Supplementary Data

Methods

Child Behavior Checklist

The Child Behavior Checklist records, in standardized format, behavioral problems and competencies of children aged 6–18 years. Normed on a nationally representative sample of 1753 youths, it includes a total problems score, as well as scores reflecting internalizing (affective and anxiety) and externalizing symptoms (attentional problems and disruptive behavior), with a *T* score above 63 considered in clinical range.

Child Depression Inventory

This 27-item self-report questionnaire measures total depression and 5 factors: negative mood, interpersonal problems, ineffectiveness, anhedonia, and negative self- esteem, with a *T* score above 65 considered above the clinical cutoff. Because this was a nonclinical sample including young children, we omitted the item asking about suicidal ideation.

Imaging procedure

Data were acquired on a 3T Trio Tim Siemens scanner (Siemens, Erlagen, Germany) by using a 32-channel head coil. T1-weighted whole-brain anatomical images (magnetization-prepared rapid acquisition gradient-echo sequence, 256×256 voxels, 1.3×1.3 mm in-plane resolution, 1.3-mm slice thickness) were acquired. After the anatomical scan, participants underwent a resting fMRI scan in which they were instructed to keep their eyes open and the screen was blanked. Resting-scan images were obtained in 67 two-mm-thick transverse slices, covering the entire brain (interleaved echo planar image sequence, T2*-weighted images; repetition time = 6 sec, echo time = 30 ms, flip angle = 90°, FOV = 256 mm, 2×2×2 mm voxels, slice thickness = 2 mm). The resting scan lasted 6.2 min (62 volumes).

Resting-state image preprocessing and noise estimation

Resting-state fMRI images were preprocessed in SPM8, using standard spatial preprocessing steps. Images were slice-time corrected, realigned to the first image of the resting scan, resampled such that they matched the first image of the resting scan voxel for voxel, normalized in Montreal Neurologic Institute space, and smoothed with a 6-mm kernel (full width at half maximum).

Physiological and other spurious sources of noise were estimated and regressed out by using the anatomical CompCor method (*aCompCor*) (Behzadi et al., 2007). A temporal band-pass filter of 0.008–0.09 Hz was applied simultaneously to all regressors in the model. Residual head motion parameters (three rotation and three translation parameters, plus another six parameters representing their first-order temporal derivatives) were regressed out. Artifact/outlier scans were also regressed out. A scan is considered an outlier if either (1) the global signal intensity of the scan is more than three standard deviations of the mean signal across the entire resting-state session, or (2) the composite head movement is greater than 1 mm. The composite head movement was computed by first converting six rotations per translation motion parameters into another set of six parameters characterizing the trajectories of six points located on the center of each of the faces of a bounding box around

Supplementary Table S1. Between-Group Connectivity Differences from (A) Left Dorsolateral Prefrontal Cortex, and (B) Subgenual Anterior Cingulate Cortex Seed When Sex Was Included as a Covariate

	BA	*Volume*	*x, y, z*	*t*	*df*	p
(A) Left DLPFC connectivity						
Nonconverted>converted						
R DLPFC	9/8	888	38, 28, 46	5.74	22	0.007
R IPL	40	1448	52, −56, 44	5.87	22	0.001
Converted>nonconverted						
None						

	BA	*Volume*	*x, y, z*	*t*	*df*	p
(B) sgACC connectivity						
Nonconverted>converted						
L IPL/postcentral gyrus	40/2	760	−40, −30, 52	6.05	22	0.01
Converted>nonconverted						
None						
Nonconverted>control						
L IPL/postcentral gyrus	40/2	1376	−42, −30, 48	5.54	28	0.001

Peak coordinates (*x y z*) based on MNI brain.
t, peak *t*-value from the cluster; *p*, FDR-corrected cluster-level *p*-value.
BA, Brodmann area; DLPFC, dorsolateral prefrontal cortex; FDR, false discovery rate; IPL, inferior parietal lobule; MNI, Montreal Neurologic Institute; sgACC, subgenual anterior cingulate cortex; volume, cluster size in microliter.

the brain. The maximum scan-to-scan movement of any of these points is then computed as the single composite movement measure. Head displacement across the resting scan did not differ significantly between the converted and nonconverted groups for either frame-to-frame translations in x, y, and z directions (converted: mean = 0.19 ± 0.11 mm; nonconverted: mean = 0.19 ± 0.08 mm; $p = 0.98$) or frame-to-frame rotations (converted: mean = 0.0043 ± 0.003; nonconverted: mean = 0.0041 ± 0.003; $p = 0.9$). The number of outliers also did not differ significantly between the two groups (converted: mean = 3.0 ± 2.9; nonconverted: mean = 3.6 ± 2.9; $p = 0.6$). The control group also did not differ significantly from the nonconverted group on these measures (ps > 0.2). Outlier images were modeled as nuisance covariates. Each outlier image was represented by a single regressor in the GLM, with a 1 for the outlier time point and 0 sec elsewhere.

Results

Connectivity differences between nonconverted and control groups

In the exploratory analysis for resilience (nonconverted vs. controls) with dorsolateral prefrontal cortex (DLPFC) and amygdala seeds, only left DLPFC connectivity showed significant difference between the two groups: The nonconverted group had lower connectivity between left DLPFC and bilateral inferior temporal gyrus than the control group. However, this difference was not significant when the nonconverted group was compared with the subset of controls who were assessed at follow-up, which may reflect the reduced statistical power for the small subset of control participants who returned for assessment.

Age-related changes in connectivity

To test whether the group differences described earlier were related to developmental differences in the participants, age-related differences in connectivity were examined for the subgenual anterior cingulate cortex (sgACC) and left DLPFC seeds. Within the entire group of at-risk children, sgACC exhibited age-related decreases in connectivity with the left insula, left superior parietal lobule, and left superior frontal gyrus. Left DLPFC exhibited an age-related increase in connectivity with the left lateral occipital cortex and a decrease in connectivity with the right frontal pole. Across the entire group of participants (at-risk and controls), the left DLPFC did not show significant age-related difference. sgACC exhibited decreased connectivity with left insula with age. None of these regions that exhibited age-related connectivity differences overlapped with the regions found in the group differences analyses (reported in Connectivity Differences Between Converted and Nonconverted Groups and Connectivity Differences Between Nonconverted and Control Groups sections).

Supplementary Reference

Behzadi Y, Restom K, Liau J, Liu TT. 2007. A component based noise correction method (CompCor) for BOLD and perfusion based fMRI. Neuroimage 37:90–101.