Cohort profile: Chinese Color Nest Project (CCNP)

Siman Liu¹, Zhe Zhang¹, Ning Yang^{1,2}, Qing Zhang^{1,3}, Quan Zhou^{1,3}, Xi-Nian Zuo^{1,2,3,4,5,6*}

1. Research Center for Lifespan Development of Mind and Brain, CAS Key Laboratory of Behavioral Sciences, Institute of Psychology, Beijing, China

2. Developmental Population Neuroscience Research Center, State Key Laboratory of Cognitive Neuroscience and Learning, Beijing Normal University, Beijing, China

3. Department of Psychology, University of Chinese Academy of Science (UCAS), Beijing, China

4. Key Laboratory of Brain and Education Sciences, School of Education Sciences, Nanning Normal University, Nanning, Guangxi, China

5. Institute for Brain Research and Rehabilitation, South China Normal University, Guangzhou, Guangdong, China

6. IDG/McGovern Institute for Brain Research, Beijing Normal University, Beijing, China

Words: 3330 (excluding the Key Features and References)

*** Corresponding author:**

Xi-Nian Zuo, PhD, Professor, <https://zuoxinian.github.io>

Developmental Population Neuroscience Research Center

State Key Laboratory of Cognitive Neuroscience and Learning

IDG/McGovern Institute for Brain Research

Beijing Normal University

Room 215, Brain Imaging Center Building

No 19 Xijiekouwai Street, Haidian District, Beijing 100875, China

Emails: xinian.zuo@bnu.edu.cn zuoxn@nnnu.edu.cn or zuoxn@psych.ac.cn

Key Features

- The ongoing CCNP was established to plot normative growth curves for brain structure and function across the human lifespan, and link age-related changes in brain imaging measures with psycho-behavioral functions at the behavioral, cognitive and emotional levels using an accelerated longitudinal design.
- CCNP comprises three phases: developmental CCNP (devCCNP: 6-20 years), standardizing CCNP (stdCCNP: 20-60 years) and aging CCNP (ageCCNP: 60-90 years).
- CCNP started from devCCNP in 2013, which has successfully acquired CCNP-SWU data with three repeated measurements at the trial stage of devCCNP, and accumulated CCNP-CAS baseline data at the second stage of devCCNP.
- CCNP-SWU consists of 201 age-sex stratified schoolchildren at enrollment (100 children followed up for 2.5 years at 1.25-year intervals). CCNP-CAS has been recruiting participants since July 2018, and has collected data from 133 eligible children so far.
- A T1-weighted MRI and two resting functional MRI scans were acquired across three waves in CCNP-SWU with the same imaging protocols on a Siemens Trio 3T scanner at Southwest University in Chongqing, China.
- CCNP-SWU obtained longitudinal biophysical, social, behavioral and cognitive data via parent-reported questionnaires, self-reported questionnaires, behavioral assessment, as well as E-Prime computer tasks.
- Data were collected on the impact of COVID-19 on children's learning and daily life from 46 children between March and May 2020. Children's emotional states during COVID-19 pandemic were also measured.
- Data are accessed by researchers and collaborators of CCNP upon agreement with the principal investigator. Requests for further information and collaboration are encouraged and should be submitted to Xi-Nian Zuo [xinian.zuo@bnu.edu.cn].

Why was the cohort set up?

Construction of normative growth curves for brain structure and function across the human life span in typically developing individuals is essential for characterizing brain morphology and connectivity changes as a function of age and monitoring neurodevelopmental status.^{1 2} The age-related trajectory of the brain in the life cycle can be used to elucidate the normative pattern of brain development, maturation and aging, and further reveal similarities and differences at different developmental stages.³⁻⁵ Growth curves for height, weight or head circumference provide important information about children's physical health, which enable pediatricians and parents to identify abnormal physical growth.⁶⁻⁹ Similarly, inadequate or excessive brain growth as estimated by deviations from the normalized distribution in growth curves may represent abnormal neurodevelopmental status that needs closer monitoring, and even interventions.

With respect to the use of brain growth curves in clinical practice, many neurological and psychiatric disorders, such as autism spectrum disorder, psychotic disorders, bipolar spectrum disorders and attention deficit hyperactivity disorder, are considered to have their origins in abnormal brain development.¹⁰⁻¹⁴ The deviations from normative brain trajectories related to neuropsychiatric conditions may help reveal the pathological and physiological changes and construct neuroimaging biomarkers, and therefore shed new light on clinical diagnosis and treatment.¹⁵⁻¹⁸ From an intervention perspective, brain growth curves also provide optimal periods for intervention and normative age-expected values that are required for further assessment of the effectiveness of an intervention program. If participants with abnormal brain development return to follow the normative pattern after receiving a specific intervention, this intervention is demonstrated to be effective in attenuating neurocognitive impairment or promoting brain development and successful aging.

Given the implications of brain growth charts in basic research and clinical application,

researchers have sought to establish brain growth curves and use them to predict cognitive deficits and neuropsychiatric conditions.^{19 20} Despite these advances, reliable and accurate growth charts for the brain are still not available. The underlying reason is that most studies rely on cross-sectional design and focus on a narrow range of ages and sample sizes, which limit their ability to accurately reflect the continuity of individual development over the course of life. In cross-sectional studies, the age-related changes shown in developmental trajectories often confound age and cohort effects.²¹⁻²³ Standard longitudinal design (i.e., pure or single-cohort longitudinal design) overcomes the shortcomings of cross-sectional design by recruiting a single cohort of participants of the same age and following them over a period of time. However, this design inevitably raises issues of time demands and sample attrition over time, and also elicits practice effects due to repeated assessments, which reduces its feasibility and efficiency in life-span studies involving a wide range of age groups.^{3 23 24}

The dilemma between cross-sectional and standard longitudinal designs highlights the need for using accelerated longitudinal designs, which recruits multiple cohorts of individuals of different ages and follows them over a relatively shorter period of time.^{25 26} Apparently, the multicohort approach is less time-consuming and more practical for creating growth curves over a long interval of the life course. Indeed, previous studies have mapped developmental trajectories over a time span of decades using accelerated longitudinal design, of which the most famous is The Seattle Longitudinal Study investigating longitudinally cognitive development from young adulthood to old age.²⁷⁻²⁹

The principal work of the ongoing study of Chinese Color Nest Project (CCNP) is to collect high-quality data on brain magnetic resonance imaging (MRI) scans and socio-psychological factors using an accelerated longitudinal design encompassing three repeated measurements on 1200 healthy individuals aged 6-85 years at enrollment. The overall aim of CCNP is to map normative growth curves for brain structure and function across the human

lifespan, and to further examine how age-related changes in brain anatomical and functional networks of the brain are related to age-related changes in psycho-behavioral functions, such as cognitive and behavioral abilities.

CCNP comprises three phases: developmental CCNP (devCCNP: 6-20 years), standardizing CCNP (stdCCNP: 20-60 years) and aging CCNP (ageCCNP: 60-90 years). CCNP starts from devCCNP in 2013, which has successfully acquired CCNP-SWU data with three repeated measurements at the trial stage of devCCNP across 5 years from 2013 to 2017, and is collecting CCNP-CAS baseline data at the second stage of devCCNP. As sub-samples of devCCNP, CCNP-SWU sample consists of 201 typically developing children aged 6–18 years at enrollment, while CCNP-CAS sample consists of 133 typically developing children so far. Each child was scheduled for three longitudinal 3T MRI scans and socio-psycho-behavioral measures with 15 months follow-up intervals. In this paper, an overview of devCCNP protocol, including study design, participants, data collection and preliminary results, is presented.

Who is in the cohort?

The trial stage implementation of devCCNP took place at Beibei District, Chongqing, China from March 2013 to January 2017. The Institute of Psychology, Chinese Academy of Sciences (CAS) and the Faculty of Psychology, Southwest University (SWU) are responsible for this pilot study called CCNP-SWU. The ongoing CCNP-CAS began in September 2017 at Beijing, China. Ethical approval was provided by the Institutional Review Board of the CAS Institute of Psychology.

The devCCNP design involves recruitment of 12 age-adjacent cohorts ranging from age 6 to 18 years followed up for 2.5 years at 1.25-year follow-up intervals. Using the devCCNP design, CCNP-SWU and CCNP-CAS aimed to recruit 192 age-sex stratified children

distributed in 12 age groups respectively, with each age group consisting of 16 children, 8 males and 8 females for purpose of gender balance (see Figure 1). In CCNP-SWU, both children and their parents/guardians were approached through lectures that explained this large-scale longitudinal cohorts and popular science activities regarding brain development in local primary and middle schools including students from the first grade of primary school to the second grade of high school. By contrast, CCNP-CAS comprises community samples recruited via the public uses social media *wechat* and popular science activities.

-Insert Figure 1 about here-

The exclusion criteria included the following: (a) children's birth weight less than 1.5kg or greater than 4.2kg; (b) children with a gestational or perinatal history of pathologies or risk factors; (c) children's height, weight, or head circumference less than the third percentile of the growth curve of Chinese children and adolescents; (d) children with a history of head injury; (e) children or one of their family members diagnosed with a neuropsychiatric disorder, such as schizophrenia, attention deficit hyperactivity disorder, autism spectrum disorder, bipolar disorder, alcohol or other drug use disorder; (f) Wechsler Intelligence Scale for Children-IV (WISC-IV) full-scale Intelligence Quotient (FSIQ) standard score lower than 80. Both children and their parents/guardians volunteered to participate in this study, and signed the informed consent before participation.

The CCNP-SWU recruitment took place between March and December in 2013. A total of 198 children volunteered to take part in this study, of which 6 were excluded due to brain cyst ($n=2$), depression disorder ($n=1$), claustrophobia ($n=1$), or WISC-IV FSIQ standard score lower than 80 ($n=2$). Therefore, 192 children were eligible for further participation, which formed the sample for the baseline assessment stage of CCNP-SWU. Because of

attrition, of the 192 original samples at baseline (Wave 1), 152 participated in the 15-month follow-up (Wave 2), representing a 79.17% retention rate from Wave 1 to Wave 2. Seven children were further included at Wave 2, of the 159 children participating at Wave 2, 106 retained in the 30-month follow-up (Wave 3), representing a 66.67% retention rate from Wave 2 to Wave 3. Also, 2 children were further included at Wave 3. Eventually, as a sub-sample of devCCNP, CCNP-SWU sample consisted of 201 children who participated at least one wave, of which 100 (49.75%) participated in all three waves, 58 (28.86%) participated in two waves, and 43 (21.39%) participated in only one wave.

The CCNP-CAS has been recruiting participants since July 2018, and has collected data from 133 eligible children thus far. Figure 2 presents age and sex distributions of CCNP-SWU and CCNP-CAS samples. Sociodemographic characteristics for CCNP-SWU and CCNP-CAS samples are illuminated in Table 1. Pearson's chi-squared tests were used to compare sample characteristics between CCNP-SWU and CCNP-CAS samples. The results indicated that children in CCNP-CAS were more likely to live in urban areas and have highly educated mothers and fathers than children in CCNP-SWU.

-Insert Figure 2 about here-

-Insert Table 1 about here-

How often have they been followed up?

Based on accelerated longitudinal design, the 12 age-adjacent cohorts were followed up every 15 months for a total of 30 months. Three repeated measurement occasions were distributed in various seasons in order to avoid season-associated variability. Data collection of CCNP-SWU for Wave 1 (baseline) was conducted from December 2013 to July 2014; data collection for Wave 2 (15-month follow-up) was conducted from April to August 2015; data

collection for Wave 3 (30-month follow-up) was conducted from September 2016 to January 2017. The mean time lag between Wave 1 and Wave 2 was 1.27 years ($SD = 0.06$; range = 1.16-1.50 years), and between Wave 2 and Wave 3 was 1.37 years ($SD = 0.07$; range = 1.22-1.56 years). The CCNP-CAS is collecting baseline data since July 2018, and will collect longitudinal data at Wave 2 and Wave 3 in the near future.

After assessment at each wave, every family received a personal development report for participation. The development report provided feedback on five aspects of children's development, including physiological characteristics (i.e., height, weight, head circumference, blood pressure, and pulse), cognitive ability, social-emotional development (social anxiety, depression, stress perception and behavioral problems), personality, and brain development. Brain development included intracranial volume (ICV), white matter (WM) volume, gray matter (GM) volume, and cerebrospinal fluid (CSF) volume, as well as the cortical thickness and surface area of seven functional networks (i.e., visual, somatomotor, dorsal attention, ventral attention, limbic, frontoparietal, and default mode networks).³⁰

What has been measured?

Table 2 lists the measures used in devCCNP across all waves to assess biophysical health and socio-psycho-behavioral factors. Objective biophysical measures were collected at each wave, including height, weight, head circumference, and biomarkers of cardiovascular health (i.e., blood pressure and pulse). The questionnaires were primarily built to collect socio-psycho-behavioral data on family and child characteristics, child behavioral problems, mood (e.g., stress, anxiety, depression, loneliness), personality characteristics, creativity, as well as video game use. Sociodemographic Questionnaire and CBCL were filled out by the parents, while the rest of the questionnaires were completed by the children.

-Insert Table 2 about here-

The Chinese Version of WISC-IV was used to measure cognitive ability.⁴⁶⁻⁴⁹ The scale consists of 10 core subtests and 4 supplementary subtests, which provide a full-scale Intelligence Quotient (FSIQ) reflecting the general cognitive ability and four indices: Verbal Comprehension Index (VCI), Perceptual Reasoning Index (PRI), Working Memory Index (WMI) and Processing Speed Index (PSI). Three E-Prime computer tasks, including the Attention Network Test, Task-Switch paradigms and Digit N-back Task, were used to assess children's alerting, orienting, executive attention, cognitive flexibility and working memory.⁵⁰⁻⁵²

Imaging data at CCNP-SWU were collected across all waves on a Siemens Trio 3T scanner at Southwest University, while imaging data at CCNP-CAS were collected on a GE Discovery MR750 3T scanner at the CAS Institute of Psychology. Two resting-state functional MRI (rfMRI) scans were acquired and separated by a T1-weighted MRI scan. The main acquisition parameters for T1-weighted MRI and rfMRI are listed in Table 3. A T2-weighted MRI scan was also performed to evaluate brain lesions. All the Child Questionnaires and Cognitive Battery Tests were completed after the imaging scans, in order to avoid the influence of physiological fatigue and affective state.

-Insert Table 3 about here-

After quality control procedures, a total of 429 high-resolution structural MRI images were acquired from 198 CCNP-SWU children. Among these children, 81 (44 girls) completed structural imaging scan 3 times, 69 (31 girls) completed twice, and 48 (30 girls) completed only once. A total of 179 CCNP-SWU children completed both structural and functional

imaging scans, of which 80 completed 3 times, 54 completed twice, and 45 completed only once. As a result, 393 sets of high-resolution structural and functional images were acquired. The volumetric brain analysis was conducted using *volBrain* pipeline to obtain brain's intracranial volume (ICV), white matter (WM) volume, gray matter (GM) volume, and cerebrospinal fluid (CSF) volume.⁵³

What has it found? Key findings and publications

Attrition analyses were conducted to compare the CCNP-SWU families who participated in all three measurement waves ($n = 100$) with these who participated in Wave 1 and then dropped out at either Wave 2 or Wave 3 ($n = 92$) on sociodemographic characteristics (see Supplementary Table S1). Attrition analyses indicated that the retained families did not significantly differ from the drop-out families in the distribution of child gender, only child or non-only child, urban areas or rural areas, maternal education status and paternal education status. However, children who attended measurement 3 times were younger than those who participated in Wave 1 and then dropped out later.

Main variables of boys and girls across two age groups (younger group less than 12 years old vs. older group greater than 12 years old) at CCNP-SWU baseline are presented in Table 4. The raw scores of extraversion, neuroticism and psychoticism assessed by Eysenck Personality Questionnaire (EPQ) were used. Independent samples t tests were conducted to compare the means of main variables between boys and girls across two age groups. There were significant gender differences in body mass index (BMI), CBCL total scores, depression, neuroticism, psychoticism, brain ICV, WM volume, GM volume, and CSF volume in younger group. As for the older group, there were significant gender differences in height, social anxiety measured by Social Anxiety Scale for Children (SASC), psychoticism, FSIQ, verbal comprehension, processing speed, brain ICV and GM volume.

-Insert Table 4 about here-

Generalized Additive Mixed Model (GAMM) was used to model growth charts of brain volume for each sex in CCNP-SWU using R (version 3.5.3, <https://www.r-project.org>).⁵⁴ The growth charts generated are shown in Figure 3. Meanwhile, Table 5 presents main variables of boys and girls across two age groups at CCNP-CAS baseline. There were detectable sex differences in CBCL total scores, social anxiety and processing speed in younger group.

-Insert Figure 3 about here-

-Insert Table 5 about here-

In order to better understand the impact of Coronavirus Disease 2019 (COVID-19) pandemic, we designed questionnaires to collect data on the impact of COVID-19 on children's learning and daily life (see Table 6). A total of 46 children (*Mage* = 11.63 years, *SD* = 3.86; 20 boys, 26 girls) from CCNP-SWU (*n* = 9) and CCNP-CAS (*n* = 37) completed the questionnaires online from March to May 2020. Two in five children (43.48%) felt a bit nervous when COVID-19 occurred and spread rapidly. More than half of children reported that their learning time, learning efficiency and exercise time were dramatically or slightly decreased, whereas their screen time was dramatically increased. COVID-19 had slight impact on family's daily routine for most families (63.04%), and had moderate or strong impact on daily routine for nearly 30% of the families. Children's emotional states during COVID-19 pandemic were also measured by four scales: Depression Anxiety Stress Scale (DASS)⁵⁵, Children's Depression Inventory (CDI)³⁸, Depression Self-rating Scale for Children (DSRSC)⁵⁶, and Childhood Anxiety Sensitivity Index (CASI)⁵⁷. Supplementary Table S2 presents the descriptive statistics.

-Insert Table 6 about here-

A previous review was published in Chinese by our group, which described the CCNP-SWU protocol for experimental design, sample selection and data collection.⁵⁸ Using the CCNP-SWU baseline brain imaging data from 84 participants, we previously reported that children exhibited similar region-specific asymmetry of dorsal anterior cingulate cortex (dACC) as in adults, and further revealed that dACC functional connectivity with default, frontoparietal and visual networks showed a region-specific asymmetry.⁵⁹ This baseline data has been released as part of the Consortium for Reliability and Reproducibility (CoRR)⁶⁰, the IPCAS 7 site (http://dx.doi.org/10.15387/fcp_indi.corr.ipcas7). Using the full baseline data, we recently observed that social anxiety was positively correlated with the GM volume in an area of the orbital-frontal cortex, and its functional connectivity with the amygdala. Intriguingly, this functional measurement mediated the relationship between social anxiety and attention avoidance while the brain traits can predict the social anxiety one-year later⁶¹. A protocol on charting brain development in schoolchildren has been developed by modelling their standard brain templates and growth charts⁶².

What are the main strengths and weaknesses?

CCNP is the first cohort to combine brain imaging, biophysical, social, behavioral and cognitive measures across nearly the full lifespan in China. To date, the accelerated longitudinal and freely available data on high-resolution structural and functional images beginning in childhood and extending into early adulthood with the same imaging protocols have been acquired, which will allow the construction of normative growth curves describing how brain morphological metrics and functional connectivity change as a function of child age across genders. In addition, longitudinal psycho-behavioral data will enable the scientific

community to investigate how age-related changes in brain structure and function are associated with age-related changes in cognitive function and behavioral performance. Particularly, CCNP offers a unique resource for examining cultural or ethnic effects on development of human brain and mind (see an example in our recent work⁶²).

This study has several limitations. First, we are aware of the inevitable sample attrition across three waves in CCNP-SWU. Although the attrition analyses suggest that child gender and family background factors did not contribute to the attrition, children who completed all three waves were younger than those who participated in Wave 1 and then dropped out of the study at either Wave 2 or Wave 3, which may introduce bias, especially when constructing growth curves and describing age-related changes. Second, the CCNP focuses exclusively on Chinese Han population, and therefore the findings may not be generalizable to other ethnic groups. There is a physiological variation between different ethnic groups, and cognitive neuroscience research on ethnic minority groups in China is also an important direction for future studies. Finally, the sample is limited to a few regions, which may limit its ability to represent Chinese general population. Due to the complexity and high cost of MRI brain scanning, it is difficult to carry out large-scale and coordinated nationwide research, which highlights the need for conducting collaborative research and promoting MRI data sharing.

Can I get hold of the data? Where can I find out more?

Baseline CCNP-SWU data on brain imaging are available to researchers via the CoRR, which is committed to open science by aggregating and openly sharing rfMRI data from multiple sources to establish test-retest reliability and reproducibility in functional connectomics.⁶⁰ The rest of the data will be publicly shared gradually and fully available to the research community when acquisition is completed. At this stage, data are only available to researchers and collaborators of CCNP. The CCNP information can be found at:

<https://climbgroup.org/research>. Requests for further information and collaboration are encouraged and considered by principal investigator (PI) Xi-Nian Zuo [xinian.zuo@bnu.edu.cn, zuoxn@nnnu.edu.cn or zuoxn@psych.ac.cn].

Funding

This work was supported by the Beijing Municipal Science and Technology Commission (Z161100002616023), Guangxi BaGui Scholarship (201621), the National R&D Infrastructure and Facility Development Program of China, Fundamental Science Data Sharing Platform (DKA2019-12-02-21), the China - Netherlands CAS-NWO Programme (153111KYSB20160020), and the Key Realm R&D Program of Guangdong Province (2019B030335001), Natural Sciences Foundation of China (Major Fund for International Collaboration: 81220108014), the Chinese Academy of Sciences Key Research Program (CAS: KSZD-EW-TZ-002), the National Basic Research Program (973 Program: 2015CB351702), and the Startup Funds for Leading Talents at Beijing Normal University.

Acknowledgements

Statistician Ting Xu is acknowledged for advice with data extraction and statistical analyses. Daniel Margulies is acknowledged for assistance on proofreading the manuscript. Research staff members Hao-Ming Dong, Yin-Shan Wang, Chao Jiang, Zhu-Qing Gong, Lei Zhang, Xue-Ru Fan and Li-Zhi Cao deserve gratitude for data extraction. Education coordinators Xu Chen, Jiang Qiu, Antao Chen, Ting-Yong Feng and Xun Liu are acknowledged for help with practical arrangements. We are also grateful to all families participating in this cohort project and all the support from schools and the communities.

Conflict of Interest

None declared.

Reference

- 1 Peterson M, Warf BC, Schiff SJ. Normative human brain volume growth. *J Neurosurg Pediatr* 2018;21(5):478–485. doi:10.3171/2017.10.PEDS17141.
- 2 Harms MP, Somerville LH, Ances BM, et al. Extending the Human Connectome Project across ages: Imaging protocols for the Lifespan Development and Aging projects. *Neuroimage* 2018;183:972–984. doi:10.1016/j.neuroimage.2018.09.060.
- 3 Zuo XN, He Y, Betzel RF, Colcombe S, Sporns O, Milham MP. Human Connectomics across the Life Span. *Trends Cogn Sci* 2017;21(1):32–45. doi:10.1016/j.tics.2016.10.005.
- 4 Zuo XN, Kelly C, Di Martino A, et al. Growing together and growing apart: regional and sex differences in the lifespan developmental trajectories of functional homotopy. *J Neurosci* 2010;30(45):15034–15043. doi:10.1523/JNEUROSCI.2612-10.2010.
- 5 Betzel RF, Byrge L, He Y, Goñi J, Zuo XN, Sporns O. Changes in structural and functional connectivity among resting-state networks across the human lifespan. *Neuroimage* 2014;102:345–357. doi:10.1016/j.neuroimage.2014.07.067.
- 6 Cole TJ. The development of growth references and growth charts. *Ann Hum Biol* 2012;39(5):382–394. doi:10.3109/03014460.2012.694475.
- 7 Yang Z, Duan Y, Ma G, Yang X, Yin S. Comparison of the China growth charts with the WHO growth standards in assessing malnutrition of children. *BMJ Open* 2015;5(2):e006107. doi:10.1136/bmjopen-2014-006107.
- 8 Ouyang F, Jiang F, Tao F, et al. Growth patterns from birth to 24 months in Chinese children: a birth cohorts study across China. *BMC Pediatr* 2018;18(1):344. doi:10.1186/s12887-018-1328-z.
- 9 Kløvgaard M, Nielsen NO, Sørensen TL, et al. Growth of children in Greenland exceeds the World Health Organization growth charts. *Acta Paediatr* 2018;107(11):1953–1965. doi:10.1111/apa.14369.
- 10 Hazlett HC, Gu H, Munsell BC, et al. Early brain development in infants at high risk for autism spectrum disorder. *Nature* 2017;542(7641):348–351. doi:10.1038/nature21369.
- 11 Ecker C, Bookheimer SY, Murphy DG. Neuroimaging in autism spectrum disorder: brain structure and function across the lifespan. *Lancet Neurol* 2015;14(11):1121–1134. doi:10.1016/S1474-4422(15)00050-2.
- 12 Jalbrzikowski M, Freedman D, Hegarty CE, et al. Structural Brain Alterations in Youth With Psychosis and Bipolar Spectrum Symptoms. *J Am Acad Child Adolesc Psychiatry* 2019;58(11):1079–1091. doi:10.1016/j.jaac.2018.11.012.

- 13 Skåtun KC, Kaufmann T, Tønnesen S, et al. Global brain connectivity alterations in patients with schizophrenia and bipolar spectrum disorders. *J Psychiatry Neurosci* 2016;41(5):331–341. doi:10.1503/jpn.150159.
- 14 Norman LJ, Carlisi C, Lukito S, et al. Structural and Functional Brain Abnormalities in Attention-Deficit/Hyperactivity Disorder and Obsessive-Compulsive Disorder: A Comparative Meta-analysis. *JAMA Psychiatry* 2016;73(8):815–825. doi:10.1001/jamapsychiatry.2016.0700.
- 15 Marquand AF, Kia SM, Zabihi M, Wolfers T, Buitelaar JK, Beckmann CF. Conceptualizing mental disorders as deviations from normative functioning. *Mol Psychiatry* 2019;24(10):1415–1424. doi:10.1038/s41380-019-0441-1.
- 16 Zabihi M, Oldehinkel M, Wolfers T, et al. Dissecting the Heterogeneous Cortical Anatomy of Autism Spectrum Disorder Using Normative Models. *Biol Psychiatry Cogn Neurosci Neuroimaging* 2019;4(6):567–578. doi:10.1016/j.bpsc.2018.11.013.
- 17 Shaw P. Maps of the Development of the Brain's Functional Architecture: Could They Provide Growth Charts for Psychiatry?. *JAMA Psychiatry* 2016;73(5):445–446. doi:10.1001/jamapsychiatry.2016.0140.
- 18 Ziegler G, Ridgway GR, Dahnke R, Gaser C; Alzheimer's Disease Neuroimaging Initiative. Individualized Gaussian process-based prediction and detection of local and global gray matter abnormalities in elderly subjects. *Neuroimage* 2014;97(100):333–348. doi:10.1016/j.neuroimage.2014.04.018.
- 19 Kessler D, Angstadt M, Sripada C. Growth Charting of Brain Connectivity Networks and the Identification of Attention Impairment in Youth. *JAMA Psychiatry* 2016;73(5):481–489. doi:10.1001/jamapsychiatry.2016.0088.
- 20 Erus G, Battapady H, Satterthwaite TD, et al. Imaging patterns of brain development and their relationship to cognition. *Cereb Cortex* 2015;25(6):1676–1684. doi:10.1093/cercor/bht425.
- 21 Spuling SM, Wurm S, Tesch-Römer C, Huxhold O. Changing predictors of self-rated health: Disentangling age and cohort effects. *Psychol Aging* 2015;30(2):462–474. doi:10.1037/a0039111.
- 22 Sutin AR, Terracciano A, Milaneschi Y, An Y, Ferrucci L, Zonderman AB. The effect of birth cohort on well-being: the legacy of economic hard times. *Psychol Sci* 2013;24(3):379–385. doi:10.1177/0956797612459658.
- 23 Twenge JM, Carter NT, Campbell WK. Age, time period, and birth cohort differences in self-esteem: Reexamining a cohort-sequential longitudinal study. *J Pers Soc Psychol* 2017;112(5):e9–e17. doi:10.1037/pspp0000122.

- 24 Hayward RD, Krause N. Forms of Attrition in a Longitudinal Study of Religion and Health in Older Adults and Implications for Sample Bias. *J Relig Health* 2016;55(1):50–66. doi:10.1007/s10943-014-9949-5.
- 25 Galbraith S, Bowden J, Mander A. Accelerated longitudinal designs: An overview of modelling, power, costs and handling missing data. *Stat Methods Med Res* 2017;26(1):374–398. doi:10.1177/0962280214547150.
- 26 Joiner RJ, Bergeman CS, Wang L. Affective experience across the adult lifespan: An accelerated longitudinal design. *Psychol Aging* 2018;33(3):399–412. doi:10.1037/pag0000257.
- 27 Schaie KW, Willis SL, Caskie GI. The Seattle longitudinal study: relationship between personality and cognition. *Neuropsychol Dev Cogn B Aging Neuropsychol Cogn* 2004;11(2-3):304–324. doi:10.1080/13825580490511134.
- 28 Hülür G, Ram N, Willis SL, Schaie KW, Gerstorf D. Cognitive dedifferentiation with increasing age and proximity of death: Within-person evidence from the Seattle Longitudinal Study. *Psychol Aging* 2015;30(2):311–323. doi:10.1037/a0039260.
- 29 Hülür G, Ram N, Willis SL, Schaie KW, Gerstorf D. Cohort differences in cognitive aging: The role of perceived work environment. *Psychol Aging* 2019;34(8):1040–1054. doi:10.1037/pag0000355.
- 30 Yeo BT, Krienen FM, Sepulcre J, et al. The organization of the human cerebral cortex estimated by intrinsic functional connectivity. *J Neurophysiol* 2011;106(3):1125–1165. doi:10.1152/jn.00338.2011.
- 31 Achenbach TM, Edelbrock CS. Manual for the child behavior checklist and revised child behavior profile. Burlington, VT: University of Vermont, Department of Psychiatry. 1983.
- 32 Liu X C, Liu L Q, Yang J, et al. Establishment of adolescent life event scale and reliability and validity test (in Chinese). *Shangdong Arch Psychiat* 1991;10:15–19.
- 33 Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. *J Health Soc Behav* 1983;24(4):385–396.
- 34 Piers EV. Piers-Harris Childrens Self-Concept Scale: Revised Manual. Los Angeles, CA: Western Psychological Services. 1984.
- 35 La Greca AM, Dandes SK, Wick P, Shaw K, Stone WL. Development of the Social Anxiety Scale for Children: Reliability and concurrent validity. *J Clin Child Psychol* 1988;17(1):84-91. doi:10.1207/s15374424jccp1701_11.
- 36 March JS, Parker JD, Sullivan K, Stallings P, Conners CK. The Multidimensional Anxiety Scale for Children (MASC): factor structure, reliability, and validity. *J Am Acad Child Adolesc Psychiatry* 1997;36(4):554–565. doi:10.1097/00004583-199704000-00019.

- 37 Spielberger CD. Manual for the State-Trait Anxiety Inventory STAI (Form Y). Palo Alto, CA: Consulting Psychologists Press, 1983.
- 38 Kovacs M. Children's depression inventory: Manual. North Tonawanda, NY: Multi-Health Systems, 1992.
- 39 Asher SR, Hymel S, Renshaw PD. Loneliness in children. *Child dev* 1984;55(4):1456-1464.
doi:10.2307/1130015.
- 40 Watson D, Clark LA, Tellegen A. Development and validation of brief measures of positive and negative affect: the PANAS scales. *J Pers Soc Psychol* 1988;54(6):1063–1070. doi:10.1037//0022-3514.54.6.1063.
- 41 Bar-On R, Parker JDA. BarOn emotional quotient inventory: Youth version. Toronto, ON, Canada: Multi-Health system, Incorporated, 2000.
- 42 Eysenck HJ, Eysenck SBG. Manual of Eysenck Personality Questionnaire (Adult and Junior). London: Hodder and Stoughton. 1975.
- 43 Torrance EP. The role of creativity in identification of the gifted and talented. *Gift Child Q* 1984;28(4):153-156. doi:10.1177/001698628402800403.
- 44 Hwang WY, Chen NS, Dung JJ, Yang YL. Multiple representation skills and creativity effects on mathematical problem solving using a multimedia whiteboard system. *Educ Technol Soc* 2007;10:191–212. doi:10.1080/03055690701423333.
- 45 Xue J, Shu H, Li H, Li W, Tian X. The stability of literacy-related cognitive contributions to Chinese character naming and reading fluency. *J Psycholinguist Res* 2013;42(5):433–450. doi:10.1007/s10936-012-9228-0.
- 46 Wechsler D. Wechsler Intelligence Scale for Children–Fourth Edition. San Antonio, TX: Psychological Corporation. 2003.
- 47 Baron IS. Test review: Wechsler Intelligence Scale for Children-Fourth Edition (WISC-IV). *Child Neuropsychol* 2005;11(5):471–475. doi:10.1080/09297040590951587.
- 48 Watkins MW, Smith LG. Long-term stability of the Wechsler Intelligence Scale for Children-Fourth Edition. *Psychol Assess* 2013;25(2):477–483. doi:10.1037/a0031653.
- 49 Zhang H. The revision of WISC-IV Chinese version (in Chinese). *Psychol Sci* 2009;32(5):1177–1179.
- 50 Fan J, McCandliss BD, Sommer T, Raz A, Posner MI. Testing the efficiency and independence of attentional networks. *J Cogn Neurosci* 2002;14(3):340–347. doi:10.1162/089892902317361886.
- 51 Schuch S, Koch I. The role of response selection for inhibition of task sets in task shifting. *J Exp Psychol Hum Percept Perform* 2003;29(1):92–105. doi:10.1037//0096-1523.29.1.92.

- 52 Zhu DF, Wang ZX, Zhang DR, et al. fMRI revealed neural substrate for reversible working memory dysfunction in subclinical hypothyroidism. *Brain* 2006;129:2923–2930. doi:10.1093/brain/awl215.
- 53 Manjón JV, Coupé P. volBrain: An Online MRI Brain Volumetry System. *Front Neuroinform* 2016;10:30. doi:10.3389/fninf.2016.00030.
- 54 van Duijvenvoorde ACK, Westhoff B, de Vos F, Wierenga LM, Crone EA. A three-wave longitudinal study of subcortical-cortical resting-state connectivity in adolescence: Testing age- and puberty-related changes. *Hum Brain Mapp* 2019;40(13):3769–3783. doi:10.1002/hbm.24630.
- 55 Lovibond PF, Lovibond SH. The structure of negative emotional states: comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories. *Behav Res Ther* 1995;33(3):335–343. doi:10.1016/0005-7967(94)00075-u.
- 56 Birmaher B. The validity of depressive disorder in childhood and the development of a self-rating scale: a research report. *J Child Psychol Psychiatry* 1981;22(1):73–88. doi:10.1111/j.1469-7610.1981.tb00533.x.
- 57 Silverman WK, Ginsburg GS, Goedhart AW. Factor structure of the childhood anxiety sensitivity index. *Behav Res Ther* 1999;37(9):903–917. doi:10.1016/s0005-7967(98)00189-2.
- 58 Yang N, He Y, Zhang Z, et al. Chinese Color Nest Project (CCNP): growing up in China. *Chin Sci Bull* 2017;62:3008–3022. In Chinese.
- 59 Wang J, Yang N, Liao W, et al. Dorsal anterior cingulate cortex in typically developing children: Laterality analysis. *Dev Cogn Neurosci* 2015;15:117–129. doi:10.1016/j.dcn.2015.10.002.
- 60 Zuo XN, Anderson JS, Bellec P, et al. An open science resource for establishing reliability and reproducibility in functional connectomics. *Sci Data* 2014;1:140049. doi:10.1038/sdata.2014.49.
- 61 Mao Y, Zuo XN, Ding C, Qiu J. OFC and its connectivity with amygdala as predictors for future social anxiety in adolescents. *Dev Cogn Neurosci* 2020; 44: 100804. doi:10.1016/j.dcn.100804.
- 62 Dong HM, Castellanos FX, Yang N, et al. Generating templates and growth charts for school-aged brain development. *bioRxiv* 2019; 747352. doi:10.1101/747352.

Figures

Figure 1. Accelerated longitudinal design for developmental component in CCNP. It has three waves of measurements including baseline at Wave 1 (purple), followup1 at Wave 2 (blue) and followup2 at Wave 3 (green). The duration between two neighboring waves is designed as 1.25 years for the purpose of avoiding a kid always visited at a same season. There are 12 age cohorts of schoolchildren and each cohort covers one integer age-interval at its baseline (C01: 6-7 years; C02: 7-8 years; ...; C12: 17-18 years). Each cohort contains equal (n) boys and girls, and thus 24n kids in total.

Figure 2. Age and sex distributions of CCNP-SWU and CCNP-CAS samples.

Figure 3. Brain volume growth charts in schoolchildren from CCNP-SWU. Growth charts are generated with their confidence intervals for the intracranial volume (ICV), white matter (WM), cerebrospinal fluid (CSF) and gray matter (GM) in males and females, respectively.

Table 1 Sociodemographic characteristics for CCNP-SWU and CCNP-CAS samples

Domain	CCNP-SWU <i>n</i> =201	CCNP-CAS <i>n</i> =133	χ^2	<i>p</i>
Child characteristics				
Child gender				
Boys	96	76	2.82	0.093
Girls	105	57		
Only child or not				
Only child	140	87	0.83	0.363
Non-only child	54	42		
Family characteristics				
Areas				
Urban areas	146	125	19.05	<0.001
Rural areas	42	6		
Maternal education				
Middle school education or less	81	3	160.43	<0.001
High school education	60	4		
Associate or bachelor's degree	51	73		
Master's or doctorate degree	3	50		
Paternal education				
Middle school education or less	66	1	143.16	<0.001
High school education	55	6		
Associate or bachelor's degree	68	62		
Master's or doctorate degree	5	61		

Table 2 List of measures used in devCCNP across all waves

	Applicable Age Range	Wave 1	Wave 2	Wave 3
Biophysical Measures				
Height, Weight, Head Circumference	-	√	√	√
Cardiovascular (Blood pressure, Pulse)	-	√	√	√
Parent Questionnaires				
Sociodemographic Questionnaire	-	√		
Child Behavior Checklist (CBCL) ³¹	6-16	√	√	√
Child Questionnaires				
Adolescent Self-Rating Life Events Checklist (ASLEC) ³²	13-20	√	√	√
Perceived Stress Scale (PSS) ³³	>10	√	√	√
Piers-Harris Children's Self-concept Scale (PHCSS) ³⁴	6-17	√		
Social Anxiety Scale for Children (SASC) ³⁵	7-16	√	√	√
Multidimensional Anxiety Scale for Children (MASC) ³⁶	8-19	√	√	√
State-Trait Anxiety Inventor (STAI) ³⁷	>6	√	√	√
Children's Depression Inventory (CDI) ³⁸	7-17	√	√	√
Children's Loneliness Scale (CLS) ³⁹	6-12	√	√	√
Positive Affect and Negative Affect Scale (PANAS) ⁴⁰	>6	√	√	√
BarOn Emotional Quotient Inventory Youth Version ⁴¹	7-18	√	√	√
Eysenck Personality Questionnaire (EPQ, Children's Version) ⁴²	7-15	√	√	√
Torrance Test of Creative Thinking (TTCT) ⁴³	-	√		
Williams Creative Test ⁴⁴	-	√	√	√
Literacy Tests (Character Naming and Reading Fluency) ⁴⁵	5-12	√	√	√
Video Game Questionnaire	-	√		
Cognitive Battery Module				
Wechsler Intelligence Scale for Children-IV-Chinese Version (WISC-IV) ⁴⁶⁻⁴⁹	6-16	√	√	√
Attention Network Test (ANT) ⁵⁰	-	√	√	√
Task-Switch Paradigm ⁵¹	-	√	√	√
Digit N-back Working Memory Task ⁵²	-	√	√	√

Table 3 The main acquisition parameters for T1-weighted MRI and rfMRI

	T1-weighted MRI	rfMRI
Sequence type	3D MPRAGE	echo planar imaging, EPI
Inversion time, TI (ms)	900	-
Echo time, TE (ms)	3.02	30
Repetition time, TR (ms)	2600	2500
Flip angle (degrees)	8	80
Bandwidth per voxel (Hz)	180	2240
Number of slices	176	38
Slice phase encoding direction	Anterior to posterior	Anterior to posterior
Slice acquisition order	Sequential ascending	Interleaved ascending
Slice thickness (mm)	1	3
Slice gap (mm)	0.50	0.33
Field of view (mm)	256	216
Acquisition matrix	256×256	72×72
Slice in-plane resolution (mm ²)	1×1	3×3
Acquisition time	8 min 19 s	7 min 45 s

Table 4 Main variables of boys and girls across two age groups at CCNP-SWU baseline

Domain	Younger Group		<i>p</i>	Older Group		<i>p</i>
	Boys <i>n</i> = 64	Girls <i>n</i> = 47		Boys <i>n</i> = 28	Girls <i>n</i> = 53	
Biophysical Measures						
Height (m)	1.39±0.11	1.36±0.09	0.157	1.62±0.10	1.57±0.05	0.022
Weight (kg)	37.51±12.61	31.25±7.63	0.002	55.02±12.29	50.60±6.67	0.090
BMI (kg/m²)	19.09±4.04	16.73±2.48	<0.001	20.18±3.25	20.57±2.68	0.580
Questionnaires						
CBCL Total Scores	25.05±16.26	17.89±12.51	0.016	26.22±20.49	21.06±16.66	0.264
Social Anxiety	4.71±4.24	4.72±3.99	0.989	7.09±3.06	8.83±3.61	0.047
Depression	10.58±6.86	7.98±5.09	0.031	12.06±6.46	13.15±5.18	0.533
EPQ Raw Scores						
Extraversion (E)	17.27±3.45	16.85±4.01	0.560	14.75±6.57	16.23±4.24	0.288
Neuroticism (N)	6.17±4.05	4.17±3.06	0.004	8.43±4.58	9.79±5.04	0.236
Psychoticism (P)	2.83±2.34	1.53±1.37	<0.001	3.04±2.15	2.04±1.63	0.022
Cognitive Battery Module						
WISC-IV Scores						
FSIQ	107.52±10.49	110.11±12.25	0.234	110.04±10.56	117.23±12.48	0.016
VCI	112.17±14.02	115.79±13.77	0.179	120.00±13.98	131.02±16.94	0.007
PRI	105.52±10.64	106.96±12.37	0.512	108.00±13.63	107.32±13.73	0.841
WMI	98.41±10.36	98.11±8.82	0.873	98.08±10.45	101.07±11.92	0.293
PSI	105.02±13.38	107.49±14.75	0.359	99.69±8.00	108.93±15.92	0.002
Brain morphological indexes						
Intracranial Volume (ICV)	1460.69±115.94	1301.07±101.10	<0.001	1463.19±120.86	1354.20±102.60	<0.001
White Matter (WM) Volume	483.53±51.67	433.43±44.21	<0.001	469.01±52.32	455.80±39.85	0.227
Gray Matter (GM) Volume	861.81±65.28	780.54±64.52	<0.001	830.03±70.59	749.99±54.74	<0.001
Cerebrospinal Fluid (CSF) Volume	115.35±37.73	87.10±28.80	<0.001	164.15±50.23	148.41±47.02	0.187

Table 5 Main variables of boys and girls across two age groups at CCNP-CAS baseline

Domain	Younger Group		<i>p</i>	Older Group		<i>p</i>
	Boys	Girls		Boys	Girls	
	<i>n</i> = 66	<i>n</i> = 49		<i>n</i> = 10	<i>n</i> = 8	
Biophysical Measures						
Height (m)	1.36±0.12	1.35±0.14	0.728	1.69±0.14	1.62±0.05	0.193
Weight (kg)	30.77±8.99	29.95±11.60	0.671	58.71±21.39	55.48±7.08	0.662
BMI (kg/m ²)	16.41±2.65	15.93±2.90	0.362	19.95±4.22	21.00±2.09	0.528
Questionnaires						
CBCL Total Scores	25.37±18.10	18.40±17.83	0.046	18.90±8.98	21.71±24.18	0.777
Social Anxiety	3.70±2.90	5.65±5.13	0.035	6.13±5.96	6.14±4.91	0.995
Depression	9.27±6.50	9.21±7.46	0.969	11.60±7.89	10.86±6.94	0.844
EPQ Raw Scores						
Extraversion (E)	19.19±4.16	17.47±3.36	0.069	17.67±3.14	19.20±3.35	0.454
Neuroticism (N)	4.31±5.23	5.76±5.54	0.279	8.00±7.48	7.60±5.90	0.925
Psychoticism (P)	3.38±3.35	2.29±2.75	0.155	4.83±4.36	4.60±5.94	0.942
Cognitive Battery Module						
WISC-IV Scores						
FSIQ	115.60±13.83	119.73±14.75	0.144	116.13±13.78	126.25±17.46	0.296
VCI	117.50±14.05	117.07±18.05	0.890	124.13±22.46	133.00±22.58	0.534
PRI	115.23±14.95	118.31±14.78	0.297	112.38±14.95	123.75±6.65	0.184
WMI	109.83±14.35	113.71±12.18	0.147	104.25±11.17	112.25±21.27	0.402
PSI	100.85±14.81	108.47±16.11	0.014	102.63±10.98	104.00±8.83	0.833

Table 6 The impact of COVID-19 on children's learning and daily life ($N = 46$)

Domain	Not paying attention	Not nervous	A bit nervous	A bit panic	Extremely panic
Nervousness or panic perceived by children when COVID-19 occurred in January 2020	3 (6.52%)	18 (39.13%)	20 (43.48%)	3 (6.52%)	2 (4.35%)
Nervousness or panic perceived by children when COVID-19 spread rapidly	2 (4.35%)	15 (32.61%)	20 (43.48%)	6 (13.04%)	3 (6.52%)
Domain	Decreased dramatically	Decreased slightly	Remained about the same	Increased slightly	Increased dramatically
Children's learning time	6 (13.04%)	18 (39.13%)	10 (21.74%)	9 (19.57%)	3 (6.52%)
Children's learning stress	8 (17.39%)	8 (17.39%)	18 (39.13%)	9 (19.57%)	3 (6.52%)
Children's learning efficiency	8 (17.39%)	19 (41.30%)	10 (21.74%)	6 (13.04%)	3 (6.52%)
Children's learning consciousness	9 (19.57%)	13 (28.26%)	17 (36.96%)	4 (8.70%)	3 (6.52%)
Children's exercise time	19 (41.30%)	9 (19.57%)	11 (23.91%)	2 (4.35%)	5 (10.87%)
Children's fun time	3 (6.52%)	4 (8.70%)	17 (36.96%)	13 (28.26%)	9 (19.57%)
Children's screen time	1 (2.17%)	0 (0%)	4 (8.70%)	10 (21.74%)	31 (67.39%)
Parental involvement in children's learning	3 (6.52%)	1 (2.17%)	21 (45.65%)	11 (23.91%)	10 (21.74%)
Parent-child interaction	3 (6.52%)	4 (8.70%)	22 (47.83%)	11 (23.91%)	6 (13.04%)
Parental conflicts	6 (13.04%)	4 (8.70%)	28 (60.87%)	7 (15.22%)	1 (2.17%)
Parent-child conflicts	8 (17.39%)	4 (8.70%)	23 (50.00%)	10 (21.74%)	1 (2.17%)
Domain	No impact	Slight impact	Moderate impact	Strong impact	Extremely strong impact
Children's diet	26 (56.52%)	10 (21.74%)	6 (13.04%)	1 (2.17%)	3 (6.52%)
Children's sleeping	22 (47.83%)	16 (34.78%)	4 (8.70%)	2 (4.35%)	2 (4.35%)
Family's daily routine	4 (8.70%)	29 (63.04%)	7 (15.22%)	6 (13.04%)	0 (0%)