Supplemental Material

Methods

Functional Brain Imaging

fMRI data acquisition Functional brain images were acquired on a 3T GE Signa scanner in two separate runs. Stimuli were presented in a block fMRI design in order to optimize signal detection and task-related effective connectivity analysis (Friston, Zarahn, Josephs, Henson, & Dale, 1999). A total of 29 axial slices (4.0 mm thickness, 0.5 mm skip) parallel to the AC-PC and covering the whole brain were imaged using a T2* weighted gradient echo spiral in-out pulse sequence with the following parameters: TR = 2 s, TE = 30 ms, flip angle = 80°, 1 interleave. The field of view was 20 cm, and the matrix size was 64 x 64, providing an in-plane spatial resolution of 3.125 mm. High resolution T1-weighted structural brain images were acquired in the same session to aid in localization of brain activation.

fMRI experimental design Children performed Addition and Subtraction verification tasks in two separate runs. Stimuli were presented in a block fMRI design in order to optimize signal detection and task-related effective connectivity analysis. Block length was randomly jittered between 22.5 and 27 seconds. For both Addition and Subtraction problems, answers were correct on 50% of the trials. The order of the accurate and inaccurate trials was randomized across participants and incorrect answers deviated by ± 2 or ± 1 from the correct answer to ensure that children were not guessing or approximating (Ashcraft & Battaglia, 1978). Accuracy and median reaction time of correctly solved problems were computed for each participant. Each equation was displayed for 5 seconds with an inter-trial interval of 500 milliseconds.

fMRI preprocessing The first 5 volumes were not analyzed to allow for signal equilibration. ArtRepair software was used to correct for excessive participant movement (http://spnl.stanford.edu/tools/ArtRepair/ArtRepair.htm). Images were realigned to correct for movement, smoothed with a 4 mm 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 slice-timing errors, spatially transformed for registration to standard MNI space, and smoothed again at 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.

fMRI multivariate pattern analysis A multivariate statistical pattern recognition-based method (Kriegeskorte, Goebel, & Bandettini, 2006) was used to identify brain regions that discriminated spatial activation patterns between HMA and LMA groups. This method utilizes a nonlinear classifier based on support-vector machine algorithms with radial basis function kernels. We used *t*-scores to examine group differences because defining response patterns in units of standard-error, rather than beta estimates, has been shown to have greater sensitivity for extracting pattern information in fMRI data (Misaki, Kim, Bandettini, & Kriegeskorte, 2010). Briefly, at each region of interest, the spatial pattern of voxels was defined by an n-dimensional vector where n in the number of voxels in the region of interest. This vector was normalized to unit mean and standard deviation. Support vector machine (SVM) classification was performed using LIBSVM software (www.csie.ntu.edu.tw/~cjlin/libsvm). For the nonlinear SVM classifier, we specified two parameters, C (regularization) and α (parameter for RBF kernel) at each searchlight position. We estimated optimal values of C, α and the generalizability of the classifier at each searchlight position by using a combination of grid search and cross-validation procedures. In earlier approaches, linear SVM was used and the free parameter C, was arbitrarily set. In the current work, however, we optimized the free parameters (C and α) based on the data, thereby designing an optimal classifier. In the M-fold cross-validation procedure, the data is randomly divided into M-folds. M-1 folds were used for training the classifier and the remaining fold was used for testing. This procedure is repeated M times wherein a different fold was left out for testing each time. We estimated class labels of the test data at each fold and computed the average classification accuracy obtained at each fold, termed here as the cross validation accuracy (CVA). The optimal parameters were found by grid searching the parameter space and selecting the pair of values (C, α) at which the M-fold cross-validation accuracy is maximized. In order to search for a wide range of values, we varied the values of C and α from 0.125 to 32 in steps of 2 (0.125, 0.25, 0.5,..., 16, 32). Here we used a leave-one-out cross-validation procedure where M = N (where N is the number of data samples in each condition/class). The resulting 3-D map of cross-validation accuracy at every voxel was used to detect brain regions that discriminated between groups. Under the null hypothesis that there is no difference between the two groups, the cross validation accuracies (CVAs) were assumed to follow the binomial distribution Bi (N, p) with parameters N equal to the total number of participants in two groups and p equal to 0.5, assuming that under the null hypothesis, the probability of each group is equal (Pereira, Mitchell, & Botvinick, 2009). The CVAs were then converted to p-values using the binomial distribution (Abrams et al., 2011).

fMRI effective connectivity analysis Psychophysiological interaction (PPI) connectivity analysis (Friston et al., 1997) was performed using a 4-mm radius sphere centered in the right amygdala cluster which showed significant hyperactivity in the HMA group (X, Y, Z = 32, -4, -22). The PPI analysis employed three regressors: a physiological variable representing the deconvolved time series within the seed region, a psychological variable representing the Complex and Simple arithmetic conditions, and a psychophysiological interaction term that represented the Hadamard cross-product of the first two regressors. PPI analyses were performed at the individual participant level and contrast images corresponding to Complex, versus Simple, Addition and Subtraction conditions were entered into a group-level *t*-test to compare task-related differences in effective connectivity between the HMA and LMA groups. Significant clusters were thresholded at $p < .05$, with FWE corrections for multiple spatial comparisons ($p < .05$, $k = 515$ voxels), as determined using the Monte Carlo simulations.

Results

Specificity of right amygdala hyperactivity in math anxiety To examine laterality differences in amygdala reactivity between the HMA and LMA groups, we contrasted left and right amygdala responses using a 2-way repeated-measures ANOVA with a between-subject factor of Group (HMA, LMA) and a within-subject factor of Hemisphere (Left, Right). The analyses revealed a significant Group x Hemisphere interaction ($F(1, 44) = 5.519$, $p = .023$). Follow-up *t*-tests revealed significant differences between the HMA and LMA groups in the right amygdala ($t(44) = -3.524$, $p = .001$), but not in the left amygdala ($t(44) = -.051$, $p = .959$). These results highlight the specificity of right amygdala hyperactivity in math anxiety.

References

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Table S1.

Scale for Early Mathematics Anxiety (SEMA)

Instructions: Now I'm going to show you some math questions. I want you to read each question and pretend that you are going to answer it. Then I want you to tell me how nervous answering that question makes you feel. So remember, you don't actually have to answer the questions, but I just want you to pretend you are going to answer them and see how it makes you feel. It could make you feel Not nervous at all, A little nervous, Somewhat nervous, Very nervous, or Very, very nervous. Do you understand?

	Not nervous at all	A little nervous	Somewhat nervous	Very nervous	Very, very nervous
Practice: Who's the President of the United States?					
1. George bought two pizzas that had six slices each. How many total slices did George have to share with his friends?					
2. Is this right?: 9 + 7 = 18					
3. How much money does Annie have if she has 2 dimes and 4 pennies?					
4. How do you write the number *four hundred and eighty two*?					
5. Draw an hour and minute hand on a clock so that it would read 3:15 PM.					
6. Draw a triangle and a square on the board.					
7. Count aloud by 5s from 10 to 55.					
8. What time will it be in 20 minutes?					
9. Is this right?: 15 - 7 = 8					
10. Daisy has more money than Ernie. Ernie has more money than Francesca. Who has more money - Daisy or Francesca?					

Instructions: Now I'm going to read you some sentences about situations that have to do with math. Try to pretend each situation is happening and think about how nervous it makes you feel. It could make you feel not Nervous at all, A little nervous, Somewhat nervous, Very nervous, or Very, very nervous. Do you understand?

	Not nervous at all	A little nervous	Somewhat nervous	Very nervous	Very, very nervous

Practice: You're about to ride a roller coaster.	
1. You are in math class and your teacher is about to teach something new.	
2. You have to sit down to start your math homework.	
3. You are adding up all the money in your piggy bank.	
4. Someone asked you to cut up an apple pie into four equal parts.	
5. You are about to take a math test.	
6. You are in math class and you don't understand something. You ask your teacher to help you.	
7. Your teacher gives you a bunch of addition problems to work on.	
8. Your teacher gives you a bunch of subtraction problems to work on.	
9. You are in class doing a math problem on the board.	
10. You are listening as your teacher explains to you how to do a math problem.	

Table S2.

Behavioral scanner performance of high-math-anxiety (HMA) and low-math-anxiety (LMA) groups

	HMA	**LMA**
Mean Accuracy ± SEM		
Complex		
Addition	67.87 ± 4.50	84.30 ± 3.21
Subtraction	60.63 ± 4.16	66.67 ± 5.19
Simple		
Addition	80.92 ± 3.58	90.82 ± 2.58
Subtraction	73.43 ± 3.73	75.60 ± 4.59
Median Response Times ± SEM		
Complex		
Addition	2826.78 ± 161.95	2782.15 ± 132.64
Subtraction	3040.98 ± 151.80	2911.13 ± 150.40
Simple		
Addition	2548.04 ± 115.23	2228.37 ± 108.56
Subtraction	2773.28 ± 118.16	2425.46 ± 131.19

Note: df = (1, 44) for all analyses.

Figure Legend

Figure S1. Increases and decreases in brain activation associated with math anxiety. Brain areas that showed activation differences between the high-math-anxiety (HMA) and low-math-anxiety (LMA) groups also demonstrated significant linear increases and decreases between math anxiety and signal level. **(a)** Increases in activation with math anxiety in right amygdala and anterior hippocampus. **(b)** Decreases in activation with math anxiety in left ventromedial prefrontal cortex (VMPFC), left intra-parietal sulcus (IPS), right dorsolateral prefrontal cortex (DLPFC) and left basal ganglia.