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Supplementary information

Global urbanicity is associated with brain and behaviour in young people

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Global urbanicity is associated with brain and behavior in young people

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Supplementary Information

Content

Supplementary Methods

1. Participants

1.1 CHIMGEN

1.1.1 Introduction

The Chinese Imaging Genetics (CHIMGEN) project was approved by the ethics committee of each center, and written informed consent was obtained from each participant. This project was initiated in 2015 and included 31 centers from 21 cities in Chinese mainland[1]. Genomic, transcriptomic, environmental, neuroimaging and behavioral data were collected from 7306 healthy Chinese Han participants (by the time of November 2020) of 18-30 years of ages to investigate genetic and environmental effects on brain and behavior. At the time of data analysis of this study (January 2018), data were available for 5425 participants.

1.1.2 Sample selection

The sample selection for the different statistical analyses of the CHIMGEN data is shown in Supplementary Fig.1.

(1) Excluding participants without lifetime residential information

Among the 5425 participants, 3336 participants had provided lifetime residential geographies. The remaining 2089 participants were excluded because they only provided their residential addresses at the time point of recruitment but they refused to provide their residential addresses at any other time points since birth. From the 3336

participants, we successfully extracted satellite-based measures of urbanicity of 3306 participants. The other 30 participants were excluded because extracting satellite measures failed in more than three years during their lifetime.

(2) Excluding participants without confounding covariates

Potentially confounding covariates including age, gender, education, site, body mass index (BMI), genetic population stratification, socioeconomic status (SES), total intracranial volume (TIV), mean cortical thickness (MCT) and total surface area (TSA) were corrected in the correlation analyses of satellite based-measure of urbanicity with brain and behavior. Complete information of confounders was available in 2176 participants, with 1130 participants being excluded from the 3306 participants with lifetime geopositioned data.

(3) Excluding participants without qualified neuroimaging data

For each neuroimaging measure, we had to exclude participants with unqualified raw imaging data and participants failed to pass the quality control (QC) during imaging data preprocessing. In the 2176 participants, 2176 participants were included in the voxel-based morphometry (VBM) analysis of gray matter volume (GMV) and 2164 participants in the surface-based morphometry (SBM) analysis of cortical thickness (CT) and surface area (SA) based on T1-weighted neuroimaging data ; 2158 participants in the Tract-based Spatial Statistics (TBSS) analysis of fractional anisotropy (FA) based on diffusion tensor imaging (DTI) data; and 2156 participants in the within-network (WNFC) and between-network (BNFC) functional connectivity analyses based on resting-state functional MRI (rsfMRI) data.

(4) Excluding participants without qualified behavioral assessments

For each behavioral measure analysis, we had to exclude participants without qualified behavioral assessment. In the 2176 participants with at least one type of the qualified MRI data, 2173 participants were finally included in the analysis of verbal learning memory, 2063 in working memory, 2139 in information processing speed, 2148 in social cognition, 2024 in cognitive control, and 2170 in mental health.

1.2 IMAGEN

1.2.1 Introduction

IMAGEN is the first European multisite and prospective project aiming to integrate different levels of environmental and biological mechanisms to identify biomarkers for developmental psychiatric disorders[2]. Comprehensive environmental factors, genetics, transcriptome, epigenetics, structural and functional neuroimaging, neurocognitive measure and mental health outcome are collected from more than 2000 14-year-old adolescents in 2009. Brain imaging measures were longitudinally assessed at age 14 years (baseline, BL) and 19 years (second follow-up, FU2). Most of neurocognitive and mental health outcome longitudinally assessed at BL, FU1 (16 years) and FU2. This project was approved by the institutional ethics committee of each center, and written informed consent was obtained from all participants.

1.2.2 Sample selection

The sample selection and loss of follow up in IMAGEN is shown in Supplementary Fig.2.

(1) Excluding participants without lifetime residential information

Among the 1411 participants of IMAGEN-FU2, 561 participants provided lifetime residential geographies. All participants's satellite-based measures of urbanicity at each year have been extracted successfully.

(2) Excluding participants without confounding assessments

From these 561 participants, we excluded 79 participants without the confounding assessments (SES, parental history of mental illness and genetic population stratification) and the remaining 482 participants were included in the further analysis.

(3) Excluding participants without qualified neuroimaging data

Among the remaining 482 participants (FU2), 415 participants were included in VBM analysis after passing QC; 420 participants in SBM analysis; 436 participants in TBSS analysis; and 351 participants in WNFC and BNFC analyses. Participants with both BL (age 14) and FU2 (age 19) imaging data after QC were used in brain development analyses, including 340 participants in VBM analysis, 325 participants in SBM analysis, 396 participants in TBSS analysis, and 83 participants in WNFC and BNFC analyses. It is notable that during IMAGEN baseline assessment in the year of 2009, resting state MRI was only carried out in 156 participants.

(4) Excluding participants without qualified behavioral assessments

Among the 482 participants (FU2), complete data of perspective taking was available in 342 participants, Ruminating Scale Questionnaire (RSQ) in 346

participants, Generalized Anxiety Scale from The Development and Well-Being Assessment Interview (DAWBA-GA) in 447 participants and Anxiety Screening for Composite International Diagnostic Interview (CIDI-DIA) in 391 participants.

2. Data collection

2.1 Residential geographies

2.1.1 CHIMGEN

In each CHIMGEN participant who had consented to provide residential information, we recorded the precise residential addresses in each year from his/her birth to recruitment and the category of each place (1=rural, 2=town, 3=city) that was determined according to the National Bureau of Statistics of China (http://www.stats.gov.cn/tjsj/ndsj/renkoupucha/2000pucha/html/append7.htm). If participants moved several times in a year (rare cases), the address where they lived more than six months was recorded. To minimize recall bias, the residential addresses of each participant were confirmed in two separate visits. In the first visit, we asked the participant to write down his/her residential addresses in paper-based assessments. In the second visit, we asked the participant to mark each residential address on an electronic map with a web-based program designed by the consortium. If the address could not be found on the map, the participant was asked to mark the nearest road or landmark on the map. Thereafter, a researcher checked the consistency of addresses provided by the participant at the two visits. When inconsistencies occurred (which was very rarely the case), the researcher asked the participant to clarify which is correct. All

participants who provided residential addresses claimed that they had correctly recalled the residential addresses at all time points in their lifetime. Finally, 3336 participants who provided their lifetime residential geographies were included in the further analysis.

2.1.2 IMAGEN

At the time of the second follow up, 561 IMAGEN participants provided their precise residential addresses of each year from their birth to recruitment and the category of each place (1=rural, 2=town, 3=city). Rural is defined as places with less than 10,000 inhabitants, town is defined as places with more than 10,000 inhabitants and less than 100,000 inhabitants and city is defined as places with more than 100,000 inhabitants. To maintain the anonymity of participants, these addresses have been obfuscated to 1km scaled longitude and latitude based on Google Earth Engine (GEE) coordinate system using code (https://github.com/crickfan/geo-anonymization) according to privacy regulation from European Commission's Article 29 Working Party (http://www.privacy-regulation.eu/en/article-4-definitions-GDPR.htm).

2.2 Remote sensing satellite data

GEE is an open access platform that makes hundreds of earth-observational satellite imagery and geospatial datasets with planetary-scale analysis available for researchers (https://earthengine.google.com/). Global human settlement layer (GHSL)[3], night-time lights (NL)[4], normalized difference vegetation index (NDVI)[5], normalized difference built-up index (NDBI)[6], normalized difference water index

(NDWI)[7] and global land cover mapping (GLCM)[8] were extracted from GEE and European Space Agency (ESA) platform to measure different urban characteristics based on the acquired individual lifetime geographies from CHIMGEN and IMAGEN-FU2. We successfully extracted satellite-based measures of urbanicity for 3306 participants from CHIMGEN and for 561 participants from IMAGEN-FU2.

2.2.1 Global Human Settlement Layer (GHSL)

GHSL produces global spatial information about the human presence on the planet over time, which is rendered in the form of built up maps, population density maps and settlement maps[3]. GHSL-POP (2016) (https://ghsl.jrc.ec.europa.eu/index.php) from the GEE platform provides population density data of 1975, 1990, 2000 and 2015 at a spatial resolution of 250m×250m (Supplementary Table 7). Based on the lifespans of participants, we used population density data of 1990, 2000 and 2015 in CHIMGEN and those of 2000 and 2015 in IMAGEN-FU2.

2.2.2 Night Light (NL)

NL reflects visible and near-infrared emission sources at night, which has been applied to measure the prosperity or urbanicity of the neighborhood surroundings[4,9-11]. NL data provide valuable insights on the distribution and magnitude of human activity on Earth. The amount of light emitted from Earth at night corresponds with electricity consumption and gross domestic product (GDP)[12,13], and is seen as a good proxy for true income growth[14] and for the distribution of economic activity[15] at different scales. Moreover, because nighttime lights are associated with human activity, they also

provide a good proxy for population counts and density[16,17] as well as can capture the distribution and patterns of human settlements[18,19], urban growth and expansion[20-23], which has been shown correlated with mental disorders[24]. The NL data of each participant were extracted from Defense Meteorological Program (DMSP) Operational Line-Scan System (OLS) Nighttime Lights Time Series Version 4 product (https://developers.google.com/earth-engine/datasets/catalog/NOAA_DMSP-OLS_NIGHTTIME_LIGHTS). The NL data (ranged from 0 to 63) had a spatial resolution of 1km ×1km and were available from 1992 to 2013 (Supplementary Table 7).

2.2.3 Normalized Difference Vegetation Index (NDVI)

Traditionally, NDVI has been used in the literature as a proxy for vegetation "greenness", live green plant canopies, vegetation seasonality, biophysical properties of vegetation canopy and productivity[25-28], as well as a proxy for the ecological effects of environmental changes on ecosystems[29]. However, because of its ability to capture the amount, type and distribution of green ("live") vegetation, NDVI is also used extensively to measure the distribution of green spaces in urban settings, as well as to estimate the exposure of different population groups to green spaces in cities[30-33]. With the increased availability of satellite imagery and the improvement in methods for analysis and interpretation, there is an ongoing increase in the research domain that links remotely-sensed derived information on green spaces (NDVI) with human cognition[34-36] and mental health[37-41]. Since NDVI varies with the seasons at least in some areas (i.e., north China and Europe), it can be used to estimate residential

greenness[30-33] rather than the coverage of vegetation. In the present study, NDVI was derived from the product of NOAA Climate Data Record (CDR) of Advanced Very High-Resolution Radiometer (AVHRR) NDVI (https://developers.google.com/earth-engine/datasets/catalog/NOAA_CDR_AVHRR_NDVI_V4). The NDVI data had a resolution of 5km×5km and were available from 1981 to 2017 (Supplementary Table 7).

2.2.4 Normalized Difference Built-up and Water Index (NDBI and NDWI)

NDBI was used to assess built-up and NDWI was used to assess water content of neighborhood surroundings, which have been applied to map urban environment[6,42]. These two measures were calculated based on band 1-7 from Landsat 7 Collection 1 Tier 1 (https://developers.google.com/earth-engine/datasets/catalog/LANDSAT_LE07_C01_T1) (Supplementary Table 7 and 25). NDBI was calculated as (B5-B4)/(B5+B4)[6] and NDWI was calculated as (B2-B4)/(B2+B4)[7]. NDBI and NDWI data were ranged from -1 to 1 and were available from 1999 to 2017 at a spatial resolution of 30 meters.

2.2.5 Global land cover mapping (GLCM)

While NDVI, NDBI and NDWI are related to vegetation, building and water, respectively, they cannot provide information for a particular land cover type. For example, high NDVI value may indicate better vegetation cover/condition, but this measure cannot distinguish between forest, cropland and grassland etc. We therefore enhanced this information with GLCM data, which has been extensively used to

characterize environmental changes and neighborhood surrounding resources[8,43,44]. Here Climate Change Initiative Land Cover dataset (CCI-LC) from ESA platform was used to extract land cover classes from 1992 to 2015 (http://maps.elie.ucl.ac.be/CCI/viewer/). Briefly, CCL-LC aimed to make the best use of available satellite data to provide an accurate percentage of land cover classes using supervised machine learning classification algorithm. The percentage here was defined as the number of pixels classified into a specific class divided by the total number of pixels within 1km radius centered at the anonymized home locations. There are 22 indicators in GLCM, which belong to 9 land cover types including cropland%, forest%, grassland%, shrubland%, bareland%, snow%, ice%, water body% and built-up%[44,45]. In the present study, only land cover types with mean percentage before 18 years of participants from CHIMGEN (n=3306) and IMAGEN-FU2 (n=561) above 1% were included in the further analysis, including the land cover types of the cropland (CHIMGEN: 64.21%; IMAGEN: 13.65%), forest (CHIMGEN: 5.00%; IMAGEN: 7.31%), grassland (CHIMGEN: 3.01%; IMAGEN: 7.54%), water body (CHIMGEN: 3.81%; IMAGEN: 1.37%) and built-up (CHIMGEN: 29.14%; IMAGEN: 67.03%).

2.2.6 Satellite-based measures of urbanicity

Finally, nine satellite-based measures of urbanicity including NL, NDVI, NDBI, NDWI, cropland%, forest%, grassland%, water body% and built-up% from CHIMGEN and IMAGEN-FU2 were included in the further analysis.

2.3 Confounding covariates data

In CHIMGEN and IMAGEN, we controlled for age, gender, education, site, BMI, genetic population stratification, TIV, MCT, TSA and SES in the correlation of satellite-based measure of urbanicity with brain and behavior. Parental history of mental illness was an exclusion criterion for CHIMGEN, but not in IMAGEN, where this variable was controlled for in IMAGEN data analysis.

2.3.1 CHIMGEN

The top four components from principle component analysis (PCA) of the genomic data were used to measure genetic population stratification using Plink v1.90b4.10[46]. The SES data collected for the CHIMGEN participants are provided in Supplementary Table 10. The objective SES information included parental education and occupation, and the subjective SES information included household financial difficulties, household and neighborhood adequacy. To balance the weights of different items, we calculated the z-score for each item of each participant, and then used the sum of the z-scores of all items to represent the normalized SES score of this participant. Of 3306 participants, we excluded 1130 participants due to incomplete confounder data (SES and genetic population stratification). The remaining 2176 participants were included in the further analysis.

2.3.2 IMAGEN

A Genetic Screening and Family History of Psychiatric Disorders Interview (GEN) for the participants was administered by the researcher at the day of the institute assessment at BL. Parents will be asked for place of birth and the ethnicity of

the adolescent's parents and grandparents as well as a history of psychopathology in the first- and second-degree relatives. The top four components from PCA of the genomic data were applied to measure genetic population stratification[46]. Parental educational category from the European School Survey Project on Alcohol and Other Drug (ESPAD) and socioeconomic/housing score from the Development and Well-Being Assessment (DAWBA) were included in IMAGEN. The socioeconomic/housing score included parental employment, household financial difficulties, and household and neighborhood adequacy, as applied in a previous IMAGEN study[47]. Details are provided in the Supplementary Table 11, The same method as in the CHIMGEN study was used to calculate a normalized SES score for each participant. Of 561 participants, we excluded 79 participants due to incomplete confounder data (SES, GEN and genetic population stratification). The remaining 482 participants were included in the further analysis.

2.4 Neuroimaging data

2.4.1 CHIMGEN

In this study, brain MRI data were acquired by 3.0-Tesla scanners from General Electrics®, Siemens® and Philips® from 28 sites of CHIMGEN. The standard parameters of the T1 weighted, DTI and resting-state fMRI sequences for different MR scanners are shown in Supplementary Tables 19-21, respectively. In order to pool the data across sites, a phantom was scanned at each site to homogenize geometric

distortions and signal uniformity. Moreover, two healthy volunteers were scanned at all sites to assess heterogeneity which was not captured by the phantom[1].

2.4.2 IMAGEN

In this study, brain MRI data were acquired from six 3.0-Tesla scanners from Siemens®, Philips®, General Electric® and Bruker®. The standard parameters of the T1 weighted, DTI and resting-state fMRI sequences for different MR scanners are shown in https://imagen-europe.com/resources/standard-operating-procedures. In order to pool the data across sites, a phantom was scanned at each site to homogenize geometric distortions and signal uniformity. Moreover, healthy volunteers were scanned periodically at all sites to assess heterogeneity which was not captured by the phantom[2].

2.5 Neuroimaging measures calculation

2.5.1 Gray matter volume (GMV)

The gay matter volume (GMV) calculation in voxel-based morphometry (VBM) analysis was conducted using Computational Anatomy Toolbox (CAT12 v1364) (http://dbm.neuro.uni-jena.de/cat) implemented in Statistical Parametric Mapping (SPM12) software package (http://www.fil.ion.ucl.ac.uk/spm) in the following steps: To exclude heterogeneity, the same steps were applied to preprocess structural neuroimaging data from CHIMGEN and IMAGEN.

(1) Bias correction

Image inhomogeneity caused by B1-field bias was corrected to accurately segment the brain tissues. The bias corrected images would have more uniform intensities within each type of the brain tissues.

(2) Segmentation

The bias-corrected structural images are segmented into gray matter (GM), white matter (WM) and cerebrospinal fluid (CSF) using a reliable segmentation model. The segmentation model is based on an adaptive Maximum A Posterior (MAP)[48] and a Partial Volume Estimation[49] technique which were used to estimate the fraction of each pure tissue type present in every voxel and thus allows for more precise segmentation without the need for a priori information about tissue probabilities.

(3) Creating population-specific tissue templates

To improve the quality of registration, population-specific tissue probability templates in Montreal Neurological Institute (MNI) space are derived from all qualified CHIMGEN participants by the DARTEL toolbox implemented in SPM12.

(4) Spatial normalization

The segmented images were spatially normalized to the population-specific templates using a two-step DARTEL algorithm and resampled into a cubic voxel of 1.5 mm. Modulation was performed on the normalized grey matter images to preserve the absolute volume of the GM tissue. For detailed information, please refer to “Features” part of the website: http://dbm.neuro.uni-jena.de/cat/index.html#VBM.

(5) Smoothing

The GMV images were smoothed with a kernel of $8 \times 8 \times 8$ mm^3 full width at half maximum. Then, the spatial preprocessed GMV maps were used for further analysis.

The total intracranial volumes (TIV) of each participant was also obtained. In CHIMGEN (n=2176) and IMAGEN-FU2 (n=482) with satellite-based measures of urbanicity and confounding data, 2176 participants from CHIMGEN and 415 participants from IMAGEN-FU2 were finally included in the VBM analysis.

2.5.2 Cortical thickness (CT) and surface area (SA)

The T1-weighted images were preprocessed and analyzed using FreeSurfer v6.0.0 (http://surfer.nmr.mgh.harvard) with following steps:

(1) Skull stripping

The automated skull-stripping was performed to separate the brain from non-brain tissues in structural MR images.

(2) Intensity normalization

Intensity non-uniformity due to variations in the sensitivity of the reception coil and gradient-driven eddy currents were corrected, and intensity-normalized images were generated.

(3) Tissue segmentation

The skull-stripped and intensity-normalized images were processed by a series of tissue segmentation procedures based on intensity and neighbor constraints. This step generates the boundary between GM and WM. The segmentation of subcortical white and gray matter structures was then performed.

(4) Surface reconstruction

A two-dimensional tessellated mesh was constructed based on the boundary between WM and GM to generate the WM surface in each hemisphere, and the WM surface was extended outwards by tracking the gray matter intensity gradient to generate the pial surface. Topology correction was performed to repair topological defects.

(5) Metric reconstruction

Surface-based metrics of the cortical thickness (CT) and surface area (SA) were calculated based on the pial and white matter surfaces.

(6) Spherical normalization

Individual surfaces were then inflated into a spherical space and registered to a spherical atlas in MNI152 space (the fsaverage atlas). Surface-based metrics for each cortical area were extracted based on the predefined surface atlas after registrating them to individual spaces using the spherical registration parameters.

(7) Smoothing

To reduce noise and the effect of misalignment during the surface-based transformation to the average template, the surface-based metrics were smoothed with a Gaussian kernel of 20 mm width. The mean cortical thickness (MCT) and the total surface area (TSA) of each participant were calculated and considered as confounding covariates in the CT and SA related analyses.

Due to the difficulties of identifying the real boundary and controversial preprocessing method of the cerebellar cortex, especially for the regions near the

midline cerebellar vermis[50], only the CT and SA of the cerebral cortex were calculated and used in the correlation of UrbanSat with brain. In CHIMGEN (n=2176) and IMAGEN-FU2 (n=482), 2164 participants from CHIMGEN and 420 participants from IMAGEN-FU2 were included in the CT and SA analyses.

2.5.3 Fractional anisotropy (FA)

The DTI images were preprocessed and analyzed using FMRIB's Software Library (FSL v5.0.10) toolbox (www.fmrib.ox.ac.uk/fsl)[51] in the following steps:

(1) Brain extraction (BET)

The non-brain tissues of the b=0 images were removed by applying the brain extraction tool (BET) implemented in FSL.

(2) Motion and distortion correction (EDDY)

A "EDDY_OPENMP" program implemented in the FSL v5.0.10 was used to evaluate and repair the image displacement and signal dropout caused by head motion, and image distortion caused by eddy current.

(3) Tensor metric calculation (DTIFIT)

The linear least square algorithm was used estimate the diffusion tensor and its derived metrics using the DTIFIT program implemented in FSL. In this step, diffusion metrics, such as three eigenvalues, fractional anisotropy (FA) and mean diffusivity (MD) were generated.

(4) Spatial normalization estimation (BBR+DARTEL)

A two-step procedure was used to estimate the co-registration parameters between individual diffusion space and MNI standard space.

(a) Individual b = 0 images were aligned to the corresponding structural images using the Boundary-Based Registration (BBR) algorithm implemented in FSL.

(b) The BBR parameters were concatenated with the DARTEL deformation field (from individual space to MNI space) generated in VBM analyses.

(c) The merged deformation field was used to register the individual diffusion data into the MNI space, or vice versa.

(5) Metric normalization

The diffusion metrics were normalized into the MNI space using the merged deformation field (BBR+DARTEL) that generated in step 4 and resampled into a cubic voxel of 2-mm.

(6) Generation of white matter skeleton

In this step, we used a revised TBSS pipeline to create the white matter skeleton. Rather than the standard TBSS pipeline[52] that directly nonlinearly align the individual FA images to the averaged FA template (FMRIB-58) in MNI space using the FNIRT program in FSL, we co-registered the individual FA images using the merged deformation field (BBR+DARTEL) that generated in step 4. Then a mean FA image was created and a mean FA skeleton of the white matter was generated using the center-of-gravity method. Each subject's aligned FA images were then projected onto the mean FA skeleton by filling the mean FA skeleton with FA values from the nearest

relevant tract center, which was achieved by searching perpendicular to the local skeleton structure for maximum value.

Finally, 2158 participants from CHIMGEN and 436 participants from IMAGEN-FU2 with qualified skeletonized maps were included the TBSS analysis.

2.5.4 Resting-state fMRI preprocessing

2.5.4.1 CHIMGEN

The resting-state fMRI data of 2176 CHIMGEN participants were preprocessed by pipeline based on SPM12 and Data Processing Assistant for Resting-State fMRI (DPARSFA v4.4)[53] with the following steps:

(1) Discarding unstable volumes

The first five functional volumes were discarded to allow signal to reach equilibrium and ensure the participants to adapt to scanning noise. After deletion, all the subjects have 175 volumes.

(2) Slice timing correction

The remaining volumes were corrected for intra-volume temporal differences using sinc-interpolation.

(3) Head motion correction

Inter-volume head motion correction is performed via a six-parameter rigid-body transformation. Specifically, each volume was first realigned to the first volume and then realigned to the mean of these volumes after the first correction. Rigid realignment was then performed to estimate and correct the motion displacement, and 19 participants were excluded from further analysis because their fMRI data had a

maximum displacement in one or more of the orthogonal directions (x, y, z) of > 2 mm or a maximum rotation (x, y, z) > 2.0 °

(4) Spatial normalization

To improve coregistration, the non-brain tissue of the mean corrected functional images and structural images were first removed. Then, the mean corrected functional images were coregistered to the corresponding structural images using the BBR method. Finally, all motion-corrected functional volumes were spatially normalized to the standard MNI space using deformation fields derived from aforementioned VBM analysis and resampled to 3-mm isotropic voxels.

(5) Smoothing

For the further independent component analysis (ICA), the normalized fMRI data were smoothed with a FWHM of 8 mm.

Finally, a total of 2156 CHIMGEN participants were finally included in the further analyses.

2.5.4.2 IMAGEN

The resting-state fMRI data of 366 IMAGEN-FU2 participants were preprocessed using FSL v5.0.9 and Advanced Normalization Tools (ANTs v1.9.2). Fifteen participants were excluded either because over 5% of scans in that subject exhibited artifacts of some kind, or if over 5% of volumes showed a frame displacement of over 0.5mm. Thus, 351 participants were finally included in the further analyses. Motion correction was carried out, applying a rigid body registration of each volume to the middle volume (FSL MCFLIRT), non-brain tissue was removed (FSL BET), and spatial smoothing was applied using a Gaussian kernel of $4 \times 4 \times 4$ mm^3. Independent component analysis (ICA) (FSL MELODIC) was run for each dataset. Artifact components were identified using an automatic classification algorithm, and

subsequently regressed from the data (ICA-AROMA v0.3). The resulting cleaned dataset was de-trended (up to a third-degree polynomial), and then co-registration to a high-resolution T1 image (FSL FLIRT using the BBR algorithm) and normalization to 2-mm isotropic MNI standard space (ANTs) were carried out. To further clean the data of physiological noise using CompCorr procedure, we created white matter (WM) and cerebrospinal fluid (CSF) masks by taking the mean of the WM and CSF segmentations from the VBM analysis, and thresholding them at 0.95, we then resliced these maps into the same space as the fMRI data. We then extracted timecourses from voxels within these regions and took the first three principal components of this signal for both WM and CSF maps. These six principal component signals should represent non-neuronal signal. We then regressed this non-neuronal signal from voxel timecourses across the rest of the brain. Lastly, preprocessed and normalized resting-state fMRI data were resliced to 3mm isotropic voxels.

2.5.5 Identification of resting state network

In CHIMGEN (n=2156) and IMAGEN-FU2 (n=351), group ICA (GICA) was used to decompose the resting-state fMRI data into independent components (ICs) to construct brain functional network using the Group ICA Of fMRI Toolbox (GIFT) software (http://mialab.mrn.org/software/gift/index.html, version 4.0b)[54], which included data reduction, ICA and back reconstruction. Data reduction was used to reduce the size of the participants' fMRI data using the principal components analysis. Two data reduction steps were carried out. After each participant's fMRI data was reduced, the participants were concatenated into one group and put through another data reduction step. ICA algorithm was then applied to the reduced data to identify ICs. The number (n=30) of ICs was automatically estimated using the minimum description

length (MDL) criterion[55]. ICASSO toolbox was used to determine the reliability of ICA algorithm. Specifically, ICA was run 100 times to obtain the final integrated output. The participant-specific time courses and spatial maps were back-reconstructed by a dual-regression method. A linear spatial regression was applied to the group-level spatial maps and participants' fMRI datasets to calculate matrix describing time courses for each component of each participant[54]. A linear temporal regression was then applied to these time-course matrices and participants' fMRI datasets to estimate participant-specific spatial maps[56]. To improve the normality of the data, we scaled the spatial component maps to z-scores[54,56]. Using GICA with the estimated 30 ICs, we identified 17 resting-state networks (RSNs) related to various cognitive and sensory-motor processes[57] that were shared in CHIMGEN and IMAGEN-FU2 (Supplementary Fig.16). For each participant-specific spatial component, the value of a voxel represents the relation of the time courses between this voxel and the participant-specific component, which was defined as within-network functional connectivity (WNFC). The correlation of the time courses between any two of the participant-specific components were defined as between-network functional connectivity (BNFC).

2.5.6 Brain structural and functional changes during adolescent development

We investigated the relation of urbanicity with adolescent brain development by calculating change rate for each imaging measure between BL and FU2 in IMAGEN, as we did before[58]. In the 340 participants with qualified structural imaging data both at BL (14 years) and FU2 (19 years), structural imaging data were pre-processed with the pairwise longitudinal tool implemented in SPM12 for longitudinal VBM analysis[59]. Finally, we obtained year-averaged GMV change maps of 340 participants,

year-averaged CT and SA change maps of 325 participants. In 83 participants with qualified fMRI data both at BL (14 years) and FU2 (19 years), we calculated WNFC and BNFC for each participant at each stage, and then we obtained the WNFC and BNFC change maps of the 83 participants.

2.6 Neuropsychological assessment

To test the overall exposure effect of urbanicity on behavior, we included different dimensions of neuropsychological and mental health assessments. In CHIMGEN (n=2176), complete quality-controlled data were available in 2173 participants for verbal learning memory, 2063 for working memory, 2139 for information processing speed, 2148 for social cognition, 2024 for cognitive control, and 2170 for mental health.

2.6.1 Verbal learning memory

The California Verbal Learning Test (CVLT) was used to test episodic verbal learning and memory, which have demonstrated sensitivity to a range of clinical conditions[60]. Briefly, the experimenter read a list of 16 nouns words loudly every second for five sessions in a fixed order. After each session, the subjects were asked to try their best to recall the words in free order. Then the experimenter recorded the numbers of correct words in immediate free memory recall within five sessions (imFM 1-5), short-term free memory recall (stFM), short-term clue memory recall (stCM), long-term free memory recall (ltFM) and long-term clue memory recall (ltCM), total numbers of insertion (TI), total numbers of repetition (TR) and long-term recognition (ltR).

2.6.2 Working memory

The classic letter N-back test (1-back and 3-back) were applied to measure working memory[61]. In the letter 1-back task, the subjects were required to match the current stimulus by the previous one in the sequence of stimuli. In the letter 3-back task, the subjects were required to match the current stimulus by the one from 2 steps earlier in the sequence of stimuli. Both 1-back and 3-back tasks have only one block including 60 trails. Each stimulus was presented for 200ms and the stimulation interval is 1800ms. The participants were instructed to respond as fast and accurately as possible after the presentation of each stimulus. Before the experiment, the subjects were given one practice test of the 1-back task. Only the subjects with accuracy more than 75% were allowed to perform the formal task. If not, they have to do the test task again. E-Prime 2.0 software (Psychology Software Tools) was used to present the stimuli and collect the results. We recorded the numbers of correct rejection stimuli (cr), hits stimuli (h), miss stimuli, false alarms stimuli, and no response stimuli, and finally calculated the accuracy ((cr+h)/60) in 1-back ($ACC_{1\text{-back}}$) and 3-back ($ACC_{3\text{-back}}$), respectively.

2.6.3 Information processing speed

The Symbols Digit Modality Test (SDMT) was applied to test attention and speed of processing ability[62]. Using a reference key, the subjects were required to pair specific numbers with given nine geometric figures after testing the first 10 items as fast and accurately as they can. Finally, we recorded the numbers of correctly and incorrectly filled digits in the 90 seconds. The total number of SDMT test is 110 score.

2.6.4 Social cognition

In CHIMGEN, a ball tossing game with a 2 2 factorial design was applied to test perspective taking (first-person vs. third-person perspective) and agency (active vs.

passive) of social cognition[63]. The subjects were required to perform active and passive tasks from two different perspectives. From the third-person perspective (3PP), three virtual characters (red, green, and blue) appeared on the screen to perform a ball tossing game. They have to perform the two tasks from the blue character's perspective instead of from their own. In the active task, subjects (blue character) were instructed to throw the ball to the red character when they were in possession of the ball. The subjects have to judge the red character's position from blue character's perspective (left or right side) by pressing the corresponding key "F" or "J". In the passive task, one of the red or green character was in possession of the ball, and subjects have to judge the ball's position from the blue character's perspective (left or right side) with a button press "F" or "J"; From the first-person perspective (1PP), the visional field of the subject was consistent with the forward vision of the blue character. Only one hand of the blue character was displayed on the screen without the body. They were also asked to perform the active and passive tasks. The whole task includes four blocks in the order of 1PP, 3PP, 3PP and 1PP block. Each block contains 18 trails including 6 active tasks and 12 passive tasks. The location of the subject, the character in possession of the ball and the relative position of the red character are all pseudo-random. The schematic representation of the ball tossing task design was shown in Supplementary Fig.21. The participants were instructed to respond as fast and accurately as possible after the presentation of each trail. Before the experiment, the participants were given 2 practice runs of the task. E-Prime 2.0 software was also used to present the stimuli and collect the results. We recorded active reaction time (1PP_ACT_RT and 3PP_ACT_RT) and accuracy (1PP ACT_ACC and 3PP_ACT_ACC) in the 1PP and 3PP, as well as passive reaction time (1PP_PAS_RT and 3PP_PAS_RT) and accuracy (1PP PAS_ACC and 3PP_PAS_ACC) in the 1PP and 3PP. The perspective taking and agency performance

were evaluated by: (a) accuracy in perspective taking (ACCpt): (3PP ACT_ACC + 3PP PAS_ACC) - (1PP ACT_ACC+1PP PAS_ACC); (b) accuracy in agency (ACCag): (3PP PAS_ACC + 1PP PAS_ACC) - (3PP ACT_ACC+1PP ACT_ACC); (c) reaction time in perspective taking (RTpt): (3PP ACT_RT + 3PP PAS_RT) - (1PP ACT_RT+1PP PAS_RT); and reaction time in agency (RTag): (3PP PAS_RT + 1PP PAS_RT) - (3PP ACT_RT+1PP ACT_RT).

In IMAGEN, perspective taking was assessed by interpersonal reactivity index (IRI) questionnaire acquired at FU2, that was used to test dispositional empathy comprising four separate but related conducts: perspective taking, fantasy, empathic concern and personal distress[64].

2.6.5 Executive control

The go/no-go test was used to measure participant's capacity for sustained attention and response control. The subjects were required to perform an action when the current stimulus was different from the previous one (e.g., press a button - Go trail) and inhibit that action when they were match (e.g., not press the same button - No-Go trail) in the sequence of stimuli. The whole task included two blocks with 21 Go trails and 189 No-Go trails in each block. The participants were instructed to respond as fast and accurately as possible after the presentation of each trail. Before the experiment, the participants were given 1 practice run of the task. E-Prime 2.0 software was used to present the stimuli and collect the results. We recorded accuracy in Go trial (ACC_{go}) and No-Go trails ($ACC_{no\text{-}go}$), respectively.

2.6.6 Mental health

In CHIMGEN, Beck Depressive Inventory (BDI) was used to measure severity of depression, and State-Trait Anxiety Inventory (STAI） was used to measure state anxiety (anxiety about an event) and trait anxiety (anxiety level as a personal characteristic). In IMAGEN-FU2, RSQ was used to measure the frequency of cognitions and behaviors of subjects during periods of depressed mood, which was only available in IMAGEN-FU2. Ruminative responding is highly associated with depression and one of its main cognitive symptoms[65,66]. Thus, in a mechanistic approach, ruminative responding can be viewed as a core variable of depressive behavior[67]. The findings of depressive symptoms in CHIMGEN that were ascertained using the BDI were supported in the RSQ findings of IMAGEN, where the BDI was not applied. CIDI-DIA and DAWBA-GA were applied to measure their anxiety state, which was available in IMAGEN-FU2.

2.6.7. Quality control for behavioral measures

We have carried our stringent quality control for each behavioral variable in the CHIMGEN sample (n=3306):

(1) We confirmed the consistency between input data and raw data to ensure the input data to be free of any input errors.

(2) We excluded participants with unreliable scores in these assessments.

(a) SDMT

The total number of the SDMT test is 110, thus the sum of the correct and incorrect numbers should be no more than 110. Then we excluded a few participants whose sum score is greater than 110. Finally, 2139 participants were included in the analysis of SDMT test.

(b) N-back task

In the practice, the correct rate of the 1-back task is used to assess the compliance of participants and only ones with the correct rate above 75% can perform the formal test. However, in the formal test, 90 participants had the correct rate of the 1-back task less than 75%, and thus we excluded these participants since we cannot ensure that they have completed the test seriously. Finally, 2063 participants were included in the analysis of N-back task.

(c) Go/No-go task

Go trials are relatively easy and theoretically have a high correct rate. However, 102 participants had less than 75% correct rate of Go trials, indicating that they did not complete the test seriously. Therefore, these participants were excluded from analysis. Here, the threshold of 75% was used to agree with the threshold of 1-back test. Finally, 2024 participants were included in the analysis of Go/No-go task.

3. Statistical analysis

3.1 Demographic statistics

We compared demographic characteristics between the final analytical sample (n=2176 for CHIMGEN; n=415 for IMAGEN-FU2) and total sample (n=5425 for CHIMGEN; n=1411 for IMAGEN-FU2) using bias-corrected bootstrapping. For each variable in CHIMGEN, after 10,000 bias-corrected bootstrapping, we estimated the distribution of the mean or frequency and calculate its 95% confidence intervals (CI). If the mean or frequency of a given variable from our final analytical sample was outside the 95% CI of the total sample, we confirmed the existence of a significant difference

between the final analytical sample and total sample in this variable (P<0.05). The same procedure was applied for IMAGEN.

3.2 Correlation analyses of mean UrbanSat with brain imaging measures

3.2.1 Gray matter volume, cortical thickness and surface area (GMV, CT and SA)

The voxel-wise multiple regression of mean UrbanSat before 18 years with brain GMV was performed in CHIMGEN (n=2176) using Statistical Parametric Mapping (SPM12) implemented in Matlab R2018a (http://www.fil.ion.ucl.ac.uk/spm) using the following formula:

$$Y=\beta_0+\beta_1X_1+\beta_2X_2+...+\beta_nX_n+e$$

The dependent variable (Y) is GMV of each voxel of brain, the independent variable (X_1) is mean UrbanSat before 18 years, the independent variables X_2 to X_n are the confounding factors, namely gender, education, site, BMI, genetic population-stratification, SES and TIV, *e* are the residuals. Statistical significance of the voxel-wise multiple regression models in the relation of mean UrbanSat with neuroimaging data was assessed by family-wise error (FWE) correction, where we corrected for voxel numbers, six imaging features (GMV, CT, SA, FA, WNFC and BNFC) and two data type (neuroimaging and behavioral data). We therefore set a significance threshold of FWE-corrected $Pc<0.05$ (equal to an uncorrected $P<(1.25\times10^{-6}/6/2)=1.01\times10^{-7}$) in brain structure analysis in CHIMGEN. To investigate the correlation of UrbanSat with brain GMV was driven by cortical thickness (CT) or surface area (SA) or both, we used the significant cluster from correlation of UrbanSat with brain GMV in CHIMGEN as spatial masks to create regions of interest (ROI) (Supplementary Fig.9), from which we extracted the mean brain metrics of all vertexes

for each participant. The results of $P<0.05$ in CT and SA analysis were set as significant.

3.2.2 Fractional anisotropy (FA)

For TBSS analysis of the white matter FA in CHIMGEN and IMAGEN-FU2, the threshold-free cluster enhancement (TFCE) option in the permutation-testing tool (permutations=5,000) in the FSL software was used to test statistical significance[68]. Multiple comparisons were corrected using a voxel-level family-wise error (FWE) method (TFCE FWE $Pc<0.05$).

3.2.3 Within-network functional connectivity (WNFC)

The WNFC of each voxel reflects temporal correlation between the time-course of BOLD signals of this voxel within a given functional network and the characteristic time-course of BOLD signals of the functional network derived from the ICA analysis. Each of the identified 17 RSNs was entered into a random-effect one-sample t-test to generate a sample-specific spatial map for the RSN (FWE correction, $P_c<0.05$) in CHIMGEN and IMAGEN, respectively. Then a voxel-wise multiple regression was applied to test the correlation between UrbanSat and WFNC in the mask of this RSN in CHIMGEN. For the voxel-wise WNFC analyses, we additionally corrected for the number of the functional networks (n=17), resulting in a FWE-corrected $P_c<0.05$ (uncorrected $P<(1.25\times10^{-6}/6/17/2)=6.13\times10^{-9}$). For each RSN, brain clusters where WNFC showed significant correlation with UrbanSat in CHIMGEN were extracted for the ROI-wise validation in IMAGEN. Additionally, voxel-wise multiple regression was also applied to test the correlation between UrbanSat and WFNC in IMAGEN.

3.2.4 Between-network functional connectivity (BNFC)

The BNFC represents temporal correlations of the characteristic time-courses of BOLD signals between any two RSNs derived from the ICA analysis. Pearson correlation was applied to calculate temporal correlations of the characteristic time-courses of BOLD signals between any pair of 17 RSNs for each participant and then converted *r* value to *z* value to improve normality. Each *z* value represents the BNFC of a given pair of RSNs of each participant. Spearman correlation was applied between UrbanSat and BNFC while controlling the confounding covariates in CHIMEGN and IMAGEN-FU2, respectively. For the pairwise BNFC analyses, statistical significance of the correlation between UrbanSat and BNFC was assessed by permutation testing in reference to a prior study[69]. A maximum correlation coefficient null distribution was generated from the permuted correlation coefficient created by randomly assigning the UrbanSat values across participants (10,000 permutations). Based on the null distribution of the maximum correlation coefficient derived from permutation testing, the statistical significance ($Pc<0.05$) was estimated for each correlation testing between UrbanSat and BNFC.

3.2.5 Meta-analysis

Although all the CHIMGEN and IMAGEN sites used 3.0 tesla MRI scanners to acquire neuroimaging data, different MRI scanners were used in different sites, which may bias our findings. To reduce the possibility, we repeated the ROI-based correlation analyses of UrbanSat with neuroimaging measures in each site (both CHIMGEN and IMAGEN) and performed meta-analysis to integrate the results. The meta-analyses pooled each center's effect size of correlation coefficient between UrbanSat and neuroimaging measure of each ROI, using an inverse variance-weighted random-effects model as implemented in the R package *metafor*

(version v2.1-0)[70]. Random effects models, compared to fixed effect models, do not make the assumption of the same effect size for each center. They estimate the mean of a distribution of effect sizes, allowing effect sizes to vary across centers due to center-specific differences (e.g., mean age). Random effects models therefore weigh within-center as well as between-center variance in the pooled effect size estimates and protect against dominating effects of the largest samples in the meta-analysis[71]. The random-effects models were fit using the restricted maximum likelihood method[72]. The Fish's z transformed correlation coefficient was used in meta-analysis.

In addition to Fish's z transformed correlation coefficient estimates, the standard errors (SE), *z*-values, *p*-values, confidence intervals (CIs) and measure of heterogeneity (I^2 statistics) were also computed in the meta-analysis. The statistics, I^2, (100% (Cochran's Q-df)/Cochran's Q) indicates the percentage of variance in a meta-analysis that is attributable to study heterogeneity, which is independent of i) the size of the meta-analysis, ii) the types of studies included in the meta-analysis, and iii) the outcome data used in the meta-analysis and hence can readily be compared across meta-analyses studies[73]. I^2 values of 0%, 25%, 50%, and 75% are considered reflective of no, low, moderate and high heterogeneity in effect size estimates across studies[73].

3.3 Correlation of brain imaging measures with age of migration

In each CHIMGEN participant who had agreed to provide the residential information, we recorded the precise residential addresses of this participant in each year from his/her birth to recruitment and the category of each place (1=rural, 2=town, 3=city) that was determined according to the National Bureau of Statistics of China

(http://www.stats.gov.cn/tjsj/ndsj/renkoupucha/2000pucha/html/append7.htm). To measure the relation between age of migration and brain, we split the 2176 CHIMGEN participants into who migrated to the city before age 14 years (n=229, mean age at migration=8.24±4.86 years old), after age 14 (n=1385, mean age at migration=17.17±2.68 years old), and life-long city-dwellers (n=562). The significant cluster (mPFC and cerebellum) from correlation of UrbanSat with brain GMV in CHIMGEN was used as a spatial mask to extract the mean brain GMV, CT and SA of all voxels/vertexes within this cluster for each participant. Then Kruskal-Wallis test is used to compare the differences of brain features among the three groups and Dunn's pairwise tests was used for *post-hoc* comparisons.

3.4 Correlation analyses of mean UrbanSat with behavioral measures

In CHIMGEN, Spearman correlation was applied to test the correlation between mean UrbanSat and each neuropsychological domain and mental health while controlling for confounding covariates. For the behavioral analysis, Bonferroni correction for the 2 data types and 21 items (Table 1 and Supplementary Table 15) was applied in the relation of UrbanSat with behavioral assessments in CHIMGEN. We therefore set a significance threshold of Bonferroni corrected P_c<0.05 (equal to an uncorrected P<(0.05/2/21)=1.19×10^{-4}) in CHIMGEN. All the significant results were validated in IMAGEN at Bonferroni corrected *Pc*<0.05 (equal to an uncorrected P<(0.05/5)=0.01).

3.5 Multiple mediation analysis

To formally test whether UrbanSat-behavior relationship can be mediated by brain structure and function, we performed multiple mediation analysis, an extension of

mediation analysis[74,75]. Mediation analysis is a path analytic approach based on regression coefficients. Taking the relation between UrbanSat (X) and depressive symptoms (Y) as an example, the central idea is that the total effect (c) of UrbanSat on depressive symptoms can be divided into direct (c') and indirect effects (a×b): The direct effect of UrbanSat is the effect of UrbanSat on depressive symptoms when the effects of potential mediators (brain structure and function) (M) have been controlled for; The indirect effect through a mediator is defined as the product of (1) the effect of UrbanSat on the mediator and (2) the effect of the mediator on depressive symptoms. Therefore, the indirect effect of UrbanSat on depressive symptoms equals the amount by which the total effect of UrbanSat on depressive symptoms drops when the mediators are taken into account (a ×b=c-c').

In multiple mediation analysis, all indirect effects are estimated in one multiple regression analysis with independent variable and all mediators as predictor variables. This means that the indirect effect of one mediator was estimated when the other mediators are taken into account. We used bootstrapping to assess the significance of the mediation effect. After 5,000 bias-corrected bootstrapping, we estimated the distribution of the indirect effect and calculate its 95% confidence intervals (CI). If zero does not fall between the resulting 95% confidence interval of the bootstrapping method, we confirmed the existence of a significant mediation effect (P<0.05). It should be emphasized that in the multiple mediation analysis of this study, mediators and dependent variables were measured contemporaneously, thus not allowing establishment of any causal directionality.

Supplementary Results

1. CFA model optimization

Firstly, we tested a CFA model including all nine satellite-based measures of urbanicity in each 90% spatiotemporal points. This model showed only moderate fit in each fold data (e.g., CFI=0.62, TLI=0.50, RMSEA=0.18, SRMR=0.09 in the first training dataset). Based on the factor loadings of the nine satellite-based measures, we removed the measure with the smallest factor loading and repeated the CFA modelling. These steps were iterated until the resulting CFA model satisfied our criteria for good model fit. The goodness of fit for each CFA modelling is shown in Supplementary Table 9 in CHIMGEN. The inclusion of the four satellite-based measures (NL, NDVI, cropland% and built-up%) achieved the best goodness of fit in all folds of training data. And even the orders of factor loadings (NL > cropland%> build-up%> NDVI) were extremely consistent. Therefore, the UrbanSat score was predicted in the test dataset when fixing the loadings from the training dataset. This process was iterated 10 times to predict out-of sample UrbanSat scores of all 3306 participants (Supplementary Fig.3). The same CFA process was performed to construct UrbanSat in IMAGEN-FU2 (n=561).

2. Bias assessments

2.1 Selection bias

Although nearly two-thirds of the variables (15/26 for CHIMGEN and 7/10 for IMAGEN) did not show significant differences between the included sample and the

excluded sample in both CHIMGEN and IMAGEN, there are differences in about one-third of the variables (11/26 for CHIMGEN and 3/10 for IMAGEN). The effect sizes of these differences are rather small and demographic variables were adjusted in our main analyses. Significant differences were observed in verbal learning memory, cognitive control and anxiety. These differences did not affect the main outcome variables of the study, depressive symptoms or perspective taking.

2.2 Sensitivity analysis

The statistical comparisons of voxel-wise multiple regression analysis of each imputed UrbanSat with whole brain GMV adjusted for all confounding covariates in 2176 participants are shown in Supplementary Fig. 6 (FWE $Pc<0.05$). We found that each imputed UrbanSat dataset was significantly correlated with the identical areas in the left mPFC and bilateral cerebellum, similar to the combined UrbanSat score following Rubin's rule. For the estimation of brain ROI level analyses, where the statistical estimate between multiple imputed UrbanSat and brain ROI was pooled in a statistically principled fashion using *mice* R package, we still replicated the results deriving from combined UrbanSat score and voxel-wise brain analysis in the main text. The estimated fractions of missing information (FMI) of UrbanSat were low for the GMVs of left mPFC (FMI=1.01%) and cerebellum (FMI=1.19%) based on *mice* R package. UrbanSat was still correlated with GMVs of the left mPFC ($P<0.001$) and cerebellum ($P<0.001$) after pooling in CHIMGEN.

To test the potential bias caused by the imputation of satellite data, sensitivity analysis was additionally performed in 1460 participants where complete brain imaging

data as well as nine complete satellite measures from birth to the age of recruitment were available without any missing data. In the 1460 participants, sensitivity analysis was performed to identify voxel-wise correlations between GMV and UrbanSat adjusted for all confounding covariates (FWE $Pc<0.05$). We achieved the same results as we have in the analysis of the 2176 participants, albeit with a slight reduction in significance, as would be expected because of the reduced sample size (Supplementary Fig.7).

With respect to UrbanSat with behaviors, FMI of UrbanSat was also low for perspective taking (FMI=0.90%) and depression index (FMI=0.67%). We replicated the results of UrbanSat with reaction time for perspective taking ($P<0.001$) and depression index ($P<0.001$).

2.3 Representativeness of sub-sample

To test whether UrbanSat based on the full sample (n=3306) is representative for the MRI sub-sample (n=2176), we re-performed the ten-fold cross validation of CFA models on the urbanicity variables in the 2176 participants. The UrbanSat constructed from the sub sample (n=2176) was practically identical to that derived from the full sample (n=3306) ($r=0.99$, $P<0.001$).

3. Voxel-wise multiple regression analysis under nonparametric testing

The voxel-wise general linear model of UrbanSat with brain GMV adjusting for confounders was performed using permutation-based nonparametric testing with threshold-free cluster enhancement (TFCE) for correcting for family-wise error (TFCE-FWE, $Pc<0.05$) as implemented in randomise for FMRIB Software Library

(FSL) v5.0.10 (https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/Randomise/UserGuide). Under the non-parametric permutation testing, the UrbanSat was positively correlated with bilateral cerebellar volume and negatively correlated with bilateral mPFC, insular, middle and inferior temporal cortex and angular cortex volume (TFCE-FWE, Pc<0.05, Supplementary Fig.5).

4. Correlation of UrbanSat with behaviors

We found a correlation of UrbanSat with the numbers of correct words in immediate free memory recall within five sessions (imFM 1-5) of the verbal learning memory (*rho*=0.08, P_c<0.05) and the accuracy of go-trail of cognitive control (*rho*=0.10, P_c<0.05) (Supplementary Table 15), but they cannot be replicated in IMAGEN-FU2 due to the lack of the assessment.

5. Correlation of WNFCs and BNFCs with age of migration

To measure the relation between age of migration with WNFCs and BNFCs, we split the CHIMGEN participants into who migrated to the city before age 14 years (n=222, mean age at migration=8.24±4.86 years), after age 14 (n=1375, mean age at migration=17.17±2.68 years), and life-long city-dwellers (n=559) (Fig.3d). We found that participants who were born in the city or migrated to an urban environment at an earlier age showed greater WNFCs in the CN (P<0.001), mVN (P=0.032) and lVN (P<0.001) as well as greater BNFCs in aDMN-CN (P<0.001), aDMN-ECN (P<0.001), aDMN-rFPN (P<0.001) and rFPN-lFPN (P<0.001) but smaller WNFC in the aDMN (P<0.001) than later migrants (Fig.4 and Supplementary Table 14).

6. Correlation of UrbanSat with WNFC and BNFC changes

Mean UrbanSat was significantly correlated with WNFC changes in the aDMN (*rho*=0.31, *P*=0.009), CN (*rho*=0.37, *P*=0.002), mVN (*rho*=0.28, *P*=0.022) and lVN (*rho*=0.25, *P*=0.032), as well as with BNFC changes in the aDMN-CN (*rho*=0.45, *P*<0.001), aDMN-ECN (*rho*=0.25, *P*=0.036), aDMN-rFPN (*rho*=0.25, *P*=0.036) and rFPN-lFPN (*rho*=0.23, *P*=0.046) in the longitudinal IMAGEN BL-FU2 sample (n=83) (Supplementary Table 12).

Supplementary Tables

Supplementary Table 1. Inclusion and exclusion criteria in CHIMGEN[1]

Categories	Items	Actions
A. Demographics	1. Age of 18-30 years	Inclusion
	2. Chinese Han without other ethnic ancestors in recent three generations	Inclusion
	3. Right-handedness confirmed by the handedness questionnaire	Inclusion
	4. Relatives have not participated in this study	Inclusion
B. Medical histories	1. Neuropsychiatric diseases (schizophrenia, anxiety, depression, epilepsy, stroke, tumors, and multiple sclerosis, etc.)	Exclusion
	2. Consciousness loss for more than 5 minutes	Exclusion
	3. Brain injury or neurosurgery	Exclusion
	4. Major physical illnesses (heart disease, hypertension, nephritis, diabetes, malignant tumors, hereditary diseases, etc.)	Exclusion
	5. Visible brain abnormalities on previous MRI examinations	Exclusion
C. Conditions	1. Alcohol or drug abuse or dependence	Exclusion
	2. The total number of cigarettes so far is more than 20	Exclusion
	3. Currently with any medication (including contraceptives)	Exclusion
	4. Taking drugs (antipsychotics, mood stabilizers, isoniazid, glucocorticoids, stimulants, etc.) that might affect the brain	Exclusion
	5. Using sedative hypnotics (benzodiazepines, barbiturates) within one month	Exclusion
	6. Neuropsychiatric disorders (three generation relatives)	Exclusion
	7. Color blindness or difficulty in color discrimination	Exclusion
	8. Women in pregnancy or in the menstrual period on the day of the experiment	Exclusion
	9. Strenuous exercise or consumption of strong tea, caffeine or alcoholic beverages on the day of the experiment	Exclusion
	10. Without enough sleep (< 7 hours) at the night before the experiment	Exclusion
D. MR contraindications	1. Metal implants	Exclusion
	2. Electronic implants (e.g. pacemakers)	Exclusion
	3. Severe claustrophobia	Exclusion

Supplementary Table 2. Inclusion and exclusion criteria in IMAGEN[2]

Categories	Items	Actions
A. Demographics	1. Child in target age (14 years)	Inclusion
B. Pregnancy and birth	1. Use of alcohol by the mother during pregnancy (>210 ml alcohol/week [e.g. 14 bottles of beer, 9 glasses of wine, 7 glasses of hard liquor])	Exclusion
	2. Diabetes of the mother during pregnancy (onset before pregnancy, treated by insulin)	Exclusion
	3. Premature birth (< 35 weeks) and/or detached placenta	Exclusion
	4. Hyperbilirubinemia requiring transfusion	Exclusion
C. Child's medical history	1. Type 1 diabetes	Exclusion
	2. Systemic rheumatologic disorders (e.g. strep throat, glomerulonephritis or endocarditis)	Exclusion
	3. Malignant tumours requiring chemotherapy (e.g. leukaemia)	Exclusion
	4. Congenital heart defects or heart surgery	Exclusion
	5. Aneurism	Exclusion
D. Neurological conditions	1. Epilepsy	Exclusion
	2. Bacterial Infection of CNS	Exclusion
	3. Brain tumour	Exclusion
	4. Head trauma with loss of consciousness >30 minutes	Exclusion
	5. Muscular dystrophy, myotonic dystrophy	Exclusion
E. Developmental conditions	1. Nutritional and metabolic diseases (e.g. failure to thrive, phenylketonuria)	Exclusion
	2. Major neuro-developmental disorders (e.g. autism)	Exclusion
	3. Hearing deficit (requiring hearing aid)	Exclusion
	4. Vision problems (strabismus, visual deficit not correctible)	Exclusion
F. Mental health and abilities	1. Treatment for schizophrenia, bipolar disorder	Exclusion
	2. IQ < 70	Exclusion
G. MR contraindications	1. Metal implants	Exclusion
	2. Electronic implants (e.g. pacemakers)	Exclusion
	3. Severe claustrophobia	Exclusion

Supplementary Table 3. Demographics of the samples used in specific statistical analysis.

Measures	Sample size (n)		Age (years)*		Gender (Male/Female)	
	CHIMGEN	IMAGEN	CHIMGEN	IMAGEN	CHIMGEN	IMAGEN
UrbanSat	3306	561	24.00 (3.00)	18.74 (0.97)	1213/2093	254/307
GMV	2176	415	24.00 (3.00)	18.71 (0.77)	769/1407	187/228
CT and SA	2164	420	24.00 (3.00)	18.71 (0.77)	766/1398	190/230
TBSS	2158	436	24.00 (3.00)	18.71 (0.77)	762/1396	192/244
WNFC and BNFC	2156	351	24.00 (3.00)	18.64 (0.71)	761/1395	158/193
CVLT-II	2173	-	24.00 (3.00)	-	768/1405	-
N-back	2063	-	24.00 (3.00)	-	728/1335	-
SDMT	2139	-	24.00 (3.00)	-	758/1381	-
PT[a]	2148	342	24.00 (3.00)	18.68 (0.82)	758/1390	143/199
Go/no-go	2024	-	24.00 (3.00)	-	716/1308	-
Depression[b]	2170	346	24.00 (3.00)	18.68 (0.82)	768/1402	144/202
Anxiety[c]	2170	447	24.00 (3.00)	18.73 (0.85)	768/1402	197/250
		391		18.70 (0.84)		176/215

*BNFC, between-network functional connectivity; CT, cortical thickness; CVLT-II, the second edition of California verbal learning test; GMV, gray matter volume; PT, perspective taking; SA, surface area; SDMT, symbol digit modalities test; TBSS, Tract-based Spatial Statistics; WNFC, within-network functional connectivity. [a]PT is measured by ball tossing game in CHIMGEN and by Interpersonal Reactivity Index in IMAGEN-FU2; [b]Depression is measured by the second edition of Beck depression inventory in CHIMGEN and by Ruminating Scale Questionnaire in IMAGEN-FU2; [c]Anxiety is measured by State Trait Anxiety Test in CHIMGEN and by Development and Well-Being Assessment Interview (upper row) and Anxiety Screening from the Composite International Diagnostic Interview (lower row) in IMAGEN-FU2.*Statistics are shown as median (quantile interval) in age variables.*

Supplementary Table 4. Comparisons of demographic variables between the final analytical sample and total sample in CHIMGEN and IMAGEN.

Variables	Total sample		Final analytical sample		*P**
	n	Statistics[#]	n	Statistics[#]	
CHIMGEN					
Age (years)	5425	24.00 (3.00)	2176	24.00 (3.00)	0.112
Gender (Male/Female)	5425	2094/3331	2176	769/1407	***<0.001***
Education (years)	5425	17.00 (3.00)	2176	17.00 (3.00)	0.183
BMI	5425	20.76 (3.21)	2176	20.76 (3.01)	0.641
SES score[a]	4846	-0.22 (7.87)	2176	-0.22 (7.86)	0.987
IMAGEN					
Age (years)	1411	18.87 (1.02)	415	18.71 (0.77)	***<0.001***
Gender (Male/Female)	1411	678/733	415	187/228	0.286
BMI	1310	20.05 (3.79)	415	20.26 (3.96)	0.362
SES score[a]	1202	0.11 (2.93)	415	0.11 (2.78)	0.734
GEN (Y/N)	1354	714/640	415	183/232	0.367

*BMI, body mass index; ES, effect size; SES, socioeconomic status; [#]Median (quantile interval) are used to describe variables. *P value is estimated by the bias-corrected bootstrapping method; [a]SES score is the sum score of normalized parental education and occupation, family unemployment stress, family financial difficulties and crisis, home inadequacy and neighborhood stress. A total of 4846 participants provide their SES information, in which 2176 are included in the study.*

Supplementary Table 5. Comparisons of demographic and behavioral variables between the included sample and the excluded sample in CHIMGEN.

Variables	Included sample		Excluded sample		*P**	*ES*
	n	Statistics#	n	Statistics#		
emographics						
Age (years)	3306	24.00 (3.00)	2119	24.00 (4.00)	***0.003***	-0.04
Gender (Male/Female)	3306	1213/2093	2119	881/1238	***<0.001***	0.05
Education (years)	3306	17.00 (3.00)	2119	17.00 (3.00)	***<0.001***	-0.06
BMI	3306	20.76 (3.03)	2119	20.76 (3.41)	0.682	-0.01
SES score[a]	2176	-0.22 (7.86)	2670	-1.02 (8.07)	***0.007***	-0.04
Behaviors						
PT and agency						
ACC_{pt}	2148	0.21 (0.38)	3197	0.21 (0.35)	0.152	-0.02
ACC_{agency}	2148	1.00×10^{-9} (0.21)	3197	1.00×10^{-9} (0.21)	0.221	-0.02
RT_{pt} (ms)	2148	1160.67 (740.39)	3197	1162.83 (730.32)	0.863	-0.002
RT_{agency} (ms)	2148	-7.44 (363.22)	3197	4.37 (369.46)	0.162	-0.02
Verbal learning memory						
imFM 1-5	2173	56.00 (12.00)	3244	55.00 (12.00)	***<0.001***	-0.05
stFM	2173	13.00 (3.00)	3244	13.00 (3.00)	***0.003***	-0.04
stCM	2173	13.00 (4.00)	3244	13.00 (4.00)	***0.003***	-0.04
ltFM	2173	13.00 (3.00)	3244	13.00 (3.00)	***<0.001***	-0.05
ltCM	2173	14.00 (3.00)	3244	14.00 (3.00)	***<0.001***	-0.05
TI	2173	4.00 (7.00)	3244	4.00 (7.00)	0.121	-0.02
TR	2173	4.00 (6.00)	3244	4.00 (6.00)	0.642	-0.01
ltR	2173	1.00 (0.00)	3244	1.00 (0.00)	0.052	-0.03
Working memory						
$ACC_{1\text{-back}}$	2063	0.92 (0.05)	3113	0.93 (0.05)	***0.012***	-0.04
$ACC_{3\text{-back}}$	2063	0.75 (0.20)	3113	0.75 (0.20)	0.938	-0.001

Information processing speed						
Correct numbers	2139	70.00 (14.00)	3230	69.00 (14.00)	0.162	-0.02
Error numbers	2139	0.00 (0.00)	3230	0.00 (0.00)	0.834	-0.003
Cognitive control						
ACC_{go}	2024	0.99 (0.02)	3032	0.99 (0.03)	0.642	-0.01
$ACC_{no\text{-}go}$	2024	0.57 (0.26)	3032	0.55 (0.26)	***0.004***	-0.04
Mental health						
BDI	2170	2.00 (5.00)	3238	2.00 (5.00)	0.356	-0.01
SA	2170	30.00 (9.00)	3238	30.00 (10.00)	0.421	-0.01
TA	2170	33.00 (9.00)	3238	33.00 (10.00)	0.080	-0.02

ACC, accuracy; BDI, Beck Depression Index; BMI , body mass index; ES, effect size; imFM 1-5, total numbers of correct words for test 1-5 in immediate free memory; ltCM, numbers of correct words in long-term clue memory; ltFM, numbers of correct words in long-term free memory; ltR, numbers of correct words in long-term recognition accuracy; PT, perspective taking; RT, reaction time; SA, state anxiety; SD, standard deviation; SES, socioeconomic status; stCM, numbers of correct words in short-term clue memory; stFM, numbers of correct words in short-term free memory; TA, trait anxiety; TI, total numbers of insert words; TR, total numbers of repeat words. *[#]Statistics are shown as median (quantile interval). *Gender is compared using Chi-square test and effect size (ES) is described as Phi coefficient (Small:<0.1; Medium:0.1-0.3: Large:>0.5)[77]; Quantitative variables are compared using Wilcoxon rank sum test and ES is described as r coefficient (r=Z/√n) (Small: <0.1; Medium: 0.1-0.3; Large:>0.5)[78]. [a]SES score is the sum score of normalized parental education and occupation, family unemployment stress, family financial difficulties and crisis, home inadequacy and neighborhood stress. A total of 4846 participants provide their SES information, in which 2176 included in the study.*

Supplementary Table 6. Comparisons of demographic and behavioral variables between the included sample and the excluded sample in IMAGEN-FU2.

Variables	Included sample		Excluded sample		*P**	ES
	n	Statistics[#]	n	Statistics[#]		
Demographics						
Age	561	18.74 (0.97)	850	18.94 (1.03)	***<0.001***	-0.09
Gender (Male/Female)	561	254/307	850	409/441	0.301	0.03
BMI	502	20.26 (3.96)	808	19.89 (3.83)	***0.042***	-0.06
SES score[a]	482	0.11 (2.78)	720	0.06 (3.27)	0.545	-0.002
GEN (Y/N)	543	289/254	811	425/386	0.767	0.01
Behaviors						
PT						
IRI	342	19.00 (5.00)	613	19.00 (5.00)	0.489	-0.02
Mental-health						
RSQ	346	35.00 (15.00)	610	36.00 (16.00)	0.678	-0.01
DAWBA-GA (Y/N)	447	355/92	806	586/220	***0.011***	0.07
CIDI-AS	391	6.00 (10.00)	727	5.00 (10.00)	0.320	-0.03

*BMI, body mass index; CIDI-AS, Anxiety Screening from the Composite International Diagnostic Interview; DAWBA-GA, Generalized Anxiety Scale from The Development and Well-Being Assessment Interview; FU1, IMAGEN first follow up assessment acquired at 16 years; FU2, IMAGEN second follow up assessment acquired at 19 years; GEN, Genetic Screening and Family History of Psychiatric Disorders Interview; IRI, Interpersonal Reactivity Index; PT, perspective taking; RSQ, Ruminating Scale Questionnaire; SES, socioeconomic status. [#]Statistics are shown as median (quantile interval); *Gender, GEN and DAWBA-GA are compared using Chi-square test and ES is shown as Phi coefficient (Small:<0.1; Medium:0.1-0.3: Large:>0.5) [76]; Quantitative variables are compared using Wilcoxon rank sum test and ES is described as r coefficient ($r=Z/\sqrt{n}$) (Small: <0.1; Medium: 0.1-0.3; Large:>0.5)[77]. [a]SES score is the sum score of normalized parental education and occupation, family unemployment stress, family financial difficulties and crisis, home inadequacy and neighborhood stress.*

Supplementary Table 7. Detailed information of remote sensing satellite-based measures of urbanicity.

Satellite measure	Platform	Data sets	Band	Time span	Temporal resolution	Spatial resolution
Population density	GEE	JRC/GHSL/P2016/POP_GPW_GLOBE_V1	Population_count	1975, 1990, 2000, 2015	10-15 years	250 meters
NL	GEE	DMSP-OLS Nighttime Lights Time Series Version 4	Stable_lights	1992-2013	Yearly	1 kilometer
NDVI	GEE	NOAA CDR AVHRR Normalized Difference Vegetation Index Version 4	NDVI	1981-2017	Daily	5 kilometers
NDWI	GEE	USGS Landsat 7 Collection 1 Tier 1 Raw Scenes	Band 2 and 4	1999-2017	16 days	30 meters
NDBI	GEE	The same as above	Band 4 and 5	1999-2017	16 days	30 meters
Land cover mapping						
Built-up%	ESA	Climate Change Initiative Land Cover datasets	-	1992-2015	Yearly	30 meters
Cropland%	ESA	The same as above	-	1992-2015	Yearly	30 meters
Forest%	ESA	The same as above	-	1992-2015	Yearly	30 meters
Grassland%	ESA	The same as above	-	1992-2015	Yearly	30 meters
Water body%	ESA	The same as above	-	1992-2015	Yearly	30 meters

ESA, European Space Agency; GEE, google earth engine; NDBI, normalized difference buildup index; NDVI, normalized difference vegetation index; NDWI, normalized difference water index; NL, night-time light

Supplementary Table 8. Numbers of imputed years of each satellite-based measure of urbanicity in 3306 participants from CHIMGEN.

Y_{birth}	$Y_{recruitment}$	n	NL (1992-2013)		GLCM (1992-2015)		NDVI (1981-2017)	
			N_{before}	N_{after}	N_{before}	N_{after}	N_{before}	N_{after}
1986	2016-2018	27	6	3-5	6	1-3	0	0-2
1987	2016-2018	45	5	3-5	5	1-3	0	0-2
1988	2016-2018	91	4	3-5	4	1-3	0	0-2
1989	2016-2018	186	3	3-5	3	1-3	0	0-2
1990	2016-2018	344	2	3-5	2	1-3	0	0-2
1991	2016-2018	447	1	3-5	1	1-3	0	0-2
1992	2016-2018	495	0	3-5	0	1-3	0	0-2
1993	2016-2018	503	0	3-5	0	1-3	0	0-2
1994	2016-2018	444	0	3-5	0	1-3	0	0-2
1995	2016-2018	367	0	3-5	0	1-3	0	0-2
1996	2016-2018	193	0	3-5	0	1-3	0	0-2
1997	2016-2018	108	0	3-5	0	1-3	0	0-2
1998	2016-2018	30	0	3-5	0	1-3	0	0-2
1999	2016-2018	12	0	3-5	0	1-3	0	0-2
2000	2016-2018	7	0	3-5	0	1-3	0	0-2
2001	2018	7	0	5	0	1-3	0	0-2

GLCM, global land cover mapping; N, numbers of participants at each birth year; NDVI, normalized difference vegetation index; NL, nighttime light; N_{before}, numbers of imputed years before the earliest year of satellite data; N_{after}, numbers of imputed years after latest year of satellite date; $Y_{birth,}$ birth year of participants; $Y_{recruitment}$, recruitment year of participants.

Supplementary Table 9. Performance of CFA models constructed by different combinations of satellite-based measures of urbanicity in the first training datasets of CHIMGEN.

Included variables	N	Excluded variables	CFI	TLI	RMSEA	SRMR	χ^2	AIC	BIC	Factor loadings
NL, NDBI, NDVI, NDWI, forest%, built-up%, water body%, grassland% and cropland%	9	-	0.623	0.497	0.178	0.092	56422.97	1575499.21	1575662.272	0.796, 0.371, 0.521, 0.543, 0.130, 0.623, 0.048, 0.061, 0.748
NL, NDBI, NDVI, NDWI, forest%, built-up%, grassland% and cropland%	8	Water body%	0.655	0.517	0.194	0.098	49071.43	1390195.72	1390341.10	0.799, 0.370, 0.520, 0.543, 0.131, 0.622, 0.063, 0.746
NL, NDBI, NDVI, NDWI, forest%, built-up% and cropland%	7	Grassland%	0.711	0.566	0.203	0.099	37885.51	1204976.22	1205103.51	0.796, 0.369, 0.521, 0.540, 0.129, 0.622, 0.751
NL, NDBI, NDVI, NDWI, built-up% and cropland%	6	Forest%	0.784	0.641	0.207	0.097	25237.75	1020415.20	1020524.34	0.791, 0.367, 0.517, 0.537, 0.619, 0.763
NL, NDVI, NDWI, built-up% and cropland%	5	NDBI	0.985	0.970	0.062	0.023	1280.07	842185.12	842275.94	0.810, 0.518, 0.484, 0.610, 0.778
NL, NDVI, built-up% and cropland%	4	NDWI	0.999	0.996	0.026	0.008	92.47	670559.72	670632.43	0.807, 0.511, 0.597, 0.793

AIC, Akaike's information criterion; BIC, Schwarz's Bayesian information criterion; CFA, confirmatory factor analysis; CFI, comparative fit index; NDBI, normalized difference buildup index; NDWI, normalized difference water index; NDVI, normalized difference vegetation index; NL, nighttime light; RMSEA, root mean square error of approximation; SRMR, standard root mean square residual; TLI, Tucker-Lewis index.

Supplementary Table 10. Items included in socioeconomic status (SES) in CHIMGEN.

Item	Coding and response scale
Maternal education	0=Primary school or below 1=Middle school 2=High school or vocational diploma 3=Three-year college diploma 4= Bachelor degree 5= PhD, MD, Master's degree
Paternal education	The same as above
Maternal occupation	0=Temporary work or unemployed 1=Manual worker or self-employed 2=Production or transportation equipment operators 3=Farmers, forestry, animal husbandry, fishery, water production personnel 4=Business and service personnel 5=Civil servant or company employee 6=Professional and technical personnel 7=Government or public institute management personnel
Paternal occupation	The same as above
Family unemployment stress [a]	0 = a lot; 1 = a little; 2 = not at all
Financial difficulties [a]	The same as above
Home inadequacy for the family's need [a]	The same as above
Neighborhood stress [a]	The same as above
Family financial crisis [a]	The same as above

[a]*The items are from SES measures of Development and Well-Being Assessment*

Supplementary Table 11. Items included in socioeconomic status (SES) in IMAGEN.

Item (n)	Coding and response scale
ESPAD	
Maternal education	0=Primary school or below 1=O levels, GCSEs or CSEs 2=NVQ or GNVQ 3=A levels or a BTEC national diploma 4=Advanced diploma 5=Bachelor degree 6=PhD, MD, Master's degree
Paternal education	The same as above
DAWBA	
Family unemployment stress	0=a lot; 1=a little; 2=no or not applicable
Financial difficulties	The same as above
Home inadequacy for the family's need	The same as above
Neighborhood stress	The same as above
Family financial crisis	0=yes; 1=no
Maternal employment	0=unemployed or unknown; 1=part-time; 2=full-time
Paternal employment	The same as above

ESPAD, European School Survey Project on Alcohol and Other Drug; DAWBA, Development and Well-Being Assessment; SES, socioeconomic status.

Supplementary Table 12. Correlations of UrbanSat with brain structure and function.

Brain metrics	CHIMGEN		IMAGEN-FU2		IMAGEN BL-FU2*	
	n	Statistics[#]	n	Statistics[#]	n	Statistics[#]
GMV						
mPFC	2176	***<0.001 (-0.12)***	415	***0.003 (-0.15)***	340	***<0.001 (0.24)***
cerebellum	2176	***<0.001 (0.14)***	415	***0.009 (0.13)***	340	0.456 (-0.04)
CT and SA						
mPFC CT	2164	0.381 (-0.02)	420	0.589 (-0.03)	325	0.967 (0.002)
mPFC SA	2164	***0.002 (-0.07)***	420	***<0.001 (-0.19)***	325	***<0.001 (0.23)***
WNFC						
aDMN	2156	***<0.001 (-0.09)***	351	***<0.001 (-0.18)***	83	***0.009 (0.31)***
CN	2156	***<0.001 (0.11)***	351	***<0.001 (0.26)***	83	***0.002 (0.37)***
mVN	2156	***<0.001 (0.07)***	351	***<0.001 (0.24)***	83	***0.022 (0.28)***
lVN	2156	***<0.001 (0.10)***	351	***<0.001 (0.24)***	83	***0.032 (0.25)***
BNFC						
aDMN-CN	2156	***<0.001 (0.12)***	351	***<0.001 (0.18)***	83	***<0.001 (0.45)***
aDMN-ECN	2156	***<0.001 (0.09)***	351	***0.008 (0.14)***	83	***0.036 (0.25)***
aDMN-rFPN	2156	***<0.001 (0.09)***	351	***<0.001 (0.19)***	83	***0.036 (0.25)***
rFPN-lFPN	2156	***<0.001 (0.10)***	351	***<0.001 (0.20)***	83	***0.046 (0.23)***

*aDMN, anterior default mode network; BNFC, between-network functional connectivity; CN, cerebellar network; CT, cortical thickness; ECN, executive control network; GMV, gray matter volume; lVN, lateral visual network; lFPN, left frontoparietal network; mPFC, medial prefrontal cortex; mVN, medial visual network; rFPN, right frontoparietal network; SA, surface area; WNFC, within-network functional connectivity; [#]Spearman correlations are used to test the correlations between UrbanSat and brain measures controlling for confounding covariates, which are shown as correlation P value (ρ value). The significant results are in bold and italic; *IMAGEN BL-FU2 measures brain structural and functional changes rate between BL of 14 years and FU2 of 19 years.*

Supplementary Table 13. Meta-analysis of UrbanSat-brain correlations from all CHIMGEN and IMAGEN-FU2 sites.

Brain metrics	*r* value	SE	*z* value	*P* value	95% CI LB	95% CI UB	I^2
GMV							
mPFC	***-0.12***	***0.02***	***-5.76***	***<0.001***	***-0.15***	***-0.07***	***0.05%***
cerebellum	***0.13***	***0.04***	***3.70***	***<0.001***	***0.06***	***0.19***	***60.21%***
CT and SA							
mPFC CT	-0.03	0.02	-1.23	0.223	-0.07	0.02	7.31%
mPFC SA	***-0.08***	***0.03***	***-2.67***	***0.007***	***-0.14***	***-0.02***	***43.44%***
WNFC							
aDMN	***-0.09***	***0.03***	***-2.94***	***0.003***	***-0.15***	***-0.03***	***41.05%***
CN	***0.13***	***0.02***	***5.92***	***<0.001***	***0.09***	***0.17***	***3.94%***
mVN	0.06	0.03	1.66	0.092	-0.01	0.12	53.10%
lVN	***0.06***	***0.03***	***2.22***	***0.032***	***0.007***	***0.12***	***35.36%***
BNFC							
aDMN-CN	0.03	0.04	0.69	0.489	-0.06	0.12	74.46%
aDMN-ECN	***0.08***	***0.04***	***2.10***	***0.042***	***0.005***	***0.16***	***65.29%***
aDMN-rFPN	0.05	0.04	1.22	0.220	-0.03	0.12	63.21%
rFPN-lFPN	***0.08***	***0.03***	***2.55***	***0.012***	***0.02***	***0.15***	***49.68%***

aDMN, anterior default mode network; BNFC, between-network functional connectivity; CN, cerebellar network; CT, cortical thickness; GMV, gray matter volume; lVN, lateral visual network; mPFC, medial prefrontal cortex; mVN, medial visual network; SA, surface area; WNFC, within-network functional connectivity; 95% CI LB and UB, 95% confidence interval lower and upper bound; The significant results are in bold and italic; Note: We exclude SUCWH center from CHIMGEN for all meta-analysis and Dublin center from IMAGEN for the meta-analysis of brain functional features, because there are only 8 and 10 participants from each site, which more than the numbers of covariates while performing Spearman correlation analysis.

Supplementary Table 14. Differences of brain features among migrated groups.

Brain metrics	n	Statistics[#]	*P* value
GMV			
mPFC	***2176***	***6.74***	***0.032***
cerebellum	***2176***	***24.27***	***<0.001***
CT and SA			
mPFC CT	2164	5.75	0.064
mPFC SA	***2164***	***37.48***	***<0.001***
WNFC			
aDMN	***2156***	***21.99***	***<0.001***
CN	***2156***	***19.53***	***<0.001***
mVN	***2156***	***6.73***	***0.032***
lVN	***2156***	***21.74***	***<0.001***
BNFC			
aDMN-CN	***2156***	***19.21***	***<0.001***
aDMN-ECN	***2156***	***15.32***	***<0.001***
aDMN-rFPN	***2156***	***16.29***	***<0.001***
rFPN-lFPN	***2156***	***26.55***	***<0.001***

[#]*Statistics are shown as H value using Kruskal-Wallis nonparametric test to compare the differences of brain features among the groups migrated before 14 years, after 14 years and lifelong city dwellers.*

Supplementary Table 15. Correlations of UrbanSat with behaviors in CHIMGEN.

Variables	N	Statistics[#]	*P* value (*rho* value)[*]
Verbal learning memory			
imFM 1-5	2173	56.00 (12.00)	***<0.001 (0.08)***
stFM	2173	13.00 (3.00)	0.360 (0.02)
stCM	2173	13.00 (4.00)	0.900 (0.01)
ltFM	2173	13.00 (3.00)	0.904 (0.01)
ltCM	2173	14.00 (3.00)	0.995 (-0.01)
TI	2173	4.00 (7.00)	0.167 (0.03)
TR	2173	4.00 (6.00)	0.010 (-0.06)
ltR	2173	1.00 (0.00)	0.147 (0.03)
Working memory			
$ACC_{1\text{-}back}$	2063	0.92 (0.05)	0.054 (0.04)
$ACC_{3\text{-}back}$	2063	0.75 (0.20)	0.013 (0.05)
Information processing speed			
Correct numbers	2139	70.00 (14.00)	0.918 (-0.01)
Error numbers	2139	0.00 (0.00)	0.715 (0.01)
Cognitive control			
ACC_{go}	2024	0.99 (0.03)	***<0.001 (0.10)***
$ACC_{no\text{-}go}$	2024	0.57 (0.26)	0.282 (-0.02)

*ACC, accuracy; imFM 1-5, total numbers of correct words for test 1-5 in immediate free memory; ltCM, numbers of correct words in long-term clue memory; ltFM, numbers of correct words in long-term free memory; ltR, numbers of correct words in long-term recognition accuracy; stCM, numbers of correct words in short-term clue memory; stFM, numbers of correct words in short-term free memory; TI, total numbers of insert words; TR, total numbers of repeat words. [#]Statistics are shown as median (quantile interval). *Spearman correlations are used to test the correlations between UrbanSat and behaviors controlling for confounding covariates, which are shown as correlation P value (rho value). The significant results (Bonferroni $P_c<0.05$; uncorrected $P<0.05/2/21=1.19\times10^{-3}$) are in bold and italic.*

Supplementary Table 16. Sex-specific correlations of UrbanSat with brain structure and function.

Brain measures	CHIMEGN				IMAGEN-FU2				IMAGEN BL-FU2*			
	Male		Female		Male		Female		Male		Female	
	n	Statistics[#]	n	Statistics[#]	n	Statistics[#]	n	Statistics[#]	n	Statistics[#]	n	Statistics[#]
GMV												
mPFC	769	***<0.001 (-0.15)***	1407	***<0.001 (-0.10)***	187	0.142 (-0.11)	228	***0.021 (-0.16)***	147	***<0.001 (0.31)***	193	***0.005 (0.21)***
cerebellum	769	***<0.001 (0.19)***	1407	***<0.001 (0.10)***	187	***0.005 (0.21)***	228	0.862 (0.01)	147	0.778 (0.02)	193	0.372 (-0.07)
CT and SA												
mPFC CT	766	0.139 (-0.05)	1398	0.978 (<0.001)	190	0.556 (-0.04)	230	0.978 (0.002)	141	0.243 (-0.10)	184	0.402 (0.06)
mPFC SA	766	0.112 (-0.06)	1398	***0.010 (-0.07)***	190	0.142 (-0.11)	230	***<0.001 (-0.26)***	141	***0.002 (0.27)***	184	***0.004 (0.22)***
WNFC												
aDMN	761	0.343 (-0.04)	1395	***<0.001 (-0.11)***	158	0.062 (-0.16)	193	***0.019 (-0.18)***	35	0.282 (0.22)	48	***0.022 (0.37)***
CN	761	***<0.001 (0.14)***	1395	***<0.001 (0.10)***	158	***0.006 (0.23)***	193	***<0.001 (0.27)***	35	***0.012 (0.49)***	48	0.133 (0.25)
mVN	761	0.069 (0.07)	1395	***0.006 (0.07)***	158	***0.001 (0.27)***	193	***<0.001 (0.25)***	35	0.952 (-0.01)	48	***0.004 (0.45)***
lVN	761	***<0.001 (0.15)***	1395	***0.004 (0.08)***	158	***0.001 (0.26)***	193	***0.004 (0.14)***	35	0.267 (0.22)	48	***0.192 (0.22)***
BNFC												
aDMN-CN	761	***0.001 (0.12)***	1395	***<0.001 (0.13)***	158	***0.008 (0.22)***	193	0.066 (0.06)	35	***0.002 (0.58)***	48	***0.012 (0.41)***
aDMN-ECN	761	0.110 (0.06)	1395	***<0.001 (0.12)***	158	***0.007 (0.22)***	193	0.389 (0.19)	35	0.789 (-0.06)	48	***0.020 (0.39)***
aDMN-rFPN	761	***0.006 (0.10)***	1395	***0.004 (0.08)***	158	***0.020 (0.20)***	193	***0.019 (0.19)***	35	0.802 (-0.05)	48	***0.020 (0.38)***

rFPN-lFPN	761	***0.042 (0.08)***	1395	***<0.001 (0.11)***	158	0.052 (0.16)	193	***0.001 (0.24)***	35	0.543 (-0.13)	48	***0.032 (0.36)***

*aDMN, anterior default mode network; BNFC, between-network functional connectivity; CN, cerebellar network; CT, cortical thickness; GMV, gray matter volume; lVN, lateral visual network; lFPN, left frontoparietal network; mPFC, medial prefrontal cortex; mVN, medial visual network; rFPN, right frontoparietal network; SA, surface area; WNFC, within-network functional connectivity. #Spearman correlations are used to test the correlations between UrbanSat and brain measures controlling for confounding covariates, which are shown as correlation P value (rho value). The significant results are in bold and italic; *IMAGEN BL-FU2 measures brain structural and functional changes rate from 14 years to 19 years.*

Supplementary Table 17. Sex-specific correlations of UrbanSat with behaviors in CHIMGEN and IMAGEN-FU2.

Item	Male			Female		
	n	Statistics[#]	*P* value (*rho* value)[*]	n	Statistics[#]	*P* value (*rho* value)[*]
CHIMGEN						
PT and agency						
ACC_{pt}	758	0.17 (0.42)	0.087 (-0.06)	1390	0.21 (0.46)	0.195 (-0.04)
ACC_{agency}	758	0.00 (0.21)	0.134 (0.06)	1390	0.00 (0.21)	0.133 (-0.04)
RT_{pt}	758	1182.28 (768.78)	***<0.001 (-0.21)***	1390	1150.38 (732.36)	***<0.001 (-0.14)***
RT_{agency}	758	-34.65 (355.19)	0.502 (0.02)	1390	8.50 (365.73)	0.882 (0.004)
Mental health						
BDI	768	1.50 (5.00)	***<0.001 (0.14)***	1402	2.00 (5.00)	***<0.001 (0.15)***
SA	768	29.00 (10.00)	0.101 (-0.06)	1402	30.00 (9.00)	0.070 (0.05)
TA	768	33.00 (10.50)	0.239 (-0.04)	1402	34.00 (10.00)	0.038 (0.06)
IMAGEN-FU2						
PT						
IRI	143	17.00 (5.00)	***0.004 (0.26)***	199	20.00 (5.00)	0.362 (0.07)
Mental health						
RSQ	144	34.00 (12.50)	***0.003 (0.27)***	202	37.00 (17.00)	0.350 (0.07)
DAWBA-GA (Y/N) [a]	197	136/61	0.831 (0.04)	250	219/31	0.561 (0.09)

CIDI-AS	176	5.00 (8.00)	0.442 (0.06)	215	7.00 (9.00)	0.041 (0.15)

ACC, accuracy; BDI, Beck Depression Index; CIDI-AS, Anxiety Screening from the Composite International Diagnostic Interview; DAWBA-GA, Generalized Anxiety Scale from The Development and Well-Being Assessment Interview; FU2, IMAGEN second follow up assessment acquired at 19 years; IRI, Interpersonal Reactivity Index; PT, perspective taking; RSQ, Ruminating Scale Questionnaire; RT, reaction time; SA, state anxiety; SD, standard deviation; TA, trait anxiety. [#]*Statistics are shown as median (quantile interval).* [*]*Spearman correlations are used to test the correlations between UrbanSat and behaviors (except for DAWBA-GA) controlling for confounding covariates.* [a]*In the DAWBA-GA, logistic regression is used to test the correlations between UrbanSat and anxiety, which is shown as P value (OR value). In CHIMGEN, the significant results (Bonferroni* $P_c<0.05$*; uncorrected* $P<0.05/2/21=1.19\times10^{-3}$*) are in bold and italic. In IMAGEN, the significant results after Bonferroni Pc<0.05 (uncorrected P<0.05/5=0.01) are in bold and italic.*

Supplementary Table 18. Multiple mediation results of UrbanSat on behavior.

Items	Perspective taking				Depression			
	CHIMGEN		IMAGEN-FU2		CHIMGEN		IMAGEN-FU2	
	Effects	95% BCI	Effects	95% BCI	Effects	95% BCI	Effects	95% BCI
Total effect of UrbanSat on behavior (c path)	***-0.372***	-	***0.116***	-	***0.424***	-	***0.159***	-
Direct effect of UrbanSat on behavior (c' path)	***-0.280***	-	***0.093***	-	***0.327***	-	***0.123***	-
Total indirect effect (ab path)	***-0.092***	***-0.132, -0.057***	***0.023***	***0.010, 0.032***	***0.097***	***0.056, 0.143***	***0.036***	***0.012, 0.056***
Individual indirect effect								
GMV and SA								
mPFC GMV	***-0.012***	***-0.028, -0.001***	***0.015***	***0.001, 0.046***	***0.022***	***0.008,0.040***	***0.019***	***0.001, 0.066***
cerebellar GMV	***-0.015***	***-0.031, -0.004***	-0.0001	-0.010, 0.007	***0.034***	***0.019, 0.056***	*0.002*	-0.003, 0.018
mPFC SA	0.004	-0.001, 0.015	-0.013	-0.014, 0.012	***-0.008***	***-0.021, -0.001***	*-0.013*	-0.056, 0.002
WNFC								
aDMN	***-0.013***	***-0.030, -0.005***	***0.020***	***0.003, 0.052***	***0.012***	***0.004, 0.024***	***0.010***	***0.002, 0.056***
CN	***-0.015***	***-0.030, -0.006***	***0.009***	***0.002, 0.046***	0.0024	-0.008, 0.013	*0.001*	-0.003, 0.026
mVN	-0.002	-0.014, 0.008	-0.005	-0.006, 0.018	***0.0103***	***0.001, 0.024***	*0.006*	-0.004,0.0462
lVN	0.005	-0.007, 0.019	-0.008	-0.022, 0.053	-0.0111	-0.027, 0.001	*-0.008*	-0.012, 0.002
BNFC								
aDMN-CN	***-0.011***	***-0.025, -0.002***	***0.016***	***0.003, 0.046***	0.008	-0.004, 0.020	*-0.0003*	-0.018, 0.002
aDMN-ECN	***-0.022***	***-0.041, -0.009***	-0.013	-0.001, 0.052	***0.019***	***0.006, 0.037***	***0.013***	***0.003, 0.068***

aDMN-rFPN	***-0.020***	***-0.037, -0.006***	***0.012***	***0.004, 0.026***	0.010	-0.003, 0.025	0.003	-0.002, 0.026
rFPN-lFPN	0.008	-0.003, 0.023	-0.011	-0.016, 0.115	-0.001	-0.013, 0.011	0.005	-0.024, 0.006

aDMN, anterior default mode network; BCI, Bootstrapped confidence interval; BNFC, between-network functional connectivity; CN, cerebellar network; CT, cortical thickness; GMV, gray matter volume; lVN, lateral visual network; lFPN, left frontoparietal network; mPFC, medial prefrontal cortex; mVN, medial visual network; rFPN, right frontoparietal network; SA, surface area; WNFC, within-network functional connectivity; The variable with significant indirect effect is in bold and italic.

Supplementary Table 19. MRI parameters of T1 weighted structural MRI for different MR scanners in CHIMGEN.

Scanners	Sequences	Matrix	Slices	FOV (mm)	ST (mm)	Resolution (mm)	Gap (mm)	TR (ms)	TE (ms)	TI (ms)	FA (°)	PAT (AF)
GE Discovery MR750	BRAVO Sagittal	256×256	188	256×256	1	1.0×1.0×1.0	0	8.16	3.18	450	12	2
GE Discovery MR750w	BRAVO Sagittal	256×256	188	256×256	1	1.0×1.0×1.0	0	6.93	2.53	450	12	2
GE Signa HDx	BRAVO Sagittal	256×256	188	256×256	1	1.0×1.0×1.0	0	8.85	3.49	450	12	2
GE Signa HDxt	BRAVO Sagittal	256×256	188	256×256	1	1.0×1.0×1.0	0	7.79	2.98	450	12	2
Philips Achieva	TFE Sagittal	256×256	188	256×256	1	1.0×1.0×1.0	0	8.16	3.73	1100	12	2
Philips Ingenia	TFE Sagittal	256×256	188	256×256	1	1.0×1.0×1.0	0	7.27	3.33	900	12	2
Siemens Skyra	MPRAGE Sagittal	256×256	192	256×256	1	1.0×1.0×1.0	0	2000	2.98	900	9	2
Siemens TrioTim	MPRAGE Sagittal	256×256	192	256×256	1	1.0×1.0×1.0	0	2000	2.26	900	12	2
Siemens Verio	MPRAGE Sagittal	256×256	192	256×256	1	1.0×1.0×1.0	0	2000	2.34	900	9	2

AF, acceleration factor; FA, flip angle; FOV, field of view; PAT, parallel acquisition technique; ST, slice thickness; TE, echo time; TI, inversion time; TR, repetition time.

Supplementary Table 20. MRI parameters of DTI for different MR scanners in CHIMGEN.

Scanners	Sequences	Matrix*	Slices	FOV (mm)	ST (mm)	Gap (mm)	Resolution (mm)	TR (ms)	TE (ms)	FA (°)	B=0	B=1000	PAT (AF)
GE Discovery MR750	SE-EPI Axial	128×128	50	256×256	3	0	2.0×2.0×3.0	6000	65	90	5	64	2
GE Discovery MR750w	SE-EPI Axial	128×128	50	256×256	3	0	2.0×2.0×3.0	10000	74	90	5	64	2
GE Signa HDx	SE-EPI Axial	128×128	50	256×256	3	0	2.0×2.0×3.0	12500	72	90	5	64	2
GE Signa HDxt	SE-EPI Axial	128×128	50	256×256	3	0	2.0×2.0×3.0	11500	72	90	5	64	2
Philips Ingenia	SE-EPI Axial	128×128	50	256×256	3	0	2.0×2.0×3.0	7950	111	90	1	32	2
Philips Achieva	SE-EPI Axial	128×128	50	256×256	3	0	2.0×2.0×3.0	6800	91	90	1	32	2
Siemens Skyra	SE-EPI Axial	128×128	50	256×256	3	0	2.0×2.0×3.0	7900	84	90	1	64	2
Siemens TrioTim	SE-EPI Axial	128×128	50	256×256	3	0	2.0×2.0×3.0	6800	91	90	1	64	2
Siemens Verio	SE-EPI Axial	128×128	50	256×256	3	0	2.0×2.0×3.0	6400	98	90	1	64	2

*AF, acceleration factor; FA, flip angle; FOV, field of view; PAT, parallel acquisition technique; ST, slice thickness; TE, echo time; TI, inversion time; TR, repetition time.*For GE scanner, the default Recon matrix is the twice of scan matrix (256 × 256 Recon matrix)*

Supplementary Table 21. MRI parameters of resting-state functional MRI for different MR scanners in CHIMGEN.

Scanners	Sequences	Matrix	Slices	FOV (mm)	ST (mm)	Gap (mm)	Resolution (mm)	TR (ms)	TE (ms)	FA (°)	Volumes	PAT (AF)
GE Discovery MR750	GRE-EPI Axial	64×64	36	220×220	3	1	3.4×3.4×4.0	2000	30	90	180	2
GE Discovery MR750w	GRE-EPI Axial	64×64	36	220×220	3	1	3.4×3.4×4.0	2000	30	90	180	2
GE Signa HDx	GRE-EPI Axial	64×64	36	220×220	3	1	3.4×3.4×4.0	2000	30	90	180	2
GE Signa HDxt	GRE-EPI Axial	64×64	36	220×220	3	1	3.4×3.4×4.0	2000	30	90	180	2
Philips Ingenia	GRE-EPI Axial	64×64	36	220×220	3	1	3.4×3.4×4.0	2000	30	90	180	2
Philips Achieva	GRE-EPI Axial	64×64	36	220×220	3	1	3.4×3.4×4.0	2000	30	90	180	2
Siemens Skyra	GRE-EPI Axial	64×64	36	220×220	3	1	3.4×3.4×4.0	2000	30	90	180	2
Siemens TrioTim	GRE-EPI Axial	64×64	36	220×220	3	1	3.4×3.4×4.0	2000	30	90	180	2
Siemens Verio	GRE-EPI Axial	64×64	36	220×220	3	1	3.4×3.4×4.0	2000	30	90	180	2

AF, acceleration factor; FA, flip angle; FOV, field of view; PAT, parallel acquisition technique; ST, slice thickness; TE, echo time; TI, inversion time; TR, repetition time.

Supplementary Table 22. Demographic data of each site in CHIMGEN.

Center	N	Age[#]	M/F	BMI[#]	Education[#]	SES[#]	PCA1[#]	PCA2[#]	PCA3[#]	PCA4[#]
TMUGH	463	24.00(3.00)	146/317	20.52(3.17)	17.00(2.00)	0.24(8.01)	0.005(0.008)	0.004(0.016)	0.002(0.011)	0.001(0.016)
TMUCIH	320	24.00(3.00)	130/190	21.10(3.58)	17.00(2.00)	0.60(7.83)	0.004(0.008)	0.005(0.017)	0.002(0.012)	0.002(0.017)
TFCH	43	24.00(2.00)	9/34	20.78(2.85)	17.00(2.00)	1.22(9.45)	0.003(0.011)	0.004(0.017)	0.001(0.011)	0.001(0.024)
CPAPFLUPH	33	23.00(3.00)	19/14	21.51(2.79)	15.00(1.00)	-2.19(4.73)	-3.64×10^{-4}(0.020)	-0.002(0.014)	0.003(0.016)	-0.004(0.015)
THH	30	24.00(4.00)	13/17	20.90(4.43)	16.50(3.00)	1.74(9.43)	0.003(0.006)	0.004(0.009)	0.003(0.011)	0.002(0.015)
HMUSH	48	21.00(1.00)	21/27	21.18(2.42)	14.00(0.50)	0.37(7.07)	0.005(0.005)	0.007(0.013)	-3.64×10^{-4}(0.011)	0.001(0.014)
SMUFH	50	24.00(2.00)	7/43	20.81(2.39)	16.50(1.00)	-0.79(8.53)	0.004(0.005)	0.010(0.009)	1.53×10^{-4}(0.011)	0.001(0.015)
DMUFAH	35	24.00(2.00)	12/23	20.76(3.51)	17.00(1.00)	-0.19(7.28)	0.004(0.006)	0.006(0.014)	0.001(0.010)	-0.001(0.017)
NMUDTH	61	22.00(2.00)	19/42	20.31(2.68)	16.00(2.00)	4.45(8.69)	-0.002(0.012)	-0.003(0.022)	0.004(0.019)	-1.79×10^{-4}(0.015)
XMUAH	122	24.00(3.00)	40/82	20.75(2.55)	17.00(2.00)	-0.25(6.45)	0.003(0.011)	0.002(0.017)	1.53×10^{-4}(0.014)	-2.41×10^{-4}(0.016)
ZUSAH	35	23.00(2.00)	12/23	20.40(1.44)	17.00(1.00)	-0.27(7.07)	-0.008(0.009)	0.002(0.009)	0.002(0.016)	-0.001(0.013)
WMUFAH	33	23.00(3.00)	13/20	20.03(3.59)	16.00(2.00)	-0.81(6.05)	-0.010(0.007)	-0.002(0.012)	0.001(0.016)	0.005(0.025)
WMUSAH	27	25.00(3.50)	9/18	20.52(2.72)	17.00(2.00)	-4.36(4.02)	-0.010(0.011)	-1.84×10^{-4}(0.005)	0.002(0.013)	0.004(0.024)
AMUFAH	44	23.00(3.00)	12/32	20.20(2.57)	16.00(2.50)	-1.85(6.33)	0.001(0.009)	0.002(0.017)	0.001(0.016)	0.001(0.020)
USTC	32	21.00(3.50)	21/11	21.45(2.63)	15.00(2.00)	4.34(10.00)	-9.41×10^{-5}(0.011)	0.001(0.015)	0.002(0.013)	0.002(0.017)
SUQH	42	26.00(2.00)	15/27	21.70(3.77)	18.00(1.00)	1.95(8.47)	0.005(0.008)	0.007(0.010)	-0.001(0.013)	-0.002(0.014)
YHH	72	20.00(1.00)	29/43	20.95(3.36)	14.00(0.50)	0.87(8.52)	0.006(0.006)	0.005(0.019)	0.001(0.010)	-0.001(0.018)
HPPH	35	24.00(2.00)	10/25	20.31(3.52)	17.00(2.00)	-2.16(4.59)	0.003(0.004)	0.008(0.010)	0.001(0.010)	-4.83×10^{-4}(0.016)
ZUFAH	241	24.00(4.00)	98/143	21.09(2.66)	17.00(2.00)	-1.30(7.62)	0.004(0.007)	0.005(0.012)	1.31×10^{-4} (0.012)	-0.001(0.016)
HUSTTH	68	24.00(2.50)	16/52	20.46(2.95)	17.00(2.00)	-0.02(8.20)	-0.010(0.016)	3.15×10^{-4}(0.010)	0.002(0.009)	-0.001(0.021)
CSUXH	45	24.00(3.00)	12/33	20.31(2.90)	18.00(2.00)	0.38(8.60)	-0.019(0.009)	-0.003(0.005)	0.006(0.009)	0.001(0.014)
GUCMFAH	37	24.00(3.00)	13/24	19.83(2.79)	17.00(3.00)	-1.70(4.63)	-0.024(0.018)	-0.008(0.010)	0.005(0.008)	-0.002(0.023)
HGH	29	23.00(4.00)	12/17	20.61(2.99)	16.00(2.00)	-2.03(7.59)	-0.026(0.026)	-0.011(0.013)	0.004(0.007)	-0.004(0.019)
FMMUTH	30	21.00(1.00)	25/5	21.77(3.01)	15.00(0.00)	3.19(6.47)	0.003(0.007)	0.007(0.014)	0.002(0.008)	0.003(0.015)

LUSH	33	25.00(4.00)	8/25	20.57(2.90)	17.00(4.00)	-1.11(9.03)	0.004(0.006)	0.003(0.014)	3.87×10^{-4}(0.014)	-0.001(0.021)
SUWCH	8	25.50(4.00)	4/4	20.14(1.14)	16.00(3.50)	-2.86(7.00)	-0.002(0.012)	-0.011(0.019)	0.004(0.027)	-0.001(0.009)
ZUPH	48	25.00(2.50)	12/36	20.51(3.96)	17.50(1.50)	-2.28(6.25)	0.004(0.006)	0.006(0.015)	-0.001(0.012)	-2.71×10^{-4}(0.015)
NMUJH	112	23.00(2.00)	32/80	20.86(3.03)	17.00(2.00)	0.36(7.37)	-0.001(0.010)	0.001(0.014)	0.002(0.016)	1.81×10^{-4}(0.017)
Total	2176	24.00(3.00)	769/1407	20.76(3.01)	17.00(3.00)	-0.22(7.86)	0.003(0.011)	0.003(0.016)	0.001(0.012)	3.16×10^{-4}(0.017)

BMI, body mass index; SES, socioeconomic status; PCA, principle component analysis; TMUGH, Tianjin Medical University General Hospital; TMUCIH, Tianjin Medical University Cancer Institute and Hospital; TFCH, Tianjin First Center Hospital; CPAPFLUPH, Pingjin Hospital, Logistics University of Chinese People's Armed Police Forces; THH, Tianjin Huanhu Hospital; HMUSH, The Second Hospital of Hebei Medical University; SMUFH, The First Hospital of Shanxi Medical University; DMUFAH, The First Affiliated Hospital of Dalian Medical University; NMUDTH, Drum Tower Hospital, Medical School of Nanjing University; XMUAH, The Affiliated Hospital of Xuzhou Medical University; ZUSAH, The Second Affiliated Hospital of Zhejiang University; WMUFAH, The First Affiliated Hospital of Wenzhou Medical University; WMUSAH, The Second Affiliated Hospital of Wenzhou Medical University; AMUFAH, The First Affiliated Hospital of Anhui Medical University; USTC, University of Science and Technology of China; SUQH, Qilu Hospital of Shandong University; YYH, Yantai Yuhuangding Hospital; ZUPH/HPPH, Zhengzhou University People's Hospital and Henan Provincial People's Hospital; ZUFAH, The First Affiliated Hospital of Zhengzhou University; HUSTTH, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology; CSUXH, Xiangya Hospital, Central South University; GUCMFAH, The First Affiliated Hospital of Guangzhou University of Chinese Medicine; HGH, Hainan General Hospital; FMMUTH, Tangdu Hospital, the Military Medical University of PLA Airforce (Fourth Military Medical University; LUSH, Lanzhou University Second Hospital; ZUPH, Zhengzhou University People's Hospital;NMUJH, Jinling Hospital, Medical School of Nanjing University. #Statistics are shown as median (quantile interval) since all variables are deviated from normal distribution in each center.

Supplementary Table 23. Demographic data of each site in IMAGEN.

Center	N	Age[#]	M/F	BMI[#]	SES[#]	GEN(Y/N)	PCA1[#]	PCA2[#]	PCA3[#]	PCA4[#]
Nottingham	87	18.63(0.49)	41/46	20.20(3.86)	-0.06(3.22)	35/52	0.005(0.001)	0.007(0.005)	-0.005(0.008)	-0.017(0.006)
Dresden	106	18.59(0.58)	51/55	19.88(2.92)	0.95(2.78)	46/60	0.004(0.001)	0.003(0.004)	-0.007(0.01)	0.024(0.01)
Berlin	56	18.61(1.08)	18/38	19.72(4.13)	0.13(2.67)	26/26	0.005(0.002)	0.003(0.005)	-0.009(0.02)	0.020(0.01)
London	93	18.83(0.63)	41/52	21.09(4.31)	0.11(2.51)	39/54	0.005(0.003)	0.006(0.006)	-0.003(0.009)	-0.017(0.01)
Mannheim	52	18.90(1.16)	24/28	20.44(4.03)	-0.54(2.33)	25/27	0.004(0.002)	0.003(0.004)	0.001(0.02)	0.012(0.02)
Dublin	21	19.37(0.76)	12/9	21.05(3.28)	1.52(3.30)	12/13	0.006(0.002)	0.006(0.004)	-0.006(0.007)	-0.041(0.007)
Total	415	18.71(0.77)	187/228	20.26(3.96)	0.11(2.78)	183/232	0.005(0.002)	0.004(0.006)	-0.004(0.01)	0.002(0.04)

BMI, body mass index; SES, socioeconomic status; PCA, principle component analysis; FU2, IMAGEN follow up 2 assessment acquired at 19 years; GEN, Genetic Screening and Family History of Psychiatric Disorders Interview; [#]Statistics are shown as median (quantile interval) in each center.

Supplementary Table 24. Detailed information of band 1-7 from Landsat 7.

Name	Wavelength	Description (30m / pixel)
Band 1	0.45-0.52 um	Band 1 (blue) surface reflectance
Band 2	0.52-0.60 um	Band 2 (green) surface reflectance
Band 3	0.63-0.69 um	Band 3 (red) surface reflectance
Band 4	0.77-0.90 um	Band 4 (near infrared) surface reflectance
Band 5	1.55-1.75 um	Band 5 (shortwave infrared 1) surface reflectance
Band 6	10.40-12.50 um	Band 6 brightness temperature
Band 7	2.08-2.35 um	Band 7 (shortwave infrared 2) surface reflectance

Extended Data Figure Legends

Extended Data Fig.1. A flow diagram of sample selection in CHIMGEN (a) and IMAGEN (b).

BDI, Beck depression inventory; BTG, ball tossing games task; BL, IMAGEN baseline assessment acquired at 14 years; CIDI-AS, Anxiety Screening from the Composite International Diagnostic Interview; CVLT-II, the second edition of California verbal learning test; DAWBA-GA, Generalized Anxiety Scale from The Development and Well-Being Assessment Interview; FC, functional connectivity; FU2, IMAGEN second follow up assessment acquired at 19 years; FU2-BL, IMAGEN FU2-BL measures brain changes rate between BL of 14 years and FU2 of 19 years; GNG, go/no-go task; IRI, Interpersonal Reactivity Index; RSQ, Ruminating Scale Questionnaire; SA, state anxiety; SBM, surface-based morphometry; SDMT, symbol digit modalities test; TA, trait anxiety; TBSS, tract-based spatial statistics; VBM, voxel-based morphometry.

Extended Data Fig.2. Schematic summary of multiple imputation and confirmatory factor analysis.

a. A flow diagram for multiple imputation and confirmatory factor analysis. b-c. Sensitivity analysis results in voxel-wise correlations of ten imputed UrbanSat (b) and combined UrbanSat (c) with brain GMV in CHIMGEN (FWE $Pc<0.05$). Each imputed UrbanSat from MICE imputation before 18 years show a significant negative correlation with left mPFC volume and a significant positive correlation with cerebellar volume adjusting confounding covariates (FWE $Pc<0.05$) (b), similar to the results derived from combined UrbanSat score following Rubin's rule (c). d. The estimated

fractions of missing information (FMI) of UrbanSat were low for the GMVs of left-mPFC-ROI (FMI=1.01%) and cerebellum-ROI (FMI=1.19%). UrbanSat was still correlated with mPFC-GMV (P<0.001) and cerebellum-GMV (P<0.001) after pooling using mice R package in CHIMGEN. e. Non-imputed mean UrbanSat before 18 years still show a significant negative correlation with mPFC-GMV and a significant positive correlation with cerebellar-GMV adjusting confounding covariates (FWE Pc<0.05) (n=1460). CFA, confirmatory factor analysis; FMI, fractions of missing information; GMV, gray matter volume; L, left; MICE, multivariate imputation by chained equations; mPFC, medial prefrontal cortex; R, right. S, satellite; Y, years.

Extended Data Fig.3. Histograms of UrbanSat in each center of CHIMGEN (a) and IMAGEN (b).

TMUGH, Tianjin Medical University General Hospital; TMUCIH, Tianjin Medical University Cancer Institute and Hospital; TFCH, Tianjin First Center Hospital; CPAPFLUPH, Pingjin Hospital, Logistics University of Chinese People's Armed Police Forces; THH, Tianjin Huanhu Hospital; HMUSH, The Second Hospital of Hebei Medical University; SMUFH, The First Hospital of Shanxi Medical University; DMUFAH, The First Affiliated Hospital of Dalian Medical University; NMUDTH, Drum Tower Hospital, Medical School of Nanjing University; XMUAH, The Affiliated Hospital of Xuzhou Medical University; ZUSAH, The Second Affiliated Hospital of Zhejiang University; WMUFAH, The First Affiliated Hospital of Wenzhou Medical University; WMUSAH, The Second Affiliated Hospital of Wenzhou Medical University; AMUFAH, The First Affiliated Hospital of Anhui Medical University; USTC, University of Science and Technology of China; SUQH, Qilu Hospital of Shandong University; YYH, Yantai Yuhuangding Hospital; ZUPH/HPPH, Zhengzhou

University People's Hospital and Henan Provincial People's Hospital; ZUFAH, The First Affiliated Hospital of Zhengzhou University; HUSTTH, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology; CSUXH, Xiangya Hospital, Central South University; GUCMFAH, The First Affiliated Hospital of Guangzhou University of Chinese Medicine; HGH, Hainan General Hospital; FMMUTH, Tangdu Hospital, the Military Medical University of PLA Airforce (Fourth Military Medical University); LUSH, Lanzhou University Second Hospital; SUWCH, West China Hospital of Sichuan University; ZUPH, Zhengzhou University People's Hospital; NMUJH, Jinling Hospital, Medical School of Nanjing University.

Extended Data Fig.4. Correlations of UrbanSat with brain GMV, SA and CT in CHIMGEN and IMAGEN.

a. Uncorrected correlation statistical maps of UrbanSat with brain GMV in CHIMGEN under non-parametric permutation testing (n=2176). b. Correlations of UrbanSat with brain GMV in CHIMGEN under Pc<0.05 in TFCE-FWE using non-parametric permutation testing (n=2176). c-d. Uncorrected correlation statistical maps of UrbanSat with brain GMV in CHIMGEN (c) and IMAGEN-FU2 (d) under parametric testing. e. The overlap results (yellow) in the voxel-wise correlation of mean UrbanSat before 18 years with brain GMV in CHIMGEN (red) and IMAGEN-FU2 (green) after controlling confounders (FWE Pc<0.05). f-g. Uncorrected vertex-wise correlation maps of UrbanSat with surface area (f) and cortical thickness (g) in CHIMGEN (n=2164). h-i. The mPFC-ROI projected onto the volumetric map (h) and fsaverage surface in Freesurfer (i).

Extended Data Fig.5. Voxel-wise correlations of individual satellite measures with brain GMV in CHIMGEN (n=2176) (a-e) and IMAGEN (n=415) (f-j).

a-e. In CHIMGEN, there are significant negative correlations of mean night-time light (a) and population density (e) with mPFC GMV and positive correlations with cerebellar GMV after controlling confounders (FWE, Pc<0.05); There are significant negative correlations of mean built-up with mPFC GMV (b) and of mean cropland with cerebellar GMV (c); There are no correlations of mean NDVI with brain GMV (d). f-j. In IMAGEN, there are significant negative correlations of mean night-time light (f), mean built-up (g) and population density (j) with mPFC GMV and positive correlations with cerebellar GMV after controlling confounders (FWE, Pc<0.05); There are no correlations of mean cropland (h) and NDVI (i) with brain GMV. GMV, gray matter volume; L, left; mPFC, medial prefrontal cortex; NDVI, normalized difference vegetation index; R, right.

Extended Data Fig.6. Forest plot of meta-analysis in CHIMGEN and IMAGEN-FU2.

Effect size of correlations of UrbanSat with mPFC GMV (a), cerebellar GMV (b), mPFC CT (c), mPFC SA (d), WNFCs in aDMN (e), CN (f), mVN (g) and lVN (h), BNFCs of aDMN-CN (i), aDMN-ECN (j), aDMN-rFPN (k) and rFPN-lFPN (l) for meta-analysis in CHIMGEN and IMAGEN-FU2. We exclude SUWCH center from CHIMGEN for all meta-analysis and Dublin center from IMAGEN for the meta-analysis of brain functional features, because there are only 8 and 10 participants from each site, which more than the numbers of covariates while performing Spearman correlation analysis.

Extended Data Fig.7. Susceptibility analysis of individual satellite measures with brain (a-d) and behaviors (e-h) using distributed lag models in CHIMGEN.

a. There are significant associations of lifetime night-time light with the mPFC-ROI GMV (ages of 4-14 years) and SA (5-12 years), WNFC in aDMN (3-11 years) during childhood and adolescence, with cerebellum-ROI GMV (3-7 years), WNFCs in CN (0-6 years), mVN (0-6 years), lVN (3-10 years), BNFCs in aDMN-CN (4-7 years), aDMN-ECN (4-6 years), aDMN-rFPN (4-6 years) and rFPN-lFPN (4-6 years) during childhood in CHIMGEN. b. There are significant associations of lifetime built-up% with the mPFC-ROI GMV (5-16 years) and WNFC in aDMN (4-14 years) during childhood and adolescence, with WNFCs in mVN and lVN (14-20 years) during adolescence, with mPFC-ROI SA (5-7 years), cerebellum-ROI GMV (1-10 years), WNFC in CN (1-10 years), BNFCs in aDMN-CN (4-10 years), aDMN-ECN (5-7 years), aDMN-rFPN (4-10 years) and rFPN-lFPN (4-6 years) during childhood in CHIMGEN. c. There are significant associations of lifetime cropland% with the mPFC-ROI GMV (5-15 years) during childhood and adolescence, with mPFC-ROI SA (5-6 years), cerebellum-ROI GMV (4-6 years), WNFCs in aDMN (4-6 years), CN (4-6 years) and lVN (4-10 years), BNFCs in aDMN-CN (0-9 years), aDMN-ECN (2-7 years), aDMN-rFPN (4-10 years) and rFPN-lFPN (4-6 years) during childhood in CHIMGEN. d. We find significant associations of lifetime NDVI with the mPFC-ROI GMV (5-15 years) and BNFC in rFPN-lFPN (6-17 years) during childhood and adolescence, with WNFCs in aDMN (5 years old) and CN (5 years old), BNFCs in aDMN-CN (4-11 years) and aDMN-rFPN (4-10 years) during childhood in CHIMGEN. There are significant correlations of lifetime night-time light (e), built-up% (f), cropland % (g) and NDVI (h) with reaction time for perspective taking performance during adolescence (ages of 5-16 years for night-time light, 4-17 years for built-up %, 5-19 years for cropland % and 4-17 years for NDVI) in CHIMGEN. Significant correlations of lifetime night-time light (e), built-up % (f), cropland % (g) and NDVI (h)

with increasing depression measured by BDI are also observed during childhood in CHIMGEN (0-6 years for night-time light, 2-9 years for built-up %, 0-9 years for cropland % and 3-11 years for NDVI). The y-axis represents the changes of brain behaviors associated with an increase of interquartile range of individual satellite measures; the x-axis is individual satellite measure lag in ages. Gray areas indicate 95% CIs. A susceptibility window is identified for the ages where the estimated pointwise 95% CI (shaded area) does not include zero. The blue solid lines indicate negative correlations and red ones indicated positive correlations. aDMN, anterior default mode network; BDI, Beck depression index; BNFC, between-network functional connectivity; CN, cerebellar network; CT, cortical thickness; GMV, gray matter volume; lVN, lateral visual network; mPFC, medial prefrontal cortex; mVN, medial visual network; RTpt, reaction time for perspective taking; SA, surface area; WNFC, within-network functional connectivity.

Extended Data Fig.8. Seventeen RSNs identified by independent component analysis in CHIMGEN.

aDMN, anterior default mode network; AN, auditory network; aSN, anterior cingulate cortex part of salience network; CN, cerebellar network; dAN, dorsal attentional network; dSMN, dosal sensorimotor network; ECN, executive control network; inSN, insular part of salience network; lFPN, left frontal parietal network; LN, language network; lVN, lateral visual network; mVN, medial visual network; pDMN, posterior default mode network; PN, precuneus network; rFPN, right frontal parietal network; RSNs, resting-state networks; vAN, ventral attentional network; vSMN, ventral sensorimotor network.

Extended Data Fig.9. Voxel-wise correlations of individual satellite measures with WNFCs and BNFCs in CHIMGEN (n=2156) and IMAGEN (n=315).

a-f. In CHIMGEN, there are negative correlations (blue) of mean UrbanSat (a) and mean night-time light before 18 years (b) with WNFC in the mPFC of the aDMN, positive correlations (red) with WNFCs in the left CV of the CN and left LG of the mVN and lVN (FWE P_c<0.05). c. There are negative correlations (blue) of mean built-up% before 18 years with WNFC in the mPFC of the aDMN and positive correlations (red) with WNFC in the left LG of the lVN (FWE P_c<0.05). d. There are negative correlations (blue) of mean cropland% before 18 years with WNFCs in the CV of the CN and the left LG of the lVN (FWE P_c<0.05). e. There is no correlation of mean NDVI with WNFC of any RSN surviving the multiple correction. f. There are negative correlations (blue) of mean population density from GHSL before 18 years with WNFC in the mPFC of the aDMN, positive correlations (red) with WNFCs in the left CV of the CN and the left LG of the mVN (FWE P_c<0.05). g-l. In IMAGEN, there are negative correlations (blue) of mean UrbanSat (g), night-time light (h), built-up% (i) before 18 years with WNFC in the mPFC of the aDMN, positive correlations (red) with WNFC in the CV of the CN (FWE P_c<0.05). j. There are negative correlations (blue) of mean cropland before 18 years with WNFC in the CV of the CN (FWE Pc<0.05). k. There is no correlation of mean NDVI with WNFC of any RSN surviving the multiple correction. l. There are negative correlations (blue) of mean population density from GHSL before 18 years with WNFC in the mPFC of the aDMN, and positive correlation (red) with WNFC in the CV of the CN (FWE, Pc<0.05). m-p. The mean built-up% (m) (N=32), cropland% (n) (N= 41), NDVI (o) (N=1) and population density (p) (N=52) show correlations with BNFCs in CHIMGEN. The red line indicates positive correlations of UrbanSat with BNFCs and blue line indicated negative correlations. N

indicates the numbers of significant correlations of BNFCs. aDMN, anterior default mode network; CV, cerebellar vermis; CN, cerebellar network; GHSL, global human settlement layers; LG, lingual gyrus; lVN, lateral visual network; mPFC, medial prefrontal cortex; mVN, medial visual network; NDVI, normalized difference vegetation index; WNFC, within-network functional connectivity.

Extended Data Fig.10. The schematic summary of ball tossing game task design, which measures perspective taking and agency performance.

ACT, active agency; 1PP, first-person perspective; 3PP, third-person perspective; PAS, passive agency.

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