Online Supplementary

**Image acquisition**

Whole-brain resting-state functional images were acquired along 32 axial slices with an echo-planar imaging sequence (repetition time = 2000 ms, echo time = 30 ms, flip angle = 90°, matrix = 64 × 64, field of view = 22 cm, voxel size = 3.5 × 3.5 × 4 mm, slice thickness = 3 mm, slice gap = 1 mm), aligned along the anterior commissure–posterior commissure line. Scan duration was 6 minutes for 24 pairs of twins and 7.5 minutes for 84 pairs of twins. During the scanning procedure, the participants were instructed to keep their eyes closed and think of nothing, without falling asleep. For spatial normalization, high-resolution T1-weighted anatomical images were acquired axially using a 3D gradient-echo pulse sequence (repetition time = 2,530 ms, echo time = 3.37 ms, flip angle = 7°, matrix = 256 × 192, slice thickness = 1.33 mm).

**Image preprocessing**

In brief, preprocessing steps included: slice timing correction; outlier detection of functional volumes; motion correction; co-registration of the anatomical image to the mean functional image; segmentation of the anatomical image into cerebrospinal fluid (CSF), white matter, and gray matter, and normalization to the standard Montreal Neurological Institute template. Subsequently, smoothing was performed using a 6-mm isotropic full-width at half-maximum Gaussian kernel to enhance the signal-to-noise ratio. After smoothing, we applied linear regression of potential confounding effects in the BOLD signal. Six time-series of head movement on translational axes of X, Y, and Z and rotational axes of pitch, roll, and yaw were obtained as confounding variables. In addition to these six head motion parameters, we concluded the various expansion terms to yield 18 additional variables to attempt to correct head motion at individual-subject level (Friston et al. 1996). For further removal of potential putative nuisance signals of white matter and CSF, an aCompCor method was applied for removing noise components from white matter and cerebrospinal areas. Within each area, five potential noise components (Chai et al. 2012) are estimated: the first computed as the average BOLD signal, and the next four computed as the first four components in a Principal Component Analysis of the covariance within the subspace orthogonal to the average BOLD signal and all other potential confounding effects. Global signal regression is also used to consider the average BOLD signal (across the entire brain) as a potential confounding effect. After denoising step, temporal frequencies below 0.008 Hz or above 0.1 Hz were removed from BOLD signal using a discrete cosine transform windowing operation to minimize border effects.

**Network analysis**

For each ROI within a network, we placed a 6-mm sphere around the coordinates of peak activation for each discrete cluster within the left and right hemisphere masks. The first eigenvariate of voxelwise raw time-series in each ROI was subtracted and de-meaned in each participant. Within-network resting-state functional connectivity was quantified using the correlation of the time-series of each ROI with all other ROIs in the network using Pearson’s r. Between-network connectivity was quantified using Pearson’s r of all the correlations between each ROI of one network and all ROIs in other networks. Thereafter, we converted r values to Z-scores using Fisher’s r to Z transformation. Finally, we averaged the Z-scores of all possible connections to compute a total network value reflecting the connectivity of all possible nodes within and between networks.

**The effect of gene markers of differential susceptibility on brain network integration**

Genomic DNA was extracted from the saliva samples of the participants. According to the manufacturer’s recommendations, a single-base primer extension assay (ABI PRISM SNaPshot Multiplex kit; ABI, Foster City, CA, USA) was performed for genotyping of polymorphisms in sensitive genes (Kim & Misra, 2007). Genotype data were processed using GeneScan Analysis version 3.7 and Genotyper version 3.7 (Applied Biosystems, Carlsbad, CA, USA). Based on past research, the following alleles were considered to confer differential susceptibility in adolescents: the valine (Val) allele of the Val66Met polymorphism (rs6265) in BDNF (Chen, Yu, Liu, & Zhang, 2015; Zhang et al., 2016), the short allele (S) of the serotonin-transporter-linked promoter region polymorphism (rs25531) in 5-HTT (Li, Berk, & Lee, 2013; Starr, Hammen, Brennan, & Najman, 2013; Stocker et al., 2017; Taylor et al., 2006), and the methionine (Met) allele of the Val158Met polymorphism (rs4680) in COMT (Stocker et al., 2017; Zhang et al., 2016).

The Mann–Whitney *U*-test was performed using SPSS software version 24 (IBM Corp; Armonk, NY, USA) to identify whether the gene markers (i.e., *BDNF*, *5-HTT*, and *COMT*) had an effect on the differential susceptibility-related brain network integration in middle adolescence. Adolescents with one or two susceptibility gene(s) were grouped to test for inter-group differences. Results showed that adolescents with the Val allele in *BDNF* exhibited significantly lower connectivity in the central executive network than did those who were homozygous for the Met allele (U = 1,270.00, p = 0.007), which survived the FDR correction. No significant differences were observed for *5-HTT* and *COMT* variants. In agreement with the twin model results, there were no significant effects of *BDNF*, *5-HTT*, and *COMT* on the interaction between the anterior salience network and the default mode network (online Supplementary Table S4).

We also created the polygenic susceptibility score to indicate the composite genetic susceptibility and examined its relationship with central executive network. We estimated the polygenic scores by simple summing, as in prior investigations (Stocker et al., 2017). Each polymorphism was assigned a score of “0” if no sensitivity allele was found at that locus, “1” if one of the alleles was found, and “2” if two of these alleles were found. Finally, these scores were added together to generate an index of polygenic susceptibility score, which ranged from 0 to 6 in our group (mean = 3.57; *SD* = 1.15). A mixed linear model was used to examine the relationship between polygenic susceptibility score and central executive network connectivity: polygenic susceptibility score as the independent variable, network connectivity as the dependent variable, family as nested variables, sex, age, birth order, and stressful life events as covariates. Results showed that the relationship between polygenic scores and central executive network connectivity is significant, *β* = −0.183, *p* < .05, indicating that the higher the polygenic susceptibility score of adolescents, the lower the functional connectivity of central executive network.

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# Table S1

# *Regions-of-Interest for the intrinsic brain networks*

|  |  |  |
| --- | --- | --- |
| Network | MNI Coordinates (x, y, z) | Label |
| Central Executive Network | -42,-63,46 | L inferior parietal lobule |
| -32,23,49 | L middle frontal gyrus |
| -40,48,-01 | L middle frontal gyrus |
| -59,-42,-12 | L middle temporal gyrus |
| -07,34,43 | L medial frontal gyrus |
| 38,26,42 | R middle frontal gyrus |
| 48,-54,47 | R inferior parietal lobule |
| 38,54,01 | R middle frontal gyrus |
| 13,02,14 | R caudate |
| 06,37,46 | R medial frontal gyrus |
| Anterior Salience Network | -06,17,47 | L dorsal anterior cingulate cortex |
| -31,47,22 | L middle frontal gyrus |
| -42,14,-03 | L anterior insula |
| 06,17,47 | R dorsal anterior cingulate cortex |
| 28,46,26 | R middle frontal gyrus |
| 42,14,-03 | R anterior insula |
| Default Mode Network | -04,-52,32 | L posterior cingulate cortex |
| -05,55,-13 | L ventromedial prefrontal cortex |
| -49,-62,34 | L temporoparietal junction |
| 04,-53,35 | R posterior cingulate cortex |
| 05,55,-13 | R ventromedial prefrontal cortex |
| 50,-57,36 | R temporoparietal junction |

*Note.* L: Left; R: Right

# Table S2.

# *Results for all the interactions between parenting environments and brain network integration.*

|  |  |  |  |
| --- | --- | --- | --- |
| Interactions | *df* | *β* | *p* |
| Maternal hostility\*CEN | 101.705 | −0.086 | 0.009 |
| Paternal hostility\*CEN | 162.200 | 0.025 | 0.133 |
| Maternal warm\*CEN | 108.207 | 0.054 | 0.187 |
| Paternal warm\*CEN | 107.123 | 0.044 | 0.292 |
| Maternal hostility\*aSN | 117.469 | −0.037 | 0.408 |
| Paternal hostility\*aSN | 113.120 | 0.075 | 0.034 |
| Maternal warm\*aSN | 108.500 | −0.015 | 0.668 |
| Paternal warm\*aSN | 109.329 | −0.030 | 0.460 |
| Maternal hostility\*aSNDMN | 107.362 | 0.028 | 0.431 |
| Paternal hostility\*aSNDMN | 103.845 | −0.093 | 0.009 |
| Maternal warm\*aSNDMN | 100.684 | 0.015 | 0.632 |
| Paternal warm\*aSNDMN | 96.860 | 0.051 | 0.134 |
| Maternal hostility\*DMN | 115.790 | −0.014 | 0.694 |
| Paternal hostility\*DMN | 111.087 | 0.046 | 0.164 |
| Maternal warm\*DMN | 120.984 | 0.003 | 0.939 |
| Paternal warm\*DMN | 114.860 | 0.007 | 0.831 |
| Maternal hostility\*CENaSN | 97.634 | −0.013 | 0.722 |
| Paternal hostility\*CENaSN | 107.450 | −0.016 | 0.639 |
| Maternal warm\*CENaSN | 103.332 | 0.012 | 0.708 |
| Paternal warm\*CENaSN | 101.971 | 0.057 | 0.068 |
| Maternal hostility\*CENDMN | 103.728 | −0.015 | 0.646 |
| Paternal hostility\*CENDMN | 108.491 | 0.032 | 0.362 |
| Maternal warm\*CENDMN | 117.200 | 0.003 | 0.922 |
| Paternal warm\*CENDMN | 110.908 | 0.035 | 0.281 |

*Note.* CEN, central executive network; aSN, anterior salience network; aSNDMN, the connectivity between the anterior salience network and default mode network; DMN, default mode network; CENaSN, the connectivity between the central executive network and anterior salience network; CENDMN, the connectivity between the central executive network and default mode network.

# Table S3.

# *Parameter estimates for competitive univariate biometric models of CEN and aSNDMN connectivity*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Functional brain network connectivity | Model | −2logL | *df* | AIC |
| CEN | ACE | −314.929 | 172 | −658.929 |
| **AE** | **−314.929** | **173** | **−660.929** |
| CE | −313.502 | 173 | −659.502 |
| E | −312.379 | 174 | −660.379 |
| aSNDMN | ACE | −171.783 | 172 | −515.783 |
| AE | −171.783 | 173 | −517.783 |
| CE | −171.594 | 173 | −517.594 |
| **E** | **−170.761** | **174** | **−518.761** |

*Note.* A, additive genetic factors; C, shared environmental factors; E, unique environmental factors. CEN, central executive network; aSNDMN, the interaction between the anterior salience network and default mode network; AIC, Akaike information criterion. The AE model (i.e., in bold) with the lowest AIC is the best-fitting model for CEN connectivity. The E model (i.e., in bold) with the lowest AIC is the best-fitting model for aSNDMN connectivity.

# Table S4

# *Results for the Mann–Whitney U-test*

|  |  |  |
| --- | --- | --- |
| Tests | Groups | *p* |
| CEN | *BDNF* | 0.007 |
| *5-HTT* | 0.166 |
| *COMT* | 0.309 |
| aSNDMN | *5-HTT* | 0.066 |
| *BDNF* | 0.465 |
| *COMT* | 0.603 |

# CEN, central executive network; aSNDMN, the interaction between the anterior salience network and default mode network.