PI) system and the Approximate Number System (ANS) (Feigenson, Dehaene, & Spelke, 2004; Odic & Starr, 2018; Piazza, 2010). The PI system precisely represents small quantities (~ four) (Feigenson & Carey, 2005), while the ANS represents approximations of larger quantities (Halberda, Ly, Wilmer, Naiman, & Germine, 2012; Revkin, Piazza, Izard, Cohen, & Dehaene, 2008). Accordingly, these two systems show different behavioral signatures. While small quantity judgments are characterized by nearly perfect precision (Kaufman, Lord, Reese, & Volkmann, 1949; Piazza, Fumarola, Chinello, & Melcher, 2011; Revkin et al., 2008), precision of large quantity judgments decreases as the numerosity increases. In numerical comparison tasks, precision on large quantities depends on the proportion between them, and not on their absolute difference; this effect has been called the ratio effect. The main distinction between the PI system and the ANS is that only the latter shows the ratio effect (Feigenson et al., 2004; Odic & Starr, 2018).

From their first year of life, infants show the behavioral and neural signatures corresponding to the ANS and PI systems (Coubart, Izard, Spelke, Marie, & Streri, 2014; Hyde & Spelke, 2011), and they use them to build numerical skills in early childhood (Hyde, Simon, Berteletti, & Mou, 2016; Starr, Libertus, & Brannon, 2013). Accordingly, children who show impairments in these systems show mathematical learning difficulties (MLD) in elementary school (Ashkenazi, Mark-Zigdon, & Henik, 2013; Heine et al., 2013; Piazza et al., 2010; Schleifer & Landerl, 2011). Less is known about the ways in which the

ANS and PI systems contribute to the more advanced mathematical skills acquired during adolescence and across a wider range of math achievement levels. Meta-analytic evidence has shown a small but stable association between non-symbolic numerical comparison abilities and math performance ($r = 0.24$, 95% CI [0.20 0.28]) in typically developing individuals aged 3-35 years (Schneider et al., 2017). Individual differences in ANS precision have also been related to superior math performance on symbolic standardized tests among adolescents who excel in math (Wang, Halberda, & Feigenson, 2017). However, there has been no direct examination of the contributions of the ANS, and in particular the PI system across the entire math achievement spectrum during adolescence. To fill these gaps in the literature, the present study sought to investigate the contributions of ANS and PI systems to math achievement in adolescence across a wide range of math ability levels.

The ANS and PI systems have been associated with anatomically distinct brain regions, with more dorsal areas associated with the processing of large quantities and more ventral regions involved in small quantities (O'Hearn et al., 2016). Small quantity processing, supported by the PI system, engages the middle temporal gyrus, lateral occipital areas, and the right temporoparietal junction (Ansari et al., 2007; He et al., 2014; O'Hearn et al., 2016; Sathian et al., 1999), while the processing of large quantities, supported by the ANS, engages the bilateral intraparietal sulcus (IPS) (Ansari et al., 2007; He et al., 2014). Small and large quantity processing share common brain areas as well. In habituation paradigms, frontal and parietal activation decreases after repeated exposure to collections of objects irrespective of their size (Demeyere, Rotshtein, & Humphreys, 2014). During number comparison tasks, parietal activation increases, relative to baseline or to symbolic representation of numbers, for both small and large quantities (Ansari, Lyons, van Eimeren,

& Xu, 2007; He, Zuo, Chen, & Humphreys, 2014). Interestingly, some of these areas, including the inferior and superior parietal lobule and the precuneus, correspond to the regions identified by meta-analytic studies as supporting abstract number processing (Sokolowski, Fias, Mousa, & Ansari, 2017), suggesting that they may be involved in the processing of numerical information regardless of its format (symbolic or non-symbolic) or its size (small or large).

Efforts have been made to link the brain correlates underlying numerical comparison tasks to different levels of math achievement. In one of the first studies exploring the neural correlates of numerical comparison abilities in mathematics learning difficulties (MLD), Price, Holloway, Räsänen, Vesterinen, and Ansari (2007) found that twelve-year-olds with MLD showed less IPS activation than their peers without math difficulties when comparing large numerosities, pointing out that abnormal activation of this region might hamper numerical development. However, further evidence for the contributions of the IPS to individual differences in math skills has been mixed. For instance, Kovas et al. (2009) did not find differences in the recruitment of the IPS between a group of ten-year-olds with low math performance and a group of high achieving children while comparing large quantities. Instead, they found that children with low math skills showed higher activation during quantity comparison in occipital areas. These results indicate that areas outside the parietal lobe also contribute to math performance. In young adults comparing quantities, Wilkey, Barone, Mazzocco, Vogel, and Price (2017) did not find a relationship between IPS and math performance, but found that increased activation in the left precuneus and left angular gyrus was related to higher scores on a standardized math test. This mixed evidence could be due to changes in the relationship between brain areas recruited while comparing quantities performance across the lifespan. In fact, in a

cross-sectional study with typically achieving participants, Haist, Wazny, Toomarian, and Adamo (2015) found that while parietal areas such as the IPS were related to higher math performance in childhood, more ventral areas, including the bilateral hippocampus and the ventral occipitotemporal cortex, as well as the precuneus were associated with higher math performance in adulthood; interestingly, there was no positive relationship between brain activations and higher math performance in adolescence. The authors suggested that these differences may reflect a change from procedure-based to memory-based problem solving strategies accompanying development (Geary & Brown, 1991). Alternatively, these findings could indicate that, as non-symbolic numerical skills develop, numerical comparison tasks can be solved in earlier stages of visual processing, as opposed to later stages of spatial and numerical processing in fronto-parietal regions (Haist et al., 2015). Together, past research has started to reveal the neural underpinnings of the core number systems and their relation to math performance in different age groups. However, while this research has focused primarily on the ANS and the IPS, the PI and its underlying underpinnings have received relatively less attention.

In spite of their importance to number development (Carey & Barner, 2019; Piazza, 2010), most studies have investigated the contributions of the core number systems and their neural underpinnings separately. In addition, those exceptions have only investigated their contributions during childhood (e.g., Heine et al., 2013). Thus, to date the contributions of those systems to math ability during adolescence, an important period for further developing critical math skills required for STEM fields and white-collar jobs (Handel, 2016), have not been investigated. To close these gaps in the literature the current study had two main aims. First, it examined whether numerical comparison abilities in the range of the ANS and PI systems differed across levels of math achievement in

adolescence. Second, it investigated the neural basis of these math performance differences and the degree to which they were related to the ANS or PI systems, or to areas involved in general processing of numerical information. To this end, we used functional magnetic resonance imaging (fMRI) to examine task-related activations during a number comparison task (cf. Ansari et al., 2007) in 16-year old adolescents ($N = 42$) that were sampled such that they represent a wide range of mathematical ability – from those who would qualify as MLD to adolescents with mathematical talent. Here, we were particularly interested in brain regions with increased activity in higher math performance and the number processing systems those regions were associated with.

Methods

Participants

A total of 51 adolescents (14.89 – 17.83 years), selected according to their performance on the Math Computation subtest of the Wide Range Achievement Test-4 (WRAT-4, Wilkinson & Robertson, 2006), participated in this study. They were required to (a) have an $IQ \geq 80$ on a short form of the Mexican adaptation of the WISC-IV (Wechsler, 2007), which included Vocabulary and Matrix Reasoning subtests, (b) have a reading speed score above the 10th percentile on the ENI Reading a Text Aloud subtest (Matute, Rosselli, Ardila, & Ostrosky, 2007), (c) be free of any fMRI contraindications (e.g., metallic implants, orthodontic braces, or claustrophobia), and (d) not meet the diagnostic criteria for attention deficit hyperactivity disorder (ADHD), based on a parent questionnaire that reproduces DSM-5 criteria (American Psychiatric Association, 2013). Part of the sample ($n = 30$) participated in a previous study on the relationship between executive functions and math performance (Abreu-Mendoza, Chamorro, Garcia-Barrera, & Matute, 2018).

Mathematical achievement levels were determined both by group (WRAT Math Computation) and individually administered (ENI Written Math) subtests. Those with mathematical learning difficulties (MLD) ($n = 14$) were defined as having a score at least 1.5 SD below the mean on the WRAT Math Computation subtest, according to the norms for first-year Mexican high school students (Abreu-Mendoza, Chamorro, & Matute, 2019) and a score below the 10th percentile on the ENI Written Math subtest (Matute et al., 2007). Typical performance (TP) ($n = 19$) was considered to be a score within the range of ± 1.5 SD on the WRAT Math computation subtest and a score above the 10th percentile on the ENI Written Math subtest. Mathematical talent (MT) ($n = 18$) was defined as a score ≥ 1.5 SD above the Mexican standard mean and a score above the 90th percentile on the ENI Written Math subtest. Nine participants were excluded after fMRI scans, due to excessive head movement (> 2 mm total displacement in one task run; 1 TP and 1 MT) or incidental findings (4 MLD, 2 TP, and 1 MT).

The final sample ($N = 42$) included 10 MLD, 16 TP, and 16 MT adolescents. Table 1 shows statistics for each of the criteria and descriptive measures of the three groups. On average, adolescents from the MT group had higher IQs ($M = 112.25$, $SD = 7.27$) than their peers from the TP ($M = 100.81$, $SD = 7.33$, $t(30) = 4.43$, $p_{\text{adj}} < .001$), which in turn had higher IQs than those of the MLD group ($M = 92.1$, $SD = 7.99$, $t(24) = 2.85$, $p_{\text{adj}} = .008$). Reading abilities differed only between the MT ($M = 11.81$, $SD = 2.14$) and MLD ($M = 9.50$, $SD = 1.58$, $t(24) = 2.95$, $p_{\text{adj}} = .02$) groups. All participants received a travel reimbursement of approximately \$15 USD at the end of the session.

Additional Measures

WISC arithmetic subtest.

To further characterize participants' math abilities, we used the Mexican version of the WISC-IV (Wechsler, 2007), which assesses the ability to solve mathematical problems presented orally.

Simple reaction time task.

To evaluate processing speed (Szűcs, Devine, Soltész, Nobes, & Gabriel, 2013), participants performed a simple reaction time task, in which they were seated at a computer and instructed to press the spacebar as soon as they saw the letter "A," which appeared with a random interstimulus interval (ISI) of 500-2000 ms. Only the letter "A" was shown, and it remained on the screen until the participant's response. During the ISI, a white cross was presented at the center of the screen. The task consisted of 30 trials, and mean reaction time across the 30 trials was used as the dependent variable for analysis.

Table 1. Group Characteristics

	MLD group <i>M (SD)</i>	TP group <i>M (SD)</i>	MT group <i>M (SD)</i>	<i>F(2,39)</i>	<i>p-value</i>	contrasts
Female ratio	6/10	8/16	8/16	-	-	-
Age	16.68 (0.55)	16.41 (0.81)	16.28 (0.86)	0.79	0.46	-
WRAT-Math computation*	14.30 (2.26)	27.31 (3.11)	36.00 (1.55)	-	-	-
ENI-Written math*	2.9 (0.57)	13.75 (3.79)	18.5 (0.89)	-	-	-
WISC-Arithmetic	8.9 (2.08)	11.00 (1.37)	12.62 (3.07)	8.01	0.001	MLD < TP & MT
WISC-IQ	92.1 (7.99)	100.81 (7.33)	112.25 (7.27)	23.62	0.001	MLD < TP < MT
ENI-Reading speed	9.5 (1.58)	10.56 (2.53)	11.81 (2.14)	3.57	0.04	MLD < MT
Simple RT	286.59 (40.44)	272.22 (38.97)	270.37 (31.99)	0.67	0.52	-

Notes. MLD = Mathematical Learning Difficulties, TP = Typical Performance, MT = Mathematical Talent. *Used for group assignment to MLD, TP or MT.

Brain Imaging

Number comparison task.

This task was an adapted version of the number comparison task used by Ansari et al. (2007). Participants were presented with two collections of dots, one after the other, and were asked to judge whether the first or the second had the larger number. There were two conditions: a small quantity condition that included collections of dots in the subitizing range (1 to 4), and a large quantity condition that included collections of dots in the estimation range (10, 20, 30, and 40). The two conditions included analogous comparison ratios (1:4, 1:3, 1:2, 2:3, 2:4, and 3:4). Thus, for instance, the 1 vs. 4 comparison in the small quantity condition was analogous to the 10 vs. 40 comparison in the large quantity condition.

Participants performed three functional runs of the task. Each run consisted of six 32-second active blocks (three blocks for each small and large quantity condition) and six 32-second resting blocks. Each active block consisted of eight trials: six that presented collections with different numerosities and two that presented the same numerosity. As in the original design of Ansari et al. (2007), trials with the same numerosity were included to prevent participants from inferring from the first collection whether the second one was necessarily larger in trials that started with 1 or 10 dots or smaller in those with 4 or 40 dots. Resting blocks consisted of a central white fixation cross. There were nine active blocks for each condition over the three runs, resulting in a total of 72 trials (including same numerosity trials) for each of the two conditions.

Each trial lasted 4000 ms, beginning with the appearance of a black screen. After 500 ms, the first collection of dots appeared for 200 ms. Then, a white fixation cross appeared for 1100 ms followed by the second collection of dots, which also appeared for 200 ms. Finally, a red fixation cross appeared for 2000 ms. During this time, participants were asked to press the left button with their right index finger if the first collection had the

larger number of dots, the right button with their right middle finger if the second collection did, or not to press either button if the two images had the same number. Figure 1 shows an example of a trial of the small and the large quantity conditions.

Figure 1. Example of trial presentation of (a) the Small Quantity and (b) the Large Quantity conditions. Both trials present the same comparison ratio (2:3), but with numerosities of their respective ranges.

Collections of dots were created using the program developed by Gebuis and Reynvoet (2011). To prevent participants from using visual properties that co-vary with number, this program manipulates (1) the area covered by the dot array (convex hull), (2) the sum of the individual dot surfaces in one array (total surface area), (3) dot diameter, and (4) the density of the dot collection (the area covered divided by the total surface area). The runs were counterbalanced to start trials with a larger or smaller numerosity. No more than three consecutive trials started with the same numerosity, and the six different comparison ratios were similarly distributed across the three runs. Blocks were presented in the following fixed order for all participants: Rest, Small, Rest, Large, Rest, Small, Rest, Large, Rest, Small, Rest, Large.

Stimuli were presented on a 40-inch LED monitor placed at the end of the scanner bore. Participants received general and task-related instructions on the monitor reflected in a mirror placed over the MRI head coil and through a set of pneumatic headphones.

Familiarization task.

Prior to the task in the scanner, participants solved a three-block familiarization task on a computer. Participants were shown the steps in the task and asked to indicate as quickly and accurately as possible after they saw the red fixation cross which image had the larger number of dots, or whether the number was the same. The first practice block consisted of six trials similar to those to be presented inside the scanner, but the images were presented for 900 ms. The second consisted of 12 trials in which the images appeared for 600 ms. The final practice block was identical to the functional run of the main task and consisted of 48 trials with the images appearing for 200 ms, the same interval as inside the scanner. Participants were given feedback on their accuracy at the end of each trial of the first practice block and at the end of the other two blocks. During this familiarization task, participants were given the opportunity to ask questions and were reminded to answer only when the red fixation cross appeared.

fMRI data acquisition

Data were collected using a 3T scanner (Philips Ingenia; Best, The Netherlands) with an 8-channel head coil. The MRI protocol included an initial T2-weighted brain volume to rule out the presence of pathologies. For co-registration of the functional images, a T1-weighted brain volume was then acquired using a high-resolution 3D Turbo Field Echo (TFE) with the following parameters: repetition time (TR) = 4900 ms, echo time (TE) = 210 ms, field of view (FOV) = 240 x 240, 170 slices, thickness = 1 mm with no gap, voxel size = 1 mm isometric. Finally, three echo-planar imaging (EPI) sequences were

acquired using the following parameters: TR = 2,000 ms, TE 30 ms, FOV = 230 x 230 x 116 mm; matrix = 96 x 94; 29 slices per volume, thickness = 4 mm with no gap, voxel size = 2.40 x 2.44 x 4 mm. The anatomical images were inspected by a neuroradiologist.

Participants who showed incidental findings were excluded from subsequent analyses.

Data analyses

In all the presented statistical analyses, our independent variable was math performance as a continuous variable (WRAT scores), instead of groups by mathematical achievement level. We used Holm's correction to correct for multiple comparisons, and it is indicated with the subscript "adj."

Behavioral data.

To examine how small and large quantity processing related to math performance, we first calculated the slope and the intercept for the linear regressions of numerical ratio (3:4, 2:3, 1:2, 1:3, 1:4) and accuracy, and the slope and the intercept for the linear regressions of numerical ratio and reaction times for each participant and for each quantity size separately. While slopes for small quantities should be close to zero, slopes for large quantities should be higher suggesting a ratio effect. Regarding intercepts, accuracy intercepts should be larger for small than for large quantities, implying a higher precision for small quantities. For reaction times, intercepts for small quantities should be smaller than those for large ones, suggesting faster responses for small quantities.

As a next step, we performed four linear mixed-effects (LME) regressions one for each measure of interest: accuracy-slope, accuracy-intercept, RT-slope, and RT-intercept to detect the relation between the intercepts and slopes on the one hand, and mathematical performance across participants on the other. In each of these regressions, we used participants as random effects, main effects of Quantity size and Math performance, their

interaction, IQ, and reading scores as fixed effects. We chose LMEs over more traditional analyses as they allow for the modeling of continuous covariates such as math performance, IQ, and reading scores as well as the two numerical comparison conditions (small and large quantity conditions). We used the R package *lme4* (Bates, Maechler, Bolker, & Walker, 2015) to carry out these analyses.

fMRI data.

T1-weighted volumes were first denoised using the script developed by Manjón, Coupé, Martí-Bonmatí, Collins, and Robles (2010). FMRI data processing was carried out using FEAT (FMRI Expert Analysis Tool) Version 6.00, from FSL (FMRIB Software Library, www.fmrib.ox.ac.uk/fsl), and registration of the functional data to the high resolution structural image used the boundary-based registration algorithm (Greve & Fischl, 2009). The high resolution structural image was registered to standard space with FLIRT (Jenkinson, Bannister, Brady, & Smith, 2002; Jenkinson & Smith, 2001). The following preprocessing steps were applied: (a) motion correction with MCFLIRT (Jenkinson et al., 2002), (b) slice-timing correction using Fourier-space time-series phase-shifting, (c) non-brain removal with BET (Smith, 2002), (d) spatial smoothing using a Gaussian kernel of FWHM 6 mm, (e) grand-mean intensity normalization of the entire 4D dataset by a single multiplicative factor, and (f) high-pass temporal filtering (Gaussian-weighted least-squares straight line fitting, with $\sigma = 50$ s). Time-series statistical analysis was carried out using FILM with a local autocorrelation correction (Woolrich, Ripley, Brady, & Smith, 2001).

In the first general linear model (GLM 1), we aimed to identify brain regions associated with performing quantity comparisons (irrespective of size) related to individual differences in the WRAT math computation scores (demeaned from the entire sample) as a

regressor in the model. We chose this subtest because it evaluates a large range of math problems and therefore represents a comprehensive characterization of mathematical ability. Active blocks, irrespective of their quantity size, were modeled in each run using a boxcar regressor convolved with a canonical double gamma hemodynamic response function. Moreover, the following nuisance regressors were also included in the model: trials in which both collections of dots presented the same numerosity, the six standard motion parameters plus the extended motion parameters (derivative, square, and derivative of square), and indicator regressors for high motion time points, indicated by a framewise displacement (FD) larger than 0.9 (Siegel et al., 2014). The number of volumes with FD larger than 0.9 did not differ across groups ($M_{MLD} = 18.2$, $SD_{MLD} = 17.78$; $M_{TP} = 7.0$, $SD_{TP} = 8.62$; $M_{MT} = 13.12$, $SD_{MT} = 14.00$; $F(2,39) = 2.18$, $p = .13$). Then, contrast estimates (Task > Rest) were averaged over runs for each participant using a fixed effects model in FLAME. Finally, group analyses were carried out using FLAME stage 1, which involved a single-group average with a covariate (demeaned WRAT math computation scores).

In a second model (GLM 2), we examined brain differences between small and large quantity comparisons for all participants. Blocks of small and large quantity conditions were also modeled in each run using a boxcar regressor convolved with a canonical double gamma hemodynamic response function. In addition to the task-related regressors and contrasts (Small quantity condition, Large quantity condition, Small > Large quantity, Large > Small quantity), we included the same nuisance regressors as in the GLM1. Contrast estimates were also averaged over runs for each participant using a fixed effects model in FLAME (FMRIB Local Analysis of Mixed Effects) (Woolrich, 2008). Group analyses were carried out using FLAME stage 1 (Woolrich, Behrens, Beckmann, Jenkinson, & Smith, 2004), including random effects.

To examine whether the regions identified in GLM 1 were modulated differently by quantity size, we extracted the percentage of signal change separately for small and large quantity conditions, and performed mixed-effects multiple regressions analyses. We used participants as random effects, and Quantity size * Math performance interaction, IQ, and reading scores as fixed effects. Here we were particularly interested in determining whether those brain regions modulated by mathematical achievement level were also modulated by quantity size.

For both GLM 1 and GLM 2, the Z (Gaussianised T/F) statistic images were thresholded using clusters determined by $Z > 3.1$ and a corrected cluster significance threshold of $p = .05$ (Worsley 2001). Moreover, as GLM 2 involved complex contrast, we restricted our analyses to the brain regions that were active in the overall activation contrast (Task > Rest). Due to the recent concerns about the use of cluster-threshold corrections, results were replicated using nonparametric correction with the command FSL Randomize ($N = 1000$ permutations, significance threshold: $p < .05$) (Winkler, Ridgway, Webster, Smith, & Nichols, 2014). Finally, anatomical labels were defined by manually entering MNI peak coordinates into the Harvard-Oxford subcortical and cortical structural probabilistic atlases within FSLView (Lancaster et al., 2007, 2000).

Functional connectivity analysis.

For each run, we extracted the beta time series for each of the functional clusters that were modulated by individual differences in math scores. We next performed Pearson's correlation analyses across each of the 15 pair of clusters within each run. Pearson's correlation coefficients were converted to z -scores using Fisher's transformation and were averaged across the three runs for each participant. Finally, we performed Pearson correlations between the average z -scores in the corresponding brain region and math

scores, controlling for IQ and reading scores. Similarly, p -values were adjusted using Holm method. Brain schematics were visualized with BrainNet Viewer (Xia, Wang, & He, 2013).

Results

Behavioral Results

Table 2 shows the mean intercepts and mean slopes for both accuracy and reaction times by Quantity size.

Table 2. Mean intercepts and slopes by quantity size for accuracy and reaction time (RT).

	Small quantities	Large quantities
	M (<i>SD</i>)	M (<i>SD</i>)
Accuracy		
Intercept	0.92 (0.09)	0.79 (0.09)
Slope	0.01 (0.03)	0.11 (0.05)
RT		
Intercept	710.03 (177.78)	656.66 (172.55)
Slope	-17.51 (32.41)	-38.44 (35.69)

Accuracy.

The upper left panel of Figure 2 shows that participants' responses were modulated by Ratio and Quantity size. Participants were more accurate while comparing small quantities (mean intercept = 0.92, $SD = 0.09$) in contrast to large quantities (mean intercept = 0.79, $SD = 0.09$). Furthermore, for small quantities, performance was stable across the different numerical ratios (mean slope = 0.01, $SD = 0.03$), while for large quantities, accuracy decreased as the ratio between the two quantities was decreased (mean slope = 0.11, $SD = 0.05$). We confirmed these accuracy differences with mixed-effect regressions and see whether they varied with math performance across adolescents. Results of these regressions with accuracy-intercept as the dependent variable showed a significant

interaction between Quantity size and Math performance ($\beta = 0.004$, $t = 3.06$, $p = .004$).

Follow-up partial correlations, controlling for IQ and reading scores, showed that participants' accuracy-intercepts for the small quantity condition were related to their math scores ($r = .37$, $p = 0.02$). There was no relationship between the accuracy-intercepts for the large quantity condition and math performance ($r = .14$, $p = .39$). We then examined whether the accuracy-slopes were modulated by quantity size and math performance. Results showed that there was not significant interaction between Quantity size and Math performance for the accuracy-slopes ($\beta = 0.0$, $t = 0.357$, $p = .72$), but only a main effect of Quantity size ($\beta = .10$, $t = 3.41$, $p = .001$), confirming that the accuracy-slope of large quantities ($M = 0.11$, $SD = 0.05$) was higher than that of small quantities ($M = 0.01$, $SD = 0.03$). Overall, these results suggest that participants who have an overall higher performance (higher accuracy-intercepts) in the small quantity condition are also those who have higher math scores (Figure 2 upper right panel); they also show that although participants' performance in the large quantity condition is modulated by the numerical ratio (Figure 2 upper left panel), math performance is not related to this ratio effect (not shown in the figure).

Reaction times.

The lower left panel of Figure 2 shows how participants' reaction times differed by Ratio and Quantity size. A visual inspection of this figure suggests that overall participants were apparently faster in the large quantity condition (mean intercept = 656.66, $SD = 172.55$) than in the small one (mean intercept = 710.03, $SD = 177.78$); however, none of two mixed-effects regression showed a significant main effect of Quantity size, nor interaction between Math and Quantity size (all p 's $> .06$).

Figure 2. Performance in the number comparison task. Mean accuracy across the numerical ratios (upper left panel). Scatterplots for the correlations between math performance (WRAT correct responses) and accuracy (ACC)-intercepts across the two quantity size conditions (upper right panels). Mean reaction times (RT) across the numerical ratios (lower left panel). Scatter plots of the correlations between math performance (WRAT correct responses) and reaction time intercepts. **Note.** The groups are displayed only for reference; analyses were performed across the entire sample.

Neuroimaging Results

Small and large quantity comparisons.

The general contrast of Task > Rest revealed that performing numerical comparisons engaged a wide network of regions, including paracingulate gyrus, the right lateral occipital cortex, the bilateral occipital poles, and the left frontal pole. In the next step, we sought to determine which of these regions were modulated by quantity size. To this end, we examined the brain regions that were differentially engaged in the contrasts Small > Large (purple) and Large > Small (dark green) quantities within the regions that were activated during the task (Task > Rest, red), across the entire sample of adolescents. These areas are shown in Figure 3. Comparing small quantities was associated with

increased activation in the left lingual gyrus, left middle temporal gyrus, bilateral superior parietal lobule and right lateral occipital cortex, whereas comparing large quantities was associated with increased activation in the bilateral occipital pole, the right frontal orbital cortex, the left paracingulate gyrus, the bilateral insular cortex, and the left occipital fusiform gyrus. Table 3 shows the cluster coordinates.

Figure 3. Brain activations for the overall activation (Task > Rest, red), and those that showed a preferential activation for small (Small > Large, purple) and large (Large > Small, dark green) quantities. Whole-brain maps were thresholded using clusters determined by $Z > 3.1$ and a (corrected) cluster significance threshold of $p < .05$.

Overall, these results suggest that the ability to compare quantities, regardless of their size, relies on a large set of brain regions, including the bilateral IPS (not a local maxima) and a set of occipital and frontal regions. However, among those regions, a set of them were specifically modulated by the number of objects within the collections

compared: bilateral parietotemporal regions were preferentially involved in comparisons of small quantities, while frontal regions (e.g., the anterior paracingulate cortex and the right frontal orbital cortex) along with occipital regions were preferentially recruited for large quantity comparisons.

Table 3. Brain Regions Showing Stronger Activations for Task > Rest, Small > Large, Large > Small Contrasts.

			Coordinates		
Local Maxima	Cluster size	Peak (Z)	x	y	z
Task > Rest					
Paracingulate gyrus	43264	8.82	0	18	42
L paracingulate gyrus		8.76	-2	10	48
R insular cortex		8.55	32	26	6
R cerebellum		8.37	46	-62	-34
R lateral occipital cortex	3735	8.07	30	-66	42
R superior parietal lobule		7.78	30	-56	44
R supramarginal gyrus		7.78	48	-42	46
R occipital pole	403	4.59	24	-88	2
R occipital pole		4.31	18	-98	-2
R lateral occipital cortex		3.69	34	-78	-4
L occipital pole	391	4.22	-14	-96	-2
L frontal pole	196	4.63	-36	52	20
Small > Large					
L lingual gyrus	1922	6.33	-38	-4	52
L precentral gyrus		4.93	-24	-12	54
L SMA		4.56	-6	0	64
L precentral gyrus		4.46	-44	-8	38
L superior parietal lobule	1724	6.88	-38	-48	58
L lateral occipital cortex		6.49	-26	-60	58
L lateral occipital cortex		5.66	-32	-74	32
R superior parietal lobule*	256	5.09	34	-50	54
R superior parietal lobule		3.87	32	-44	38
R lateral occipital cortex		3.84	22	-70	60
L middle temporal gyrus	229	7.29	-48	-58	6
L lateral occipital cortex		3.43	-44	-56	-6
R lateral occipital cortex	116	6.02	52	-54	6
R middle temporal gyrus		5.98	50	-64	2
Large > Small					

L paracingulate	967	6.35	-4	32	32
R frontal pole	688	5.12	40	36	8
R frontal pole		3.64	38	56	2
R frontal pole		3.53	32	58	14
L occipital fusiform gyrus	521	7.1	-12	-84	-18
L lingual gyrus		5.93	8	-84	-18
L lateral occipital cortex		5.08	-30	-80	-12
L cerebellum		4.83	-28	-76	-28
R frontal orbital cortex	511	5.74	34	22	-8
R insular cortex		3.29	28	12	-12
L occipital pole	353	9.12	-16	-96	6
L occipital pole		7.89	-12	-94	-4
R occipital pole	352	7.23	16	-94	0
R lateral occipital cortex		6.56	28	-88	6
R occipital pole		6.18	14	-90	-10
L insular cortex	297	6.18	-38	16	-10

Note. For each cluster, 3 sub-peaks are reported that at least are more than 8mm apart. * = according the nonparametric correction analyses, this brain area was marginally significant ($p = .05001$).

Neural underpinnings of numerical comparison abilities and math achievement.

Next, we examined whether any of the brain regions involved in the numerical comparison task were associated with math performance across participants. Several brain regions (bilateral precuneus, left hippocampus, right lateral occipital cortex, left lingual gyrus, right cuneal cortex, and right lingual gyrus) were modulated by the WRAT math computation scores such that adolescents with higher math performance showed greater task-related activity in these regions (Task > Rest, Figure 4). The positive association between task-related activity and math performance remained significant after controlling for IQ, reading speed, and multiple comparisons in all regions (Table 4).

Figure 4. Scatterplots for the correlation between the activity of functional clusters and the WRAT math computation scores. **Note.** MLD = Mathematical Learning Difficulties, TP = Typical Performance, MT = Mathematical Talent. The participant groups are displayed only for reference; analyses were performed across the entire sample.

Table 4. Functional Clusters Showing a Correlation with the WRAT Math Computation Scores

Local Maxima	Cluster size	Peak (Z)	Coordinates			<i>r</i> -values	partial <i>r</i> -values
			x	y	z		
R precuneus	768	5.16	16	-48	42	0.64	0.47*
R precuneus		4.47	10	-54	50		
L precuneus		4.33	-2	-52	42		
L hippocampus	547	5.21	-32	-28	-6	0.70	0.48*
L temporal fusiform cortex		4.62	-34	-40	-14		
L temporal fusiform cortex		3.93	-42	-26	-12		
L superior temporal gyrus		3.81	-46	-18	-8		
R Lateral occipital cortex	522	4.39	50	-78	4	0.63	0.41*
R Lateral occipital cortex		3.95	56	-64	6		
R Lateral occipital cortex		3.53	42	-78	18		
R Lateral occipital cortex		3.39	38	-66	6		
L lingual gyrus	442	4.05	0	-70	2	0.49	0.40*
L lingual gyrus		4.03	-18	-56	-10		
R lingual gyrus		4	2	-74	-2		

L lingual gyrus		3.95	-10	-62	-6		
R cuneal cortex	339	4.33	24	-66	24	0.58	0.48*
R cuneal cortex		3.89	16	-72	26		
R cuneal cortex		3.69	8	-72	28		
R precuneus		3.62	8	-62	18		
R lingual gyrus	308	4.35	24	-54	-6	0.59	0.51*

Note. For each cluster, 3 sub-peaks are reported that at least are more than 8mm apart. Correlation values estimated based on extracted signal change. Partial correlation coefficients controlling for IQ and reading speed scores. * $p_{adj} < .05$ for multiple tests using Holm's method.

We next examined whether the brain regions that varied with math performance were modulated differently according to quantity size. Aside of the expected main effects of Math, results from the mixed-effects regressions showed that only the right lateral occipital cortex showed a main effect of Quantity size ($\beta = 0.29$, $t = 2.15$, $p = .04$): greater activity in the small quantity condition (mean % signal change = 0.54, SD = 0.45) than in the large quantity condition (mean % signal change = 0.32, SD = 0.41).

Figure 5. Quantity size effect in right lateral occipital cortex. Each dot represents an individual data point, while diamonds represent the mean for each condition. **Note.** MLD = Mathematical Learning Difficulties, TP = Typical Performance, MT = Mathematical Talent. Error bars represent bootstrapped 95% CI. The participant groups are displayed only for reference, analyses were performed across the entire sample * $p < .05$

In summary, a region with activity modulated according to the continuum of math performance was preferentially involved in small quantity processing, suggesting a fundamental contribution of the PI system to math achievement in adolescence. In addition, a number of brain regions (the left hippocampus, the bilateral precuneus, the bilateral lingual gyrus, and the right cuneal cortex) that were engaged across both small and large quantities were also positively associated with performance, suggesting that more general processes involved in the comparison of different non-symbolic quantities also play an important role in heterogeneity in math performance.

Functional connectivity analyses.

Individuals with MLD often show a hyper-connectivity both in resting-state (Jolles et al., 2016) and in task-related connectivity (Rosenberg-Lee et al., 2015), as compared with those with typical math performance. We thus examined how interactions among the brain areas associated with math achievement differed with math ability in adolescence. Functional connectivity analyses were conducted by computing the pairwise correlations between task-related activation over time in all six functional clusters. We then related the strength of connectivity between clusters to individual differences in math achievement across the entire adolescent sample. After correcting for multiple tests and controlling for IQ and reading scores (Table 6 for detailed statistics), connectivity between several brain regions was negatively modulated by the WRAT math computation scores, including connectivity between right cuneal cortex and the right lingual gyrus ($r = -.56, p_{\text{adj}} = .003$), between the right lateral occipital cortex and the right lingual gyrus ($r = -.46, p_{\text{adj}} = .04$) and between the bilateral precuneus and the right lingual gyrus ($r = -.51, p_{\text{adj}} = .01$) (see Figure 6). In all of these connectivity patterns, adolescents with higher math performance showed less connectivity when comparing different magnitudes. Together, these results suggest that

adolescents with lower math performance is characterized by a lesser task-related response in brain areas crucial for numerical quantity processing, while at the same time they show a pattern of hyper-connectivity between those brain areas during task performance.

Table 5. Mean (SD) *r*- to *z*-values for Association Strengths across Pairs of Regions Correlated with Math Performance after Controlling for IQ and Reading Speed.

Pairs	<i>z</i> -scores (mean)	<i>z</i> -scores (SD)	partial <i>r</i> -values	<i>p</i> -values
1. BP-LHipp	0.49	0.18	-0.31	0.0511
2. BP-RLOcc	0.60	0.24	-0.07	0.6887
3. BP-LLG	0.65	0.21	-0.43	0.0051
4. BP-RCC	0.80	0.19	-0.35	0.0253
5. BP-RLG	0.45	0.20	-0.51	0.0007
6. LHipp-RLOcc	0.36	0.22	-0.07	0.6674
7. LHipp-LLG	0.67	0.16	-0.07	0.6551
8. LHipp-RCC	0.43	0.17	-0.19	0.2455
9. LHipp-RLG	0.46	0.20	0.00	0.9992
10. RLOcc-LLG	0.65	0.23	-0.27	0.0900
11. RLOcc-RCC	0.66	0.20	-0.18	0.2691
12. RLOcc-RLG	0.58	0.20	-0.46	0.0030
13. LLG-RCC	0.81	0.18	-0.38	0.0142
14. LLG-RLG	1.05	0.20	-0.20	0.2134
15. RCC-RLG	0.66	0.20	-0.56	0.0002

Notes. BP = Bilateral precuneus, LHipp = Left hippocampus, RCC = Right cuneal cortex, RLG = Right lingual gyrus, RLOcc = Right lateral occipital cortex. *r*-values represent the partial correlation coefficient after controlling for IQ and reading scores. *P*-values that remained significant after controlling for multiple tests (Holm's method) are shown in bold.

Figure 6. Graphical representation of connectivity in regions correlated with math performance across the entire sample. Scatter plots for connections that were associated with WRAT math computations scores. Notes. MLD = Mathematical Learning Difficulties, TP = Typical Performance, MT = Mathematical Talent, BP = Bilateral precuneus, LLG =

Left lingual gyrus, LHipp = Left hippocampus, RCC = Right cuneal cortex, RLG = Right lingual gyrus, RLOcc = Right lateral occipital cortex. **Note:** The participant groups are displayed only for reference, analyses were performed across the entire sample.

Discussion

The present study examined the contributions of the ANS and PI systems to numerical skills in adolescence and across the continuum of math achievement. By examining adolescents with varied math performance while they compared quantities in the range of the PI system (1 to 4 objects) and the ANS (> 4 objects), we showed that participants with low math performance were also those less accurate in comparing small quantities. Crucially, brain regions involved in the processing of small quantities (right lateral occipital cortex) and regions recruited during the processing of both ranges of quantities (left hippocampus, bilateral precuneus, right cuneal, and bilateral lingual cortex) were associated with individual differences in math performance. Together, these findings suggest that mechanisms related to the PI system and mechanisms shared between that system and the ANS play a critical role for math performance during adolescence.

Adolescents in our study showed the behavioral signatures of the PI system and the ANS. Overall, they were more accurate at comparing collections of four objects or less than comparing collections of larger quantities with equal ratios as showed in Ansari et al., (2007). Moreover, their accuracy in the large quantity condition showed a ratio effect, since participants' accuracy decreased as the ratio between the quantities to be compared decreased (Odic & Starr, 2018).

At the brain level, we found different patterns of activity associated with the processing of small and large quantities. Small quantity comparisons showed greater activation in parietotemporal regions. These results in some way corroborate findings in

adults, who show greater activity in the temporal gyrus while enumerating small quantities than large ones (Sathian et al., 1999) or while passively watching changes in the numerosity of small collections (Demeyere et al., 2014). In contrast, comparing large quantities was associated with increased activation in frontal and occipital areas in the present study. Specifically, increased activity in the anterior cingulate gyrus could reflect the greater difficulty of comparing large quantities (Duncan & Owen, 2000). Consistent with this interpretation, Wilkey et al. (2017) showed that activity in the anterior cingulate gyrus was modulated by the difficulty imposed by the numerical ratio in comparison tasks involving large numerosities: higher anterior cingulate gyrus activity was related to harder numerical ratios. Greater activity in occipital areas while comparing large quantities is also consistent with Ansari et al. (2007). An alternative interpretation is that this results might reflect the different visual properties between small and large quantities; however, there is recent evidence suggesting that a first stage of large quantity processing occurs in visual areas (Fornaciai & Park, 2018).

Why is comparing small quantities related to mathematical performance? To compare two collections of objects, the PI system follows a two steps mechanism. The first step of this mechanism, object individuation, consists of selecting an element based on its location, and has an upper limit of four elements. The following step, object identification, consists of encoding object characteristics, and has been related to the superior IPS and the lateral occipital complex (Xu & Chun, 2009). However, occipital activity has been shown to increase when two collections with the same small quantity, but different spatial configurations, are presented one after the other (Demeyere et al., 2014), suggesting that these areas represent small numbers as categories. In the current study, task-related activity in occipital areas was enhanced in adolescents with higher math ability. This result hints to

the idea that a difficulty in comparing small quantities might not be due to a deficit in individuating objects but might be related to a later process that allows the representation of small numbers as categories. This interpretation finds an additional support in our behavioral finding that the slope for small quantities did not correlate with math performance, suggesting that regardless of math level, individuals can correctly individualize/subitize objects. It also finds support in a recent behavioral study showing no association between the number of elements that children and adults can individuate or subitize and their math performance (Anobile, Arrighi, & Burr, 2019). Other studies have also found that children with MLD have difficulty in recognizing patterns of dots with small numbers of dots, and with large numbers of dots in canonical patterns (e.g., a dice-like arrangement) (Ashkenazi et al., 2013), a process that is related with the lateral occipital cortex.

The role of the hippocampus during number comparison tasks has received little attention. Notably, in the current study, adolescents with the lowest mathematical scores showed no hippocampal preferential engagement in the quantity comparison task, while adolescents with high scores showed reliable activation in this brain region (Figure 4). What may the role of the hippocampus during a number comparison task be, and how is it related to math performance and the core number systems? One study reported that activity in the bilateral hippocampus during a number comparison task was negatively correlated with mathematical performance in adulthood, whereas in occipital regions performance was positively correlated (Haist et al., 2015). The authors interpreted these activity patterns to mean that adults with higher math performance solved the comparison task in earlier visual stages, in the occipital areas, while those with lower performance retrieved their responses from long-term memory involving the hippocampus. Importantly, in contrast to that study,

where participants saw the two collections of dots simultaneously, adolescents in the present study saw the two collections of dots sequentially, giving them the opportunity to retrieve the corresponding symbol (the number word) of the first numerosity when present with the second collection of dots. Encountering the collections of dots sequentially may have encouraged participants to use retrieval-based strategies, as opposed to relying on visual cues like comparing dot sizes, which would have been misleading, as visual properties alone did not indicate which collection was larger. This idea is corroborated by studies suggesting that participants who base their responses on whether a collection of dots “looks like” a specific quantity are those who respond faster in enumeration tasks (Gandini, Lemaire, & Dufau, 2008). Moreover, impairment in retrieving arithmetical facts has been linked to mathematical learning difficulties (Geary & Brown, 1991), and greater retrieval abilities have been related to exceptional mathematical skill (Pesenti et al., 2001). Taken together, hippocampal activity during the present number comparison task may reflect greater use of retrieval-based strategies, which leads to better performance on this task on both quantity ranges and on mathematical tests.

Previous studies have reported that children with MLD show a hyper-connectivity between fronto-parietal regions and the IPS while solving arithmetic problems (Rosenberg-Lee et al., 2015), and between parietal, occipital, and frontal regions and the IPS during rest (Jolles et al., 2016). Corroborating and extending these results to adolescents, we demonstrated that adolescents with lower math performance showed stronger correlations between parietal, temporal, and occipital areas while comparing numerosities. As previously suggested (Rosenberg-Lee et al., 2015), the greater correlation across these brain areas could result in encoding irrelevant information that would result in impaired performance. Specifically, low math performance could be related to the use of distracting

strategies such as encoding visual information (e.g., dot size, total extended area) that might be misleading on which of the two collections of dots has the larger numerosity. Consistent with this idea, the hyper-connectivity pattern associated with lower math performance was clustered around visual areas that were generally involved in the task (the right cuneal cortex, and lingual gyrus) and the processing of small quantities (the right lateral occipital cortex).

In the present study, we found no association between math performance and performance in the large quantity condition. One explanation for this lack of differences could be the difficulty of the comparisons we employed. Although there is no standard means of measuring ANS accuracy, the task should have enough variability in the difficulty of numerical comparisons to capture individual differences in the ANS. In our study, the most difficult comparison involved a 3:4 ratio, which even four-year-olds can successfully solve (Abreu-Mendoza & Arias-Trejo, 2015; Odic, 2018). However, more difficult comparisons could not be employed, as there would have been no analogous comparisons for the small quantity condition—the PI system can only track up to four objects. This explanation seems unlikely as there was no ceiling effect in the large quantity condition, which suggests that there was enough variability to detect differences across the groups. Alternatively, contributions of the ANS to math performance may be smaller during adolescence than during childhood. Although meta-analytic evidence suggests that the ANS contributes to math ability across the lifespan (Schneider et al., 2017), results are mixed for later stages of development. While some studies have found no correlations between math performance and accuracy or reaction time in a large quantity comparison task (Haist et al., 2015; Kovas et al., 2009), other studies have found such relationships with reaction time (Wilkey et al., 2017) or with W , a measure of ANS precision (Wang et al., 2017). These

apparently contradictory results call for further studies with older participants and for studies with longitudinal designs.

Although, as expected, we found activation of the IPS for both small and large quantity comparisons, this activity was not related to participants' math performance. As the IPS represents one of the key areas for the abstract representation of numerical quantities and is modulated both by quantity size (Cutini, Scatturin, Moro, & Zorzi, 2014; Demeyere et al., 2014) and by symbolic and non-symbolic representations of quantities (Sokolowski et al., 2017), this result could suggest that different math achievement levels in adolescents are not related to impaired or enhanced number processing, but to other domain-general mechanisms involved in numerical comparisons.

One limitation of our study is its sample size, especially the number of participants below the 10th percentile of math ability. Originally, we aimed for a larger sample of adolescents with low math ability, but the sample size was significantly reduced by the number of adolescents with incidental findings ($n = 7$). This number is larger than those reported in the fMRI literature (Vernooij et al., 2007), but we believe the number of incidental findings may be underreported, as studies rarely include review by an expert clinician as part of the protocol. Including this criterion in our protocol increased our confidence that differences in the brain patterns are not due to atypical neuroanatomical differences. While our main analyses were based on the entire sample of adolescents ($N = 42$) and therefore were relatively well powered, future research with larger samples, especially at both ends of the achievement spectrum can help elucidate mechanisms of individual differences in each of the achievement groups. Furthermore, we focused on matching the cognitive abilities of the two pairs of adjacent groups (MLD/TP, and TP/MT), but there were differences between the IQ scores of the TP and MT groups. However, since

the associations between brain activity and math scores were still significant after controlling for IQ and reading speed scores, general differences in IQ are unlikely to be the primary source of the individual differences we found. One last consideration is that we did not control for executive functions. While the contribution of various executive functions such as working memory, inhibitory control and task switching have been previously demonstrated, the present study focused on investigating the contributions of core systems to math performance, and considering the effects of executive functions was beyond the scope of this study.

In conclusion, the present study aimed to investigate the degree to which the two core number systems, the PI system and the ANS, contribute to mathematical achievement in adolescence. By evaluating numerical comparison abilities in the ranges of both systems, we showed that the PI system distinguishes adolescents with mathematical learning difficulties from their peers with mathematical talent. More importantly, brain activity patterns in adolescents across a range of mathematical ability suggest that the link between the core number systems and mathematical performance during adolescence might be related not to numerical representation but to the general domain processes they entail.

Compliance with Ethical Standards

Informed consent: All participants and their parents gave written informed consent.

Ethical approval: The ethics committee of the University of Guadalajara approved this study (approval number ET112015-205), which follows the guidelines established in the Mexican General Health Law and the Helsinki Declaration.

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