

Macroeconomic income inequality, brain structure and function, and mental health

Received: 18 February 2025

Accepted: 26 August 2025

Published online: 30 September 2025

 Check for updates

A list of authors and their affiliations appears at the end of the paper

Income inequality, a structural property of societies characterized by the unequal distribution of resources, is associated with adverse mental health outcomes during adolescence, which is a sensitive period of neurodevelopment. While previous research has explored the impact of individual-level socioeconomic factors on brain structure and function, the neurobiological mechanisms linking structural inequality to mental health disparities remain poorly understood. Here, using data from the Adolescent Brain Cognitive Development study, we investigated the associations between state-level income inequality, indexed by the Gini coefficient, and brain structure and functional connectivity in over 8,000 children aged 9–10 years (from 17 states in the USA). We analyzed whole-brain cortical thickness and surface area, and volume and region-specific measures of thickness and surface area, as well as functional connectivity within and between 12 brain networks, controlling for several individual-level and state-level confounders (for example, income, educational attainment, state-level incarceration rate and Medicaid expansion status). Mediation analyses were conducted to test whether brain metrics linked income inequality to mental health outcomes at 6-month and 18-month follow-ups. Higher income inequality was associated with reduced cortical thickness and surface area across widespread brain regions, as well as altered functional connectivity between multiple brain networks. Lower cortical volume and surface area, as well as connectivity between the default mode and dorsal attention networks, mediated the association between higher structural income inequality and greater mental health problems. Our findings reveal income inequality as a unique societal-level determinant of neurodevelopment and mental health, independent of individual socioeconomic status. Policies aimed at reducing inequality and strengthening social cohesion to mitigate its neurobiological and mental health impacts are needed.

Economic inequality, characterized by the unequal distribution of income and wealth in a society, is associated with mental health and wellbeing outcomes beyond the influence of household income^{1–3}. This may be particularly relevant during adolescence—a dynamic period of neurodevelopment when the brain undergoes rapid maturation and many mental health disorders begin to emerge^{4,5}. Research increasingly underscores the link between higher income inequality and a range of adverse mental health outcomes in young people, including elevated

rates of depression, anxiety and behavioral disorders^{6–9}. Inequality-related stressors may contribute to heightened mental health vulnerabilities by shaping neurodevelopmental pathways, particularly those involved in emotion regulation and social cognition. Although numerous studies have examined how individual-level income is associated with brain development^{10,11}, few have considered the broader role of structural income inequality in brain development and mental health. Income inequality has risen worldwide in recent decades¹². Investigating

✉ e-mail: divyangana.rakesh@kcl.ac.uk

whether and how inequality becomes neurobiologically embedded and heightens the risk of psychopathology during adolescence could provide valuable insights. Absolute poverty—typically defined as the inability to meet basic needs and operationalized based on thresholds set by the government and/or economists—has known effects on neurobiology¹⁰. If structural inequality has similar measurable associations, addressing it may gain broader acceptance across political ideologies.

Income inequality, which refers to the disproportionate concentration of income within a small fraction of the population, can fundamentally alter the social environment and is a distinct construct from poverty. While income inequality can exacerbate poverty by concentrating resources among a small proportion of the population, it is a structural characteristic of a society that can influence mental health through unique pathways—such as increased social comparison, which is a fundamental process through which individuals evaluate themselves by comparing their attributes, abilities and achievements to those of others¹³, and reduced social cohesion—not captured by individual income or poverty alone^{1,3}. Inequality fosters relative deprivation, social comparison and perceptions of limited social mobility^{1,3}. This creates conditions that induce chronic stress, a well-established risk factor for psychopathology¹⁴. Although evidence from adolescent samples is limited, biological evidence is aligned with the idea that inequality contributes to increased stress. A study of over 19,000 individuals across four European countries found that C-reactive protein levels, a marker of inflammation, were lowest in more equal societies (for example, Switzerland) and highest in more unequal ones (for example, Portugal)¹⁵. Experimental findings are also consistent with this: Shapiro et al.¹⁶ showed that short-term exposure to inequality triggers physiological stress responses. Increased stress levels could explain the well-established links between inequality and mental health^{1,3,17}.

Stress neurobiology research shows that chronic stress exposure is associated with neural pathways involved in emotion regulation and cognitive control¹⁸, which are relevant for mental health. Extensive research has linked low individual income to altered brain structure and function, such as reduced cortical thickness and surface area and changes in functional connectivity^{19,20}, factors closely associated with mental health²¹. Importantly, the association of individual socioeconomic status (SES) with brain volume has been shown to vary across European countries, with associations being stronger in some countries than others²²—potentially reflecting broader structural factors such as inequality—a hypothesis that remains untested. Apart from a study examining electrophysiological brain dynamics in adults²³ and a few studies examining links of local income disparity with gray matter^{24,25}, the role of structural income inequality in shaping brain structure and function and, crucially, behavior outcomes in youth, remains unexplored. This gap underscores the critical need to explore how income inequality may influence neurobiology and mental health, independent of individual income.

In this study, we leverage population-based data from the Adolescent Brain Cognitive Development (ABCD) study to assess associations between state-level income inequality, indexed by the Gini coefficient, and brain structure and functional connectivity in children aged 9–10 years. Specifically, we examine the associations of inequality with cortical thickness and surface area, analyzing both whole-brain and region-specific measures, as well as functional connectivity within and between 12 brain networks. Finally, we evaluated whether any implicated brain structure or connectivity metrics mediated the relationship between state-level inequality and mental health 6 and 18 months later, aiming to elucidate the pathways through which structural inequality contributes to mental health disparities. Overall, the present study aims to examine the neural mechanisms through which income inequality is associated with adolescent mental health. By examining neurobiological pathways, we aim to better understand how inequality contributes to mental health disparities and inform potential interventions.

Table 1 | Demographic information

Characteristic	<i>n</i> or mean ± s.d.
No. of subjects (<i>n</i> female)	10,071 (4,871)
Non-Hispanic white (<i>n</i>)	5,591
Age (years)	9.92 ± 0.62
Gini coefficient (2017)	0.47 ± 0.02
Income-to-needs ratio	3.65 ± 2.4
Parent educational attainment (years)	15.28 ± 2.52
Parent mental health problems	21.16 ± 17.91
TANF (US\$)	530.38 ± 173.99
Incarceration rate (per 100,000)	689.42 ± 219.9
Total mental health problems	6.8 ± 5.41
Mean FDR	0.23 ± 0.21

TANF is a monthly temporary assistance for needy families.

Results

The sample consisted of 10,071 children (4,871 female; 56% non-Hispanic white; Table 1) from across 17 states in the USA ($N = 8,412$ for functional connectivity after excluding unusable scans). We used linear mixed-effects models to examine associations of income inequality (operationalized as the Gini coefficient) with average cortical thickness, total cortical volume, total surface area, regional cortical thickness ($n = 34$ variables) and surface area ($n = 34$ variables), and within- and between-network connectivity ($n = 78$ variables). Our analyses control for multiple key covariates, including participant age and sex assigned at birth, scanner model, in-scanner motion (for connectivity variables), household income-to-needs ratio, parental educational attainment, parent mental health and state-level variables including incarceration rate, Temporary Assistance for Needy Families (TANF) and Medicaid expansion status. We also accounted for the nested family structure. These covariates were included to isolate the unique contribution of structural inequality to brain and mental health outcomes. False discovery rate (FDR) corrections ($P_{\text{FDR}} < 0.05$) were applied within cortical thickness, surface area and functional connectivity analyses.

Inequality and brain structure

Higher income inequality was significantly associated with lower overall cortical volume ($\beta = -2.93$, s.e.m. 0.49, $t = -6.04$, $P < 0.001$), average cortical thickness ($\beta = -1.33$, s.e.m. 0.55, $t = -2.41$, $P = 0.016$) and total surface area ($\beta = -2.99$, s.e.m. 0.49, $t = -6.06$, $P < 0.001$; Fig. 1a–c). Further, higher income inequality was associated with widespread patterns of lower cortical thickness (Fig. 1d and Table 2) and surface area (Fig. 1e and Table 2) across frontal, temporal, parietal and occipital regions ($n = 48$ variables). For a few regions, inequality was associated with higher thickness and surface area, including for the bank of superior temporal sulcus (STS) and supramarginal thickness, and parahippocampal area. The complete model output for all associations is available in Supplementary Table 2.

In sensitivity analyses, we adjusted for the average cortical thickness for thickness models and the total surface area in surface area models (Supplementary Table 4). Briefly, thickness results remained largely unchanged (22 out of 24 variables were still significant), whereas some surface area results were no longer significant (12 out of 22 variables remained significant). This suggests that inequality is associated with regional structure, over and above global effects.

Inequality and brain connectivity

Similarly, we found a significant relationship between inequality and several ($n = 46$) connections between and within functional networks. Higher inequality was associated with alterations in connectivity within

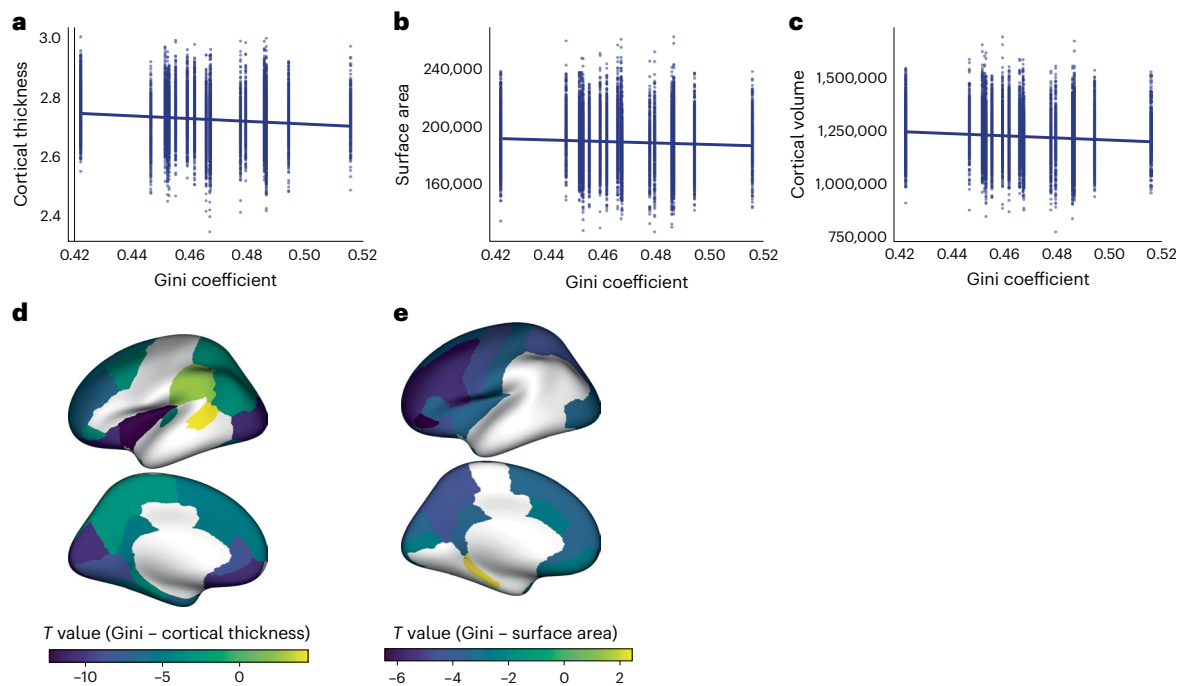


Fig. 1 | Relationship between Gini coefficient and brain structure. **a–c**, The association between Gini coefficient and average cortical thickness (**a**), total surface area (**b**) and total cortical volume (**c**). **d,e**, The *t*-statistic values from

linear mixed-effects models for significant associations between Gini coefficient and regional cortical thickness variables (**d**) and surface area variables (**e**). Only areas with significant associations are depicted in the figure.

and between networks involved in higher-order cognition and attention, such as the cingulo-opercular network (CON), dorsal attention network (DAN), default mode network (DMN), frontoparietal network (FPN) and ventral attention network (VAN). Inequality was also linked to connectivity in networks related to sensory and motor functions, including the auditory network (AN), sensorimotor network (SMN) and visual network (VN) (Fig. 2 and Table 3). The complete model output for all associations is available in Supplementary Table 3.

Additionally, to directly assess whether income inequality explained additional variance beyond individual-level SES, we compared models with and without the Gini coefficient for a few representative models (global brain measures and the first two significant connectivity variables). We found that including income inequality significantly improved the model fit for all brain outcomes tested and resulted in small but consistent increases in marginal R^2 when the Gini coefficient was added to the models (Supplementary Table 5). This suggests that the Gini coefficient explains unique variance above individual-level SES and other covariates in the model. The main effects of parent income to needs and educational attainment are presented in Supplementary Tables 11 and 12.

Inequality, brain structure and connectivity and mental health

We then leveraged structural equation modeling, including the same covariates as the linear mixed-effects models, to test the role of the implicated brain variables as mediators of the association of inequality with total mental health problems at 6 months and 18 months later. The FDR was used to adjust for multiple comparisons within each set of analyses. Fit indices indicated acceptable to excellent fit for the structure models (root mean square error of approximation: mean 0.013, s.d. 0.004; comparative fit index: mean 0.997, s.d. 0.002; Tucker–Lewis index: mean 0.97, s.d. 0.023) and connectivity models (root mean square error of approximation: mean 0.016, s.d. 0.003; comparative fit index: mean 0.993, s.d. 0.004; Tucker–Lewis index: mean 0.93, s.d. 0.038). There was a significant total effect of inequality on mental health at the 18-month follow-up but not the 6-month follow-up (Supplementary Tables 6–10). We found a significant indirect effect

for total surface area and cortical volume, and connectivity between the DAN and DMN for the association between inequality and total mental health problems at both 6 months and 18 months later. Specifically, higher inequality was associated with lower surface area and volume and higher (that is, less negative) DMN–DAN connectivity, which were in turn associated with higher mental health problems (Fig. 3 and results for 6 months provided in the Supplementary Information). These results were significant even when total mental health problems at baseline were accounted for in sensitivity analyses (see Supplementary Information for the model output).

Discussion

The present study provides new evidence on the neural mechanisms through which structural income inequality contributes to psychopathology. Our findings show that structural inequality is associated with measurable differences in brain structure and functional connectivity, which have implications for subsequent mental health outcomes during early adolescence. Higher income inequality was associated with reduced cortical thickness and surface area across widespread brain regions spanning all four lobes of the brain, which is in line with our whole-brain findings. The present study also revealed that structural income inequality was associated with alterations in functional connectivity within and between multiple cortical brain networks, including both higher-order cognitive and sensorimotor systems. These findings of widespread associations between inequality and brain structure and connectivity extend prior research on the impact of individual socioeconomic factors^{10,11,19,20,26–32} on brain development by highlighting the role of structural income inequality as a unique societal-level determinant that operates independently of individual-level SES. Importantly, total brain volume and surface area, as well as connectivity between the DMN and DAN, mediated links between inequality and mental health 6 months and 18 months later.

Given the evidence showing that inequality fundamentally alters the social environment—resulting in lower levels of social cohesion, trust and social capital, as well as higher levels of social comparison¹³—and the crucial role that social relationships play in our health

Table 2 | Inequality and regional cortical thickness and surface area

Brain region	β	s.e.m.	t	P	P _{FDR}	Semi-partial R ²
Bank of superior temporal sulcus thickness	0.053	0.012	4.357	<0.001	<0.001	0.0019
Caudal anterior cingulate thickness	-0.064	0.012	-5.253	<0.001	<0.001	0.0030
Caudal middle-frontal thickness	-0.046	0.012	-3.799	<0.001	<0.001	0.0016
Cuneus thickness	-0.132	0.012	-11.094	<0.001	<0.001	0.0124
Entorhinal thickness	-0.075	0.012	-6.284	<0.001	<0.001	0.0042
Fusiform thickness	-0.051	0.012	-4.197	<0.001	<0.001	0.0019
Inferior parietal thickness	-0.038	0.012	-3.276	0.001	0.002	0.0012
Isthmuscingulate thickness	-0.067	0.012	-5.436	<0.001	<0.001	0.0031
Lateral occipital thickness	-0.108	0.011	-10.087	<0.001	<0.001	0.0095
Lateral orbitofrontal thickness	-0.144	0.012	-11.975	<0.001	<0.001	0.0147
Lingual thickness	-0.109	0.012	-9.244	<0.001	<0.001	0.0083
Medial orbitofrontal thickness	-0.121	0.012	-10.228	<0.001	<0.001	0.0099
Parahippocampal thickness	-0.036	0.012	-3.010	0.003	0.004	0.0010
Paracentral thickness	-0.031	0.012	-2.612	0.009	0.013	0.0007
Parsorbitalis thickness	-0.034	0.012	-2.831	0.005	0.007	0.0007
Pericalcarine thickness	-0.122	0.012	-10.296	<0.001	<0.001	0.0111
Precentral thickness	-0.025	0.012	-2.120	0.034	0.045	0.0006
Precuneus thickness	-0.040	0.012	-3.296	<0.001	0.002	0.0011
Rostral anterior cingulate thickness	-0.103	0.012	-8.756	<0.001	<0.001	0.0078
Rostral middle-frontal thickness	-0.094	0.012	-7.780	<0.001	<0.001	0.0065
Superior frontal thickness	-0.063	0.012	-5.174	<0.001	<0.001	0.0028
Superior parietal thickness	-0.044	0.012	-3.648	<0.001	<0.001	0.0014
Supramarginal thickness	0.029	0.011	2.545	0.011	0.015	0.0004
Temporal pole thickness	-0.043	0.012	-3.580	<0.001	<0.001	0.0014
Transverse temporal thickness	-0.038	0.012	-3.147	0.002	0.003	0.0009
Insula thickness	-0.146	0.012	-12.256	<0.001	<0.001	0.0152
Caudal anterior cingulate area	-0.031	0.012	-2.593	0.01	0.017	0.0007
Caudal middle-frontal area	-0.058	0.012	-5.033	<0.001	<0.001	0.0023
Cuneus area	-0.043	0.012	-3.609	<0.001	<0.001	0.0012
Isthmuscingulate area	-0.036	0.012	-3.144	0.002	0.003	0.0009
Lateral occipital area	-0.037	0.011	-3.353	<0.001	0.002	0.0009
Lateral orbitofrontal area	-0.046	0.011	-4.073	<0.001	<0.001	0.0015
Medial orbitofrontal area	-0.032	0.011	-2.874	0.004	0.008	0.0006
Parahippocampal area	0.028	0.012	2.377	0.017	0.028	0.0005
Parsopercularis area	-0.059	0.012	-5.061	<0.001	<0.001	0.0025
Parsorbitalis area	-0.069	0.011	-6.191	<0.001	<0.001	0.0035
Parstriangularis area	-0.041	0.011	-3.580	<0.001	<0.001	0.0012
Pericalcarine area	-0.032	0.012	-2.582	0.01	0.017	0.0007
Postcentral area	-0.041	0.011	-3.683	<0.001	<0.001	0.0010
Precentral area	-0.045	0.011	-4.143	<0.001	<0.001	0.0013
Precuneus area	-0.048	0.011	-4.212	<0.001	<0.001	0.0017
Rostral anterior cingulate area	-0.039	0.012	-3.338	<0.001	0.002	0.0011
Rostral middle-frontal area	-0.060	0.011	-5.488	<0.001	<0.001	0.0026
Superior frontal area	-0.044	0.011	-3.939	<0.001	<0.001	0.0014
Superior parietal area	-0.047	0.012	-4.097	<0.001	<0.001	0.0014
Frontal pole area	-0.072	0.011	-6.399	<0.001	<0.001	0.0036
Temporal pole area	-0.025	0.011	-2.200	0.028	0.043	0.0005
Insula area	-0.038	0.011	-3.358	<0.001	0.002	0.0011

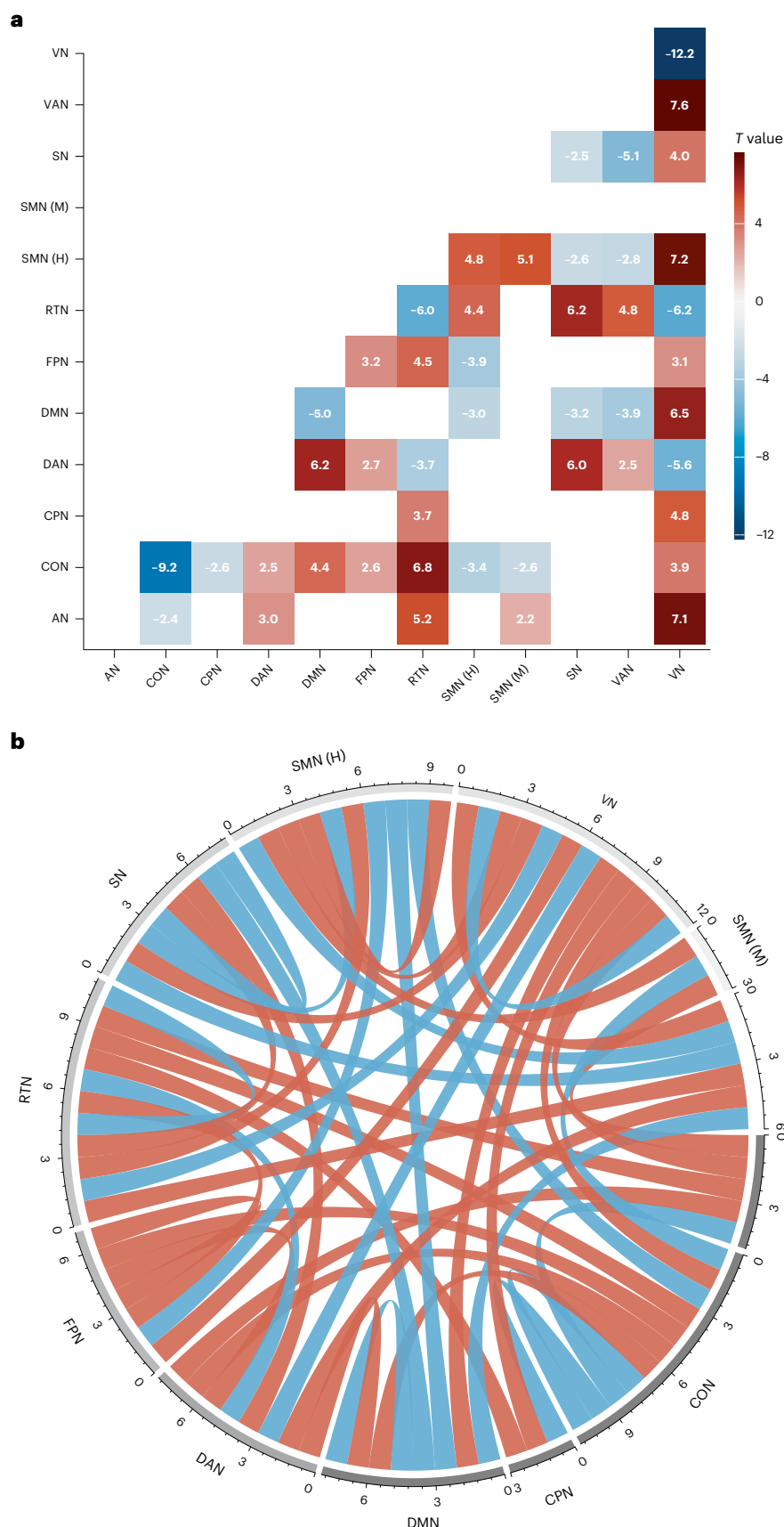


Fig. 2 | Relationship between Gini coefficient and resting-state functional connectivity. **a**, A heat map of the t -statistic values (from linear mixed models) of the relationship between Gini coefficient and significant connectivity variables after correction for multiple comparisons ($n = 46$). Only the bottom half of

the matrix has been displayed for ease of readability. **b**, A chord diagram for significant connections. Red and blue chords represent positive and negative associations, respectively.

Table 3 | Inequality and functional connectivity

Connectivity variable	β	s.e.m.	t	P	P_{FDR}	Semi-partial R^2
AN to CON	-0.031	0.013	-2.385	0.017	0.03	0.0007
CON to CON	-0.115	0.013	-9.158	<0.001	<0.001	0.0101
CPN to CON	-0.034	0.013	-2.610	0.009	0.018	0.0009
CON to DMN	0.056	0.013	4.382	<0.001	<0.001	0.0024
DMN to DMN	-0.063	0.012	-5.033	<0.001	<0.001	0.0033
DAN to DMN	0.078	0.012	6.246	<0.001	<0.001	0.0048
AN to DAN	0.039	0.013	3.010	0.003	0.006	0.0011
CON to DAN	0.034	0.013	2.532	0.011	0.021	0.0007
CON to FPN	0.034	0.013	2.571	0.01	0.019	0.0008
DAN to FPN	0.035	0.013	2.686	0.007	0.015	0.0009
FPN to FPN	0.041	0.013	3.163	0.002	0.004	0.0010
AN to RTN	0.066	0.013	5.156	<0.001	<0.001	0.0032
CON to RTN	0.087	0.013	6.765	<0.001	<0.001	0.0055
CPN to RTN	0.049	0.013	3.667	<0.001	<0.001	0.0016
DAN to RTN	-0.049	0.013	-3.719	<0.001	<0.001	0.0018
FPN to RTN	0.059	0.013	4.482	<0.001	<0.001	0.0026
RTN to RTN	-0.076	0.013	-5.986	<0.001	<0.001	0.0046
DMN to SN	-0.042	0.013	-3.168	0.002	0.004	0.0012
DAN to SN	0.079	0.013	6.020	<0.001	<0.001	0.0044
RTN to SN	0.080	0.013	6.153	<0.001	<0.001	0.0047
SN to SN	-0.033	0.013	-2.531	0.011	0.021	0.0008
CON to SMN (H)	-0.045	0.013	-3.406	<0.001	0.002	0.0015
DMN to SMN (H)	-0.039	0.013	-3.020	0.003	0.006	0.0011
FPN to SMN (H)	-0.051	0.013	-3.902	<0.001	<0.001	0.0018
RTN to SMN (H)	0.058	0.013	4.439	<0.001	<0.001	0.0024
SN to SMN (H)	-0.034	0.013	-2.615	0.009	0.018	0.0008
SMN (H) to SMN (H)	0.062	0.013	4.793	<0.001	<0.001	0.0026
AN to SMN (M)	0.028	0.013	2.201	0.028	0.047	0.0005
CON to SMN (M)	-0.035	0.013	-2.641	0.008	0.017	0.0009
SMN (H) to SMN (M)	0.065	0.013	5.061	<0.001	<0.001	0.0030
DMN to VAN	-0.050	0.013	-3.865	<0.001	<0.001	0.0020
DAN to VAN	0.032	0.013	2.452	0.014	0.025	0.0008
RTN to VAN	0.062	0.013	4.797	<0.001	<0.001	0.0029
SN to VAN	-0.066	0.013	-5.093	<0.001	<0.001	0.0031
SMN (H) to VAN	-0.037	0.013	-2.813	0.005	0.011	0.0010
VN to VAN	0.096	0.013	7.580	<0.001	<0.001	0.0068
AN to VN	0.092	0.013	7.060	<0.001	<0.001	0.0062
CON to VN	0.051	0.013	3.881	<0.001	<0.001	0.0019
CPN to VN	0.064	0.013	4.827	<0.001	<0.001	0.0029
DMN to VN	0.081	0.013	6.452	<0.001	<0.001	0.0050
DAN to VN	-0.073	0.013	-5.590	<0.001	<0.001	0.0038
FPN to VN	0.040	0.013	3.102	0.002	0.005	0.0013
RTN to VN	-0.080	0.013	-6.156	<0.001	<0.001	0.0046
SN to VN	0.052	0.013	4.001	<0.001	<0.001	0.0019
SMN (H) to VN	0.093	0.013	7.188	<0.001	<0.001	0.0064
VN to VN	-0.148	0.012	-12.229	<0.001	<0.001	0.0165

Within-network connectivity is signified by the name of the network repeated twice (for example, VN to VN).

and wellbeing³³, it is unsurprising that inequality is associated with higher stress levels³⁴. While not directly measured in our study, we speculate that these social changes and increased stress levels probably

contribute to the profound impacts on the brain outcomes in children observed in our study. We discuss these ideas further below.

A key finding of this study is that youth living in states with higher income inequality have, on average, lower surface area and thickness across widespread regions in the brain, spanning the frontal, parietal, temporal and occipital lobes. The implicated regions support a range of functions including executive function, emotion regulation, reward processing, attention and sensory integration, socioemotional processing and visual processing^{35–40}. Inequality was also associated with differences in functional connectivity within and between numerous functional systems involved in both sensorimotor and higher-order cognitive functions. Together, these findings indicate that income inequality may shape brain development in a diffuse and pervasive manner, potentially influencing a wide range of cognitive, emotional and behavioral outcomes in children and adolescents. Importantly, our findings are consistent with and extend prior work on individual SES showing similarly widespread associations of SES with brain structure and connectivity^{19,20,29} and associations between SES and a range of outcomes in children^{41–44}. We speculate that such widespread patterns may be a consequence of inequality-related chronic stress. While both household income and inequality generate chronic stress, with potential biological consequences, they may do so via different psychosocial pathways. For instance, absolute poverty may trigger stress via material deprivation and income insecurity, while inequality may amplify status anxiety and social comparison as inequality heightens the salience of socioeconomic hierarchies, leading to increased upward social comparisons and feelings of inadequacy^{3,45,46}. Social comparison—a psychological process through which individuals evaluate themselves relative to others¹³—is heightened in unequal societies where status hierarchies are more salient. This fosters upward comparison and contributes to status anxiety, a persistent worry about one's social standing⁴⁷. According to the status anxiety hypothesis, individuals in more unequal societies may experience greater stress about their social rank—even if they are not economically deprived. Supporting this, relative income (for example, income rank) is often a stronger predictor of psychological distress and life satisfaction than absolute income, particularly in high-inequality areas^{48–51}. Experimental and observational studies have also linked higher inequality to increased materialism, status seeking and conspicuous consumption⁵². For children and adolescents, who are particularly sensitive to social comparison⁵³, this may translate into a heightened preoccupation with peer status, social rejection and negative self-evaluation⁵⁴, all of which lead to higher stress levels⁵⁵. Growing up in the context of higher income inequality is also associated with greater victimization in adolescence⁵⁶.

Further, inequality may also contribute to higher levels of adolescent stress indirectly. For example, ample evidence shows that inequality degrades mental health in adults^{1,3,17}, and poor parent mental health is associated with greater family conflict and reduced parental support⁵⁷, both of which may contribute to adolescent stress. Biological and experimental evidence is in line with the idea that inequality contributes to stress^{15,16}. Experiencing chronic stress may disrupt the hypothalamic–pituitary–adrenal axis and elevate cortisol levels, noradrenaline and adrenaline⁵⁸. While short-term stress responses may be protective, chronic stress places strain on the brain and other organ systems⁵⁸. In the brain, chronic stress may disrupt synaptic homeostasis by impairing the balance between synapse formation and pruning, driven in part by prolonged glucocorticoid exposure⁵⁹. This can lead to widespread synaptic loss and reduced synaptic density⁵⁹, which may contribute to the widespread connectivity alterations in large-scale functional networks observed in the present study. Additionally, chronic stress can reduce dendritic arborization complexity, potentially driving reductions in cortical volume and thickness^{60,61}. Further research is needed to test these pathways directly.

Income inequality not only exacerbates chronic stress but may also deprive adolescents of the protective effects of strong social

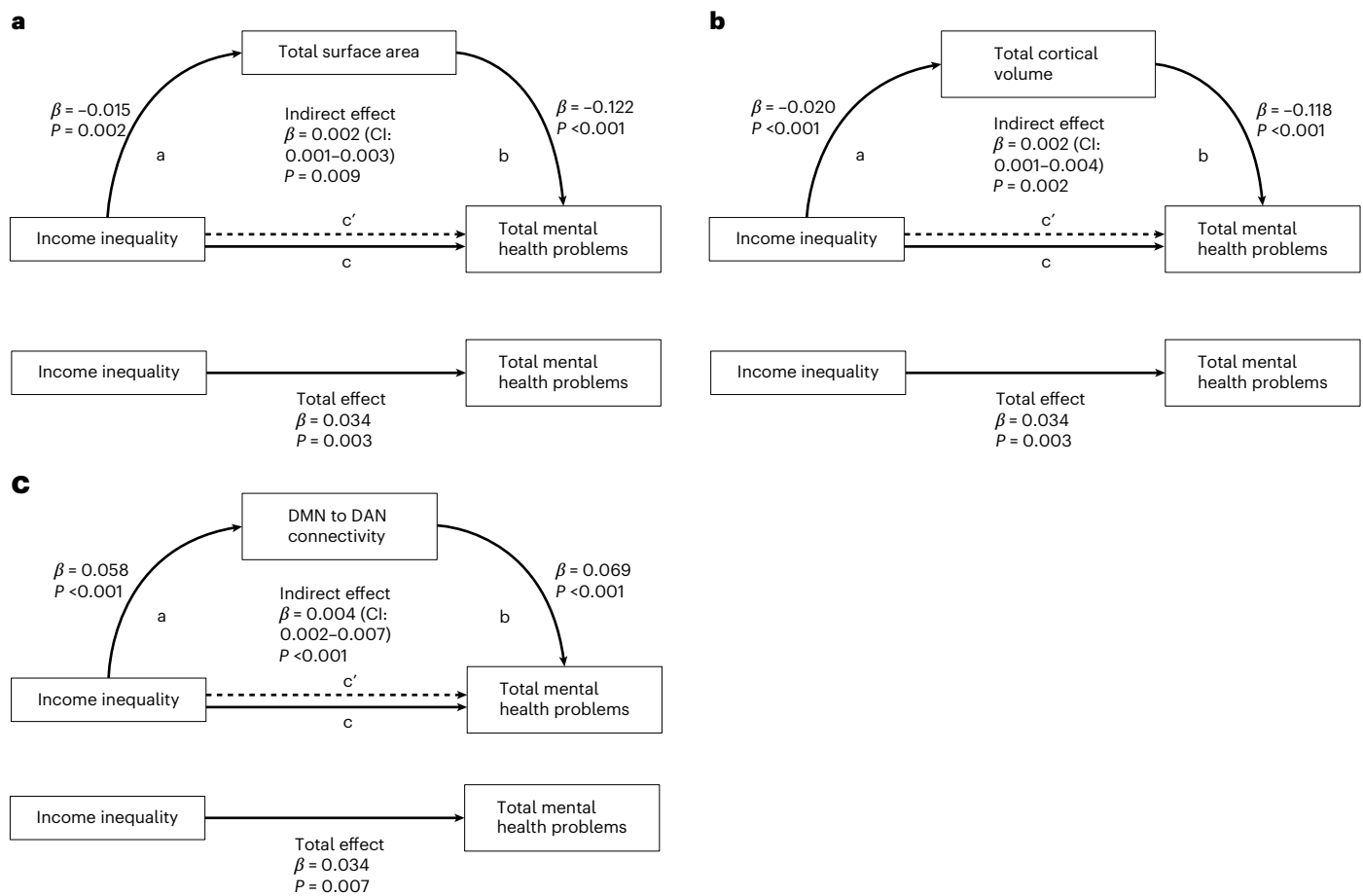


Fig. 3 | Neural mediators of the link between income inequality and mental health problems 18 months later. a–c. The neural mediators between income inequality and total mental health problems for total surface area (a), total cortical volume (b) and DMN to DAN connectivity (c).

ties, such as emotional support and shared resources, which may buffer these associations. For example, income inequality erodes social capital—defined as trust, networks and norms of reciprocity within communities—which is critical for fostering social cohesion and mental wellbeing⁶². Communities with high levels of inequality tend to experience greater segregation, reduced civic participation and weaker social networks, all of which can amplify feelings of isolation and mistrust⁶³, contributing to the maintenance or exacerbation of chronic stress. This chronic stress may ultimately influence brain structure and function as described earlier.

Another central finding of our study is that whole-brain cortical surface area and cortical volume, and connectivity between the DMN and DAN, mediated the association between income inequality and mental health problems. These results are consistent with prior work showing that the DMN and DAN are involved in emotion regulation, and disruptions in their connectivity have been associated with various mental health disorders^{64–66}. Furthermore, our findings build on prior research showing associations between reduced cortical volume and surface area and various forms of psychopathology (for example, depression, anxiety and externalizing disorders)^{67–71}. Our results suggest that income inequality may contribute to these associations by shaping neurodevelopment, although further research is needed to disentangle the mechanisms underlying these links. Notably, only a small subset of brain variables associated with income inequality mediated these links, leaving the exact contribution of these neural alterations to behavioral outcomes uncertain. We speculate that it is possible such effects would be evident in outcomes not examined in the present study—such as emotion regulation and cognitive function—over

over a longer developmental timespan, such as late adolescence or young adulthood.

Implications for policy and intervention

Our findings suggest that structural income inequality is associated with neurobiological differences, even after accounting for absolute income and poverty. These brain differences, in turn, help explain links to adverse mental health outcomes. As such, structural inequality should be considered a harmful social determinant with clear biological sequelae, meriting attention in efforts to improve population mental health, regardless of political ideology. In other words, addressing absolute poverty alone is likely to be inadequate and policies aimed at reducing inequality, improving social capital and cohesion, and mitigating the effects of social comparison are needed. We have discussed possible interventions in depth in a recent paper (see ref. 3 for a review). Briefly, economic reform including progressive taxation, increased social safety nets and universal healthcare are needed to alleviate the stressors that disproportionately affect children in more unequal societies³. Further, efforts to promote social capital, such as community-building initiatives and investments in public infrastructure, could mitigate the detrimental effects of inequality on mental health by fostering trust and social cohesion^{1–3}. Interventions targeting status anxiety, such as programs promoting emotion regulation, social connectedness and feelings of self-worth, may help reduce the salience of social comparison among adolescents. In particular, schools could play a critical role by creating inclusive environments that minimize socioeconomic disparities and emphasize belonging and connectedness to promote mental health in young people⁷². Given our findings

of links between structural inequality and brain structure and function, and evidence suggesting that inequality is associated with worse outcomes for everyone, even those not struggling financially^{2,17}, such measures are urgently needed.

Limitations and future directions

Despite its strengths, this study has several limitations: (1) while the Gini coefficient we used provides a robust measure of income inequality, it did not capture other inequities, such as wealth disparities or access to healthy nutrition, that may also influence brain development. Although we relied on the Gini coefficient, other indices, such as the proportion of total income earned, Atkinson index, income ratios or the Robin Hood index may offer complementary insights⁷³. For instance, the Theil index allows for the decomposition of inequality into between-group and within-group components^{74,75} (for example, between race versus within race), offering a more granular understanding of how different dimensions of inequality may relate to brain development. Future work could benefit from incorporating multiple measures of inequality to provide a more nuanced understanding of how different aspects of income distribution may differentially relate to brain outcomes. (2) Our findings are correlational. Experimental studies (for example, from behavioral economics) and longitudinal neuroimaging research, ideally grounded in causal inference frameworks, are needed to establish causal pathways. (3) While we speculate that the brain differences observed in our study may be due to the chronic stress associated with inequality, we did not measure perceived stress or biological markers of stress (for example, cortisol levels) directly. As such, any interpretations should be made with caution. Future work should test whether both self-reported and physiological indicators of stress mediate links between inequality and brain structure and function. Relatedly, stress and its neurodevelopmental consequences caused by structural factors such as inequality, and individual-level factors including poverty are not easily dissociable. (4) We chose to focus on state-level income inequality, which captures broader macrosocial factors and has been underexplored in developmental cognitive neuroscience. Future work should test the unique, distinct and joint effects of local inequality versus state inequality to better understand how different social contexts contribute to developmental outcomes⁷⁶. (5) In our dataset, 21 sites span only 17 states, with 15 out of 17 states represented by a single site. This precluded us from including site as a random effect without compromising our ability to estimate state-level associations. While we controlled for scanner manufacturer and model, future research with broader geographic sampling and multiple sites per state could better disentangle site-specific variability from state-level predictors of brain structure and function. (6) The ABCD study does not include data from states with the highest poverty rates in the USA (for example, Mississippi, Louisiana and New Mexico). These findings therefore may not be generalizable to structurally disadvantaged states. However, our findings of inequality being associated with brain structure and function even in states with comparatively lower levels of poverty highlights the relevance of state-level contextual factors beyond absolute deprivation. (7) Averaging left and right hemisphere values may have masked potential hemispheric differences. This could be explored in future work with specific hypotheses. (8) This study examined whole-brain patterns and overall psychopathology and cannot comment on associations relevant for specific mental health domains. Future work should investigate more specific pathways to delineate risk and resilience mechanisms for distinct mental health domains. (9) We did not examine the role of residential segregation and homogeneity, which may influence children's development through shared pathways with inequality such as low social capital, fragmentation, exclusion and lack of belonging^{76–78}. Future work that examines the extent to which these exposures share common versus distinct pathways is needed. Further, it would also be valuable to examine whether racial homogeneity within a state or region influences the strength of the association between

inequality and children's outcomes in future work. Future research should examine the environmental and biological mechanisms linking inequality to brain structure and connectivity, such as neighborhood cohesion, prosocial behavior, parental stress, family conflict and stress pathways. Finally, while effect sizes are small, small effects can accumulate and have meaningful effects at the population level⁷⁹.

Conclusions

This study advances our understanding of how income inequality shapes child brain structure and function and mental health. Our findings highlight how structural inequality becomes biologically embedded to influence mental health. Addressing inequality at the societal level is essential to fostering environments that support healthy neurodevelopment and mental wellbeing for all children.

Methods

Participants

This study utilized data from the ABCD study (release 5.1), an ongoing large-scale, multisite, longitudinal research study from the USA. Baseline data were collected from September 2017 to August 2018. The present study used neuroimaging data from the baseline time point and self-reported mental health from 6-month (when self-reported mental health was first assessed⁸⁰) and 18-month (the last time point before the COVID-19 pandemic) follow-ups. The ABCD study aims to comprehensively track psychological and neurobiological development from late childhood to late adolescence. The study is conducted across 21 research sites (from 17 states). The participating sites cover about 20% of the 9–10-year-old population in the USA. Schools within a 50-mile radius of each site—across public, charter and private institutions—were selected using probability sampling within the 21 defined catchment areas (see ref. 81 for more information). Participants took part in clinical interviews, neuroimaging sessions, neurocognitive testing and completed various surveys. Written informed consent was obtained from parents or caregivers, and children provided assent. All participant rights were safeguarded by local institutional review boards. After excluding participants based on imaging quality and missing data on covariates, 10,071 children remained in the final analysis sample for brain structure and 8,412 for functional connectivity. Detailed demographic information for the sample has been provided below.

Measures

Inequality. We focused on structural inequality at the state level, which is intended to capture broader, system-level socioeconomic stratification—the policies, norms and institutional frameworks that shape income distribution at a population level. Inequality at the state level was assessed using the Gini coefficient, one of the most widely used measures of income inequality^{2,34,73}, making it comparable with previous research. The Gini coefficient quantifies the extent to which income distribution among individuals or households within a population deviates from perfect equality. Values range from 0 (complete equality, where everyone has the same income) to 1 (complete inequality, where one person has all the income and everyone else has none). It is typically calculated from the Lorenz curve, which plots the cumulative proportion of income earned against the cumulative proportion of the population, ranked from poorest to richest. The coefficient represents the area between the Lorenz curve and the line of perfect equality, divided by the total area under the line of perfect equality. State-level Gini coefficient values were acquired for the year 2017 from the US Census Bureau. Importantly, larger geographic units, such as states or nations, offer more consistent and robust findings on the relationship between inequality and various outcomes than inequality at a smaller geographical scale such as the neighborhood^{34,82}. For example, Wilkinson and Pickett⁸² found that the proportion of analyses reporting a supportive association between income inequality and health

outcomes was 83% among international studies, 73% in studies using large subnational units (for example, states) and only 45% in studies using small areas such as neighborhoods. Similarly, Hsieh and Pugh⁸³ concluded that consistent associations between income inequality and violent crime were found in studies using national or state-level data, but not in studies using smaller geographic units³⁴. This pattern has been echoed in later multilevel meta-analyses^{34,84}, supporting the idea that state-level measures more reliably capture meaningful variation in inequality. Further, inequality is a relatively stable construct and can be assumed to precede neurobiological changes temporally. More importantly, brain structure and function cannot influence state-level income inequality, making reverse causality a non-issue in this context. We report associations between the state-level Gini coefficient and state-level median income and racial homogeneity (percentage white) and income-to-needs ratio (averaged for individuals in the state) in Supplementary Table 1.

Mental health. We utilized youth-reported symptoms of psychopathology on the Brief Problem Monitor, which assesses symptoms over the past week using 19 items drawn from the Child Behavior Checklist, Teacher's Report Form and Youth Self-Report^{85,86}. Items are rated as 0 ('not true'), 1 ('somewhat true') or 2 ('very true') and are categorized into three domains (attention, internalizing and externalizing). We utilized the total problems raw score, which included scores on internalizing, externalizing and attention symptoms. Internal consistency in our sample was high (Cronbach's $\alpha = 0.85$), indicating good reliability. The present study used data from two time points: the 6-month (the time point at which self-reported mental health was first assessed) and 18-month follow-up (which was the last timepoint of complete data before the pandemic). This was done to examine whether brain structure and connectivity mediated associations between inequality and mental health both in the short term and over a longer period, thereby testing the robustness and persistence of any observed effects.

Race and ethnicity. Race and ethnicity data were collected through two questions: (1) "What race do you consider the child to be?" (Asian, Black or African American, white) and (2) "Is the child of Hispanic/Latino/Latina descent?" (yes or no). Responses were categorized into five groups: Asian, Hispanic, non-Hispanic Black, non-Hispanic white and multiracial/multiethnic, and this classification is used in the study's data releases. This variable was binarized into non-Hispanic white and non-white.

Covariates. Models were adjusted for a range of theoretically motivated covariates⁸⁷. The mean educational attainment of parents/caregivers (in years) was calculated by averaging the education levels of both parents/caregivers. In cases where data for both were unavailable, the information for the available parent or caregiver was used. The income-to-needs ratio was determined by dividing the median value of the household's income band (as defined by the ABCD study) by the federal poverty line for the respective household size. Parental mental health was the (responding) parent's total raw score on the self-reported Adult Self Report instrument of broad psychopathology. Additionally, we accounted for the average TANF benefit at the state level^{88,89} as low assistance for needy families can exacerbate inequality as well as increase individual-level stress, which in turn can influence neurodevelopment. Further, we covaried for incarceration rate⁹⁰ (that is, the number of individuals incarcerated in the state out of every 100,000 in population), as more unequal states may have higher levels of crime, which can influence brain development and mental health, as well as Medicaid expansion (binary variable) as an indicator of whether the state had expanded Medicaid eligibility⁹¹. In sensitivity analyses for our mediation models, we accounted for parent-reported youth mental health problems (total problems subscale) based on the Child Behavior Checklist⁹².

Imaging acquisition, preprocessing and connectivity data

The imaging procedures used here have been comprehensively outlined by Casey et al.⁹³. Neuroimaging was performed following standardized protocols across multiple sites using 3T magnetic resonance imaging scanners from Siemens, Phillips or General Electric, equipped with 32-channel head coils. A high-resolution 3D T1-weighted image with 1 mm voxel size was obtained for all participants. Further, four or five 5 min resting-state scans (eyes open) were performed to ensure a minimum of 8 min of relatively low-motion data. For further details, refer to Hagler et al.⁹⁴. The preprocessing was carried out by the ABCD data analysis and informatics core, utilizing a uniform pipeline (for detailed procedures and quality control, refer to Hagler et al.⁹⁴). Motion correction was implemented in real-time at the Siemens and GE sites using dedicated software tools. Both automated and manual methods were employed to assess data quality, and all images were reviewed by trained professionals to detect artifacts or abnormalities. Artifact severity in the cortical reconstructions of the postprocessed images was rated on a scale from 0 to 3, with 3 indicating the highest level of artifact. Based on these ratings, technicians recommended the inclusion of only those images rated 0 for further analysis. Signal-to-noise ratios and head motion were assessed using automated tools.

FreeSurfer version 7.1.1 was used for cortical surface reconstruction and parcellation (Desikan–Killiany atlas). In this study, we focused on cortical thickness and surface area (34 variables each). Since no lateralized effects were hypothesized and prior work on individual-level environmental factors and brain structure has not yielded consistent results for lateralized effects¹⁰, values for the left and right hemispheres were averaged for the analysis. This is consistent with ours and others' prior work on this sample^{19,95}, and a study by Taylor et al.⁹⁶ showed that SES is largely consistently associated with volume in the left and right hemisphere in the ABCD sample. Scans were excluded if they did not meet the quality control inclusion criteria outlined by the data analysis, informatics and resource center of ABCD (see release notes for details).

Functional magnetic resonance imaging time courses were projected onto FreeSurfer's cortical surface. Using these time courses, within- and between-network connectivity (Pearson correlation) was calculated based on the Gordon parcellation scheme (36) for 12 predefined resting-state networks: AN, CON, cinguloparietal network, DAN, DMN, FPN, retrosplenial temporal network (RTN), SMN (hand (H)), SMN (mouth (M)), salience network (SN), VAN and VN. These connectivity measures were then Fisher z-transformed, resulting in 78 dependent variables, 66 between-network connectivity variables and 12 within-network connectivity variables (with within-network connectivity representing the average correlation across all pairs of regions within each network). Scans were excluded if they did not meet the quality control inclusion criteria outlined by the ABCD data analysis, informatics and resource center (see release notes for details).

Statistical analyses

To examine the effects of state-level income inequality on brain structure and functional connectivity, we conducted linear mixed-effects models (using the *lme4* package in R). State-level income inequality, indexed by the Gini coefficient, was included as the main predictor, with brain structure (cortical thickness and surface area, 34 variables each) and functional connectivity (across 12 brain networks, 78 variables in total) as the dependent variables (with separate models for each outcome). We corrected for multiple comparisons using the FDR within each set of analyses for thickness, area and connectivity ($P_{\text{FDR}} < 0.05$). *P* values were obtained using the *lmerTest* package. We ran three additional models for total cortical volume, total surface area and average cortical thickness. We included participant age at baseline, sex, scanner type and average framewise displacement (for connectivity measures), income-to-needs ratio at baseline, parent educational attainment at baseline and parent mental health problems at baseline as covariates to control for potential confounding factors. We additionally

adjusted for TANF, incarceration rate and Medicaid expansion status (from 2016–2017) at the state level and included a random effect for family ID. All numerical variables were standardized for analyses. Semi-partial R^2 values were obtained using the *partR2* package in R. Given the small number of states ($n = 17$) and adjustments for key individual-level covariates (for example, age, sex, income-to-needs ratio, parent educational attainment and parent mental health) and site and state-level variables (for example, scanner manufacturer and model, state-level policies and cash assistance, and incarceration rates), clustering or random effects at the state or site level were deemed redundant as the included covariates adequately account for potential confounding and site-related variability. Since some covariates might arguably lie on the causal pathway from inequality to youth mental health (for example, parent mental health issues), the estimates obtained from our model are conservative. However, including this covariate adjusts for other environmental factors that may be associated with parent mental health issues—such as neglect, inconsistent caregiving and substance abuse—as well as genetic propensity to mental health problems. This approach allowed us to isolate effects associated with inequality to a greater extent. Further, to tease apart regional effects from global effects, we adjusted for average thickness (for regional thickness models) and total surface area (for regional surface area models). Model output for this additional analysis has been provided in Supplementary Table 4. Additionally, sensitivity analyses adjusting for racial homogeneity at the state-level (that is, percentage white) have been provided in Supplementary Tables 18–21.

On secondary analyses, race/ethnicity was modeled as a moderator of the association between inequality and brain structure and connectivity to account for intersectional influences. As above, we corrected for multiple comparisons using the FDR within each set of analyses for thickness, area and connectivity ($P_{\text{FDR}} < 0.05$). These results have been reported and are discussed in the Supplementary Information.

For the significant variables identified in the linear mixed-effects models, we performed mediation analysis using structural equation modeling in the lavaan package in R. The analysis aimed to investigate whether brain structure or functional connectivity metrics mediated the relationship between state-level income inequality and total mental health symptoms assessed both 6 months and 18 months later. Scanner manufacturer/model, family ID (to account for family structure) and mean framewise displacement (for functional connectivity variables) were regressed out of the brain measures (that is, the mediator). All covariates (for example, sex, baseline income-to-needs ratio, baseline parental education and baseline parent psychopathology, 2016–2017 Medicaid, TANF and incarceration rate) were included as predictors in both the brain and outcome equations of the mediation models to ensure effects of interest were adjusted for these variables. Additionally, interview age at baseline was modeled in the ‘a’ path and interview age at the respective mental health assessment (either the 6-month or 18-month follow-up) was modeled as a covariate in the ‘b’ path. The structural models were not saturated and included only theoretically driven paths. To assess the significance of indirect effects, we employed a bootstrapping procedure with 5,000 resamples to obtain bias-corrected confidence intervals (CIs) and P values for the indirect pathways. As before, we corrected for multiple comparisons within each set of analyses (that is, thickness, surface area and connectivity; $P_{\text{FDR}} < 0.05$). A moderated mediation model was conducted for variables where race/ethnicity moderates the association between inequality and brain variables (results reported in the Supplementary Information). In a sensitivity analysis, we tested whether results were robust to the inclusion of total mental health problems at baseline as a covariate.

Reporting summary

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

Data availability

The ABCD study data used in this project are publicly available (<https://abcdstudy.org/>). Access to the data is granted to qualified researchers via a data use agreement. For further information on how to obtain access to this dataset, visit the NIH Brain Development Cohorts data sharing platform (<https://www.nbdc-datahub.org/>).

Code availability

All data analyses used readily available programs (for example, open-source R code). No custom code was used.

References

- Patel, V. et al. Income inequality and depression: a systematic review and meta-analysis of the association and a scoping review of mechanisms. *World Psychiatry* **17**, 76–89 (2018).
- Wilkinson, R. G. & Pickett, K. *The Spirit Level: Why Equality Is Better for Everyone* (Penguin, 2010).
- Rakesh, D. et al. Economic inequality and mental health: causality, mechanisms, and interventions. *Annu. Rev. Clin. Psychol.* **21**, 353–377 (2025).
- Solmi, M. et al. Age at onset of mental disorders worldwide: large-scale meta-analysis of 192 epidemiological studies. *Mol. Psychiatry* **27**, 281–295 (2022).
- Rakesh, D., Dehestani, N. & Whittle, S. in *Encyclopedia of Adolescence* 2nd edn (eds Troop-Gordon, W. & Neblett, E. W.) (Academic, 2024); <https://www.sciencedirect.com/science/article/pii/B978032396023600124X>
- Dierckens, M. et al. National-level wealth inequality and socio-economic inequality in adolescent mental well-being: a time series analysis of 17 countries. *J. Adolesc. Health* **66**, S21–S28 (2020).
- Pabayo, R., Dunn, E. C., Gilman, S. E., Kawachi, I. & Molnar, B. E. Income inequality within urban settings and depressive symptoms among adolescents. *J. Epidemiol. Community Health* **70**, 997–1003 (2016).
- Elgar, F. J., Gariépy, G., Torsheim, T. & Currie, C. Early-life income inequality and adolescent health and well-being. *Soc. Sci. Med.* **174**, 197–208 (2017).
- Farmer, G., MacDonald, S. W., Yamamoto, S. S., Wilkes, C. & Pabayo, R. Neighbourhood income inequality and general psychopathology at 3-years of age. *J. Can. Acad. Child Adolesc. Psychiatry* **31**, 135 (2022).
- Rakesh, D. & Whittle, S. Socioeconomic status and the developing brain—a systematic review of neuroimaging findings in youth. *Neurosci. Biobehav. Rev.* **130**, 379–407 (2021).
- Rakesh, D., Whittle, S., Sheridan, M. A. & McLaughlin, K. A. Childhood socioeconomic status and the pace of structural neurodevelopment: accelerated, delayed, or simply different? *Trends Cogn. Sci.* **27**, 833–851 (2023).
- Horowitz, J. M., Igielnik, R. & Kochhar, R. Trends in income and wealth inequality. *Pew Research Center* <https://www.pewresearch.org/social-trends/2020/01/09/trends-in-income-and-wealth-inequality/> (2020).
- Wilkinson, R. & Pickett, K. The enemy between us: the psychological and social costs of inequality. *Eur. J. Soc. Psychol.* **47**, 11–24 (2017).
- Lupien, S. J., Juster, R.-P., Raymond, C. & Marin, M.-F. The effects of chronic stress on the human brain: from neurotoxicity, to vulnerability, to opportunity. *Front. Neuroendocrinol.* **49**, 91–105 (2018).
- Layte, R. et al. A comparative analysis of the status anxiety hypothesis of socio-economic inequalities in health based on 18,349 individuals in four countries and five cohort studies. *Sci. Rep.* **9**, 796 (2019).
- Shapiro, M. S., Rylant, R., de Lima, A., Vidaurre, A. & van de Werfhorst, H. Playing a rigged game: inequality's effect on physiological stress responses. *Physiol. Behav.* **180**, 60–69 (2017).

17. Wilkinson, R. & Pickett, K. *The Inner Level: How More Equal Societies Reduce Stress, Restore Sanity and Improve Everyone's Well-Being* (Penguin, 2018).
18. McEwen, B. S. Allostasis and allostatic load: Implications for neuropsychopharmacology. *Neuropsychopharmacology* **22**, 108–124 (2000).
19. Rakesh, D., Zalesky, A. & Whittle, S. Assessment of parent income and education, neighborhood disadvantage, and child brain structure. *JAMA Netw. Open* **5**, e2226208 (2022).
20. Rakesh, D., Zalesky, A. & Whittle, S. Similar but distinct—effects of different socioeconomic indicators on resting state functional connectivity: findings from the Adolescent Brain Cognitive Development (ABCD) study. *Dev. Cogn. Neurosci.* **51**, 101005 (2021).
21. Whittle, S., Zhang, L. & Rakesh, D. Environmental and neurodevelopmental contributors to youth mental illness. *Neuropsychopharmacology* **50**, 201–210 (2024).
22. Walhovd, K. B. et al. Education and income show heterogeneous relationships to lifespan brain and cognitive differences across European and US cohorts. *Cereb. Cortex* **32**, 839–854 (2021).
23. Baez, S. et al. Structural inequality and temporal brain dynamics across diverse samples. *Clin. Transl. Med.* **14**, e70032 (2024).
24. Vargas, T. G., Damme, K. S. F. & Mittal, V. A. Differentiating distinct and converging neural correlates of types of systemic environmental exposures. *Hum. Brain Mapp.* **43**, 2232–2248 (2022).
25. Parker, N. et al. Income inequality, gene expression, and brain maturation during adolescence. *Sci. Rep.* **7**, 7397 (2017).
26. Farah, M. J. Socioeconomic status and the brain: prospects for neuroscience-informed policy. *Nat. Rev. Neurosci.* **19**, 428–438 (2018).
27. Farah, M. J. The neuroscience of socioeconomic status: correlates, causes, and consequences. *Neuron* **96**, 56–71 (2017).
28. Rakesh, D., Seguin, C., Zalesky, A., Cropley, V. & Whittle, S. Associations between neighborhood disadvantage, resting-state functional connectivity, and behavior in the adolescent brain cognitive development study: the moderating role of positive family and school environments. *Biol. Psychiatry Cogn. Neurosci. Neuroimaging* **6**, 877–886 (2021).
29. Sripada, C. et al. Socioeconomic resources are associated with distributed alterations of the brain's intrinsic functional architecture in youth. *Dev. Cogn. Neurosci.* **58**, 101164 (2022).
30. Rakesh, D., Sadikova, E. & McLaughlin, K. A. Associations among socioeconomic disadvantage, longitudinal changes in within-network connectivity, and academic outcomes in the ABCD study. *Dev. Cogn. Neurosci.* **74**, 101587 (2025).
31. Jednoróg, K. et al. The influence of socioeconomic status on children's brain structure. *PLoS ONE* **7**, e42486 (2012).
32. Noble, K. G. et al. Family income, parental education and brain structure in children and adolescents. *Nat. Neurosci.* **18**, 773–778 (2015).
33. Cohen, S. Social relationships and health. *Am. Psychol.* **59**, 676–684 (2004).
34. Pickett, K. E. & Wilkinson, R. G. Income inequality and health: a causal review. *Soc. Sci. Med.* **128**, 316–326 (2015).
35. Alvarez, J. A. & Emory, E. Executive function and the frontal lobes: a meta-analytic review. *Neuropsychol. Rev.* **16**, 17–42 (2006).
36. Stuss, D. T. Functions of the frontal lobes: relation to executive functions. *J. Int. Neuropsychol. Soc.* **17**, 759–765 (2011).
37. Grill-Spector, K. & Malach, R. The human visual cortex. *Annu. Rev. Neurosci.* **27**, 649–677 (2004).
38. Pozzi, E., Vijayakumar, N., Rakesh, D. & Whittle, S. Neural correlates of emotion regulation in adolescents and emerging adults: a meta-analytic study. *Biol. Psychiatry* **89**, 194–204 (2021).
39. Posner, M. I. & Petersen, S. E. The attention system of the human brain. *Annu. Rev. Neurosci.* **13**, 25–42 (1990).
40. Olson, I. R., Plotzker, A. & Ezzyat, Y. The enigmatic temporal pole: a review of findings on social and emotional processing. *Brain* **130**, 1718–1731 (2007).
41. Rakesh, D., Lee, P. A., Gaikwad, A. & McLaughlin, K. A. Annual research review: associations of socioeconomic status with cognitive function, language ability, and academic achievement in youth: a systematic review of mechanisms and protective factors. *J. Child Psychol. Psychiatry* **66**, 417–439 (2025).
42. Lawson, G. M., Hook, C. J. & Farah, M. J. A meta-analysis of the relationship between socioeconomic status and executive function performance among children. *Dev. Sci.* **21**, e12529 (2018).
43. Bradley, R. H. & Corwyn, R. F. Socioeconomic status and child development. *Annu. Rev. Psychol.* **53**, 371–399 (2002).
44. Reiss, F. Socioeconomic inequalities and mental health problems in children and adolescents: a systematic review. *Soc. Sci. Med.* **90**, 24–31 (2013).
45. Cheung, F. & Lucas, R. E. Income inequality is associated with stronger social comparison effects: the effect of relative income on life satisfaction. *J. Pers. Soc. Psychol.* **110**, 332–341 (2016).
46. Walasek, L. & Brown, G. D. A. Income inequality and status seeking: searching for positional goods in unequal US states. *Psychol. Sci.* **26**, 527–533 (2015).
47. Delhey, J., Schneickert, C. & Steckermeier, L. C. Sociocultural inequalities and status anxiety: redirecting the Spirit Level Theory. *Int. J. Comp. Sociol.* **58**, 215–240 (2017).
48. Wood, A. M., Boyce, C. J., Moore, S. C. & Brown, G. D. A. An evolutionary based social rank explanation of why low income predicts mental distress: a 17 year cohort study of 30,000 people. *J. Affect. Disord.* **136**, 882–888 (2012).
49. Osafo Hounkpatin, H., Wood, A. M., Brown, G. D. A. & Dunn, G. Why does income relate to depressive symptoms? Testing the income rank hypothesis longitudinally. *Soc. Indic. Res.* **124**, 637–655 (2015).
50. Boyce, C. J., Brown, G. D. A. & Moore, S. C. Money and happiness: rank of income, not income, affects life satisfaction. *Psychol. Sci.* **21**, 471–475 (2010).
51. Boyce, W. T., Sokolowski, M. B. & Robinson, G. E. Toward a new biology of social adversity. *Proc. Natl Acad. Sci. USA* **109**, 17143–17148 (2012).
52. Pybus, K., Power, M., Pickett, K. E. & Wilkinson, R. Income inequality, status consumption and status anxiety: an exploratory review of implications for sustainability and directions for future research. *Soc. Sci. Humanit. Open* **6**, 100353 (2022).
53. Harter, S. *The Construction of the Self, Second Edition: Developmental and Sociocultural Foundations* (Guilford Publications, 2015).
54. Wang, J.-L., Wang, H.-Z., Gaskin, J. & Hawk, S. The mediating roles of upward social comparison and self-esteem and the moderating role of social comparison orientation in the association between social networking site usage and subjective well-being. *Front. Psychol.* **8**, 233971 (2017).
55. He, D., Shen, X. & Liu, Q.-Q. The relationship between upward social comparison on SNSs and excessive smartphone use: a moderated mediation analysis. *Child. Youth Serv. Rev.* **116**, 105232 (2020).
56. Elgar, F. J. et al. Association of early-life exposure to income inequality with bullying in adolescence in 40 countries. *JAMA Pediatrics* **173**, e191181 (2019).
57. Van Loon, L. M. A., Van de Ven, M. O. M., Van Doesum, K. T. M., Witterman, C. L. M. & Hosman, C. M. H. The relation between parental mental illness and adolescent mental health: the role of family factors. *J. Child. Fam. Stud.* **23**, 1201–1214 (2014).
58. Shonkoff, J. P. et al. The lifelong effects of early childhood adversity and toxic stress. *Pediatrics* **129**, e232–e246 (2012).

59. Hall, B. S., Moda, R. N. & Liston, C. Glucocorticoid mechanisms of functional connectivity changes in stress-related neuropsychiatric disorders. *Neurobiol. Stress* **1**, 174–183 (2015).
60. Eiland, L. & Romeo, R. D. Stress and the developing adolescent brain. *Neuroscience* **249**, 162–171 (2013).
61. Liston, C. & Gan, W.-B. Glucocorticoids are critical regulators of dendritic spine development and plasticity in vivo. *Proc. Natl Acad. Sci. USA* **108**, 16074–16079 (2011).
62. Ehsan, A., Klaas, H. S., Bastianen, A. & Spini, D. Social capital and health: a systematic review of systematic reviews. *SSM Popul. Health* **8**, 100425 (2019).
63. Kawachi, I., Kennedy, B. P., Lochner, K. & Prothrow-Stith, D. Social capital, income inequality, and mortality. *Am. J. Public Health* **87**, 1491–1498 (1997).
64. Owens, M. M. et al. Investigation of psychiatric and neuropsychological correlates of default mode network and dorsal attention network anticorrelation in children. *Cereb. Cortex* **30**, 6083–6096 (2020).
65. Jirsaraie, R. J. et al. Mapping the neurodevelopmental predictors of psychopathology. *Mol. Psychiatry* **30**, 478–488 (2024).
66. Xu, Z., Zhao, W., Wang, H., Tian, Y. & Lei, X. Functional connectivity between dorsal attention and default mode networks mediates subjective sleep duration and depression in young females. *J. Affect. Disord.* **325**, 386–391 (2023).
67. van Tol, M.-J. et al. Regional brain volume in depression and anxiety disorders. *Arch. Gen. Psychiatry* **67**, 1002–1011 (2010).
68. Romer, A. L., Ren, B. & Pizzagalli, D. A. Brain structure relations with psychopathology trajectories in the ABCD study. *J. Am. Acad. Child Adolesc. Psychiatry* **62**, 895–907 (2023).
69. Shen, X. et al. Brain structural associations with depression in a large early adolescent sample (the ABCD study). *EClinicalMedicine* **42**, 101204 (2021).
70. Shad, M. U., Muddasani, S. & Rao, U. Gray matter differences between healthy and depressed adolescents: a voxel-based morphometry study. *J. Child Adolesc. Psychopharmacol.* **22**, 190–197 (2012).
71. Li, Q., Whittle, S. & Rakesh, D. (2025). Longitudinal associations between greenspace exposure, structural brain development, and mental health and academic performance during early adolescence. *Biol. Psychiatry* <https://doi.org/10.1016/j.biopsych.2025.03.026> (2025).
72. Raniti, M., Rakesh, D., Patton, G. C. & Sawyer, S. M. The role of school connectedness in the prevention of youth depression and anxiety: a systematic review with youth consultation. *BMC Public Health* **22**, 2152 (2022).
73. Maio, F. G. D. Income inequality measures. *J. Epidemiol. Community Health* **61**, 849–852 (2007).
74. Hero, R. E. & Levy, M. E. The racial structure of inequality: consequences for welfare policy in the United States. *Soc. Sci. Q.* **99**, 459–472 (2018).
75. Hero, R. E. & Levy, M. E. The racial structure of economic inequality in the United States: understanding change and continuity in an era of “great divergence”. *Soc. Sci. Q.* **97**, 491–505 (2016).
76. Vargas, T., Conley, R. E. & Mittal, V. A. Chronic stress, structural exposures and neurobiological mechanisms: a stimulation, discrepancy and deprivation model of psychosis. *Int. Rev. Neurobiol.* **152**, 41–69 (2020).
77. Erdem, Ö., Prins, R. G., Voorham, T. A. J. J., van Lenthe, F. J. & Burdorf, A. Structural neighbourhood conditions, social cohesion and psychological distress in the Netherlands. *Eur. J. Public Health* **25**, 995–1001 (2015).
78. Emerson, S. D., Minh, A. & Guhn, M. Ethnic density of regions and psychiatric disorders among ethnic minority individuals. *Int. J. Soc. Psychiatry* **64**, 130–144 (2018).
79. Funder, D. C. & Ozer, D. J. Evaluating effect size in psychological research: sense and nonsense. *Adv. Methods Pract. Psychol. Sci.* **2**, 156–168 (2019).
80. Barch, D. M. et al. Demographic and mental health assessments in the adolescent brain and cognitive development study: updates and age-related trajectories. *Dev. Cogn. Neurosci.* **52**, 101031 (2021).
81. Garavan, H. et al. Recruiting the ABCD sample: design considerations and procedures. *Dev. Cogn. Neurosci.* **32**, 16–22 (2018).
82. Wilkinson, R. G. & Pickett, K. E. Income inequality and population health: a review and explanation of the evidence. *Soc. Sci. Med.* **62**, 1768–1784 (2006).
83. Hsieh, C.-C. & Pugh, M. D. Poverty, income inequality, and violent crime: a meta-analysis of recent aggregate data studies. *Crim. Justice Rev.* **18**, 182–202 (1993).
84. Kondo, N. et al. Income inequality and health: the role of population size, inequality threshold, period effects and lag effects. *J. Epidemiol. Community Health* **66**, e11 (2012).
85. Achenbach, T. M., McConaughy, S. H., Ivanova, M. Y. & Rescorla, L. A. *Manual for the ASEBA Brief Problem Monitor for Ages 6–18* (ASEBA).
86. Achenbach, T. M. & Rescorla, L. *Manual for the ASEBA School-Age Forms and Profiles: An Integrated System of Multi-Informant Assessment* (ASEBA, 2001).
87. Saragosa-Harris, N. M. et al. A practical guide for researchers and reviewers using the ABCD study and other large longitudinal datasets. *Dev. Cogn. Neurosci.* **55**, 101115 (2022).
88. Increases in TANF cash benefit levels are critical to help families meet rising costs. *Center on Budget and Policy Priorities* <https://www.cbpp.org/research/income-security/increases-in-tanf-cash-benefit-levels-are-critical-to-help-families-meet-0> (2014).
89. Weissman, D. G., Hatzenbuehler, M. L., Cikara, M., Barch, D. M. & McLaughlin, K. A. State-level macro-economic factors moderate the association of low income with brain structure and mental health in US children. *Nat. Commun.* **14**, 2085 (2023).
90. Maruschak, L. Correctional populations in the United States, 2017–2018. <https://bjs.ojp.gov/library/publications/correctional-populations-unitedstates-2017-2018> (2020).
91. Data.Medicaid.gov. Centers for Medicare and Medicaid Services. <https://data.medicare.gov/> (2021).
92. Achenbach, T. M. in *Encyclopedia of Clinical Neuropsychology* (Springer, 2018); https://doi.org/10.1007/978-3-319-56782-2_1529-3
93. Casey, B. J. et al. The Adolescent Brain Cognitive Development (ABCD) study: imaging acquisition across 21 sites. *Dev. Cogn. Neurosci.* **32**, 43–54 (2018).
94. Hagler, D. J. et al. Image processing and analysis methods for the Adolescent Brain Cognitive Development study. *Neuroimage* **202**, 116091 (2019).
95. Hackman, D. A. et al. Association of local variation in neighborhood disadvantage in metropolitan areas with youth neurocognition and brain structure. *JAMA Pediatrics* **175**, e210426 (2021).
96. Taylor, R. L., Cooper, S. R., Jackson, J. J. & Barch, D. M. Assessment of neighborhood poverty, cognitive function, and prefrontal and hippocampal volumes in children. *JAMA Netw. Open* **3**, e2023774 (2020).

Acknowledgements

D.R. acknowledges support from a Young Investigator Grant from the Brain and Behaviour Research Foundation (no. 32908) and a New Investigator Research Grant from the UKRI Medical Research Council (no. MR/Z506667/1). T.V. acknowledges funding from the National Institute of Mental Health (NIMH) (no. R37-MH119194-05S2). Data used in the preparation of this article were obtained from the ABCD study (<https://abcdstudy.org>) held in the NIMH Data Archive.

This is a multisite, longitudinal study designed to recruit more than 11,000 children ages 9–10 years old and follow them over 10 years into early adulthood. The ABCD study is supported by the National Institutes of Health and additional federal partners under award numbers U01DA041048, U01DA050989, U01DA051016, U01DA041022, U01DA051018, U01DA051037, U01DA050987, U01DA041174, U01DA041106, U01DA041117, U01DA041028, U01DA041134, U01DA050988, U01DA051039, U01DA041156, U01DA041025, U01DA041120, U01DA051038, U01DA041148, U01DA041093, U01DA041089, U24DA041123 and U24DA041147. A full list of supporters is available at <https://abcdstudy.org/federal-partners.html>. A listing of participating sites and a complete listing of the study investigators can be found at https://abcdstudy.org/consortium_members/. ABCD consortium investigators designed and implemented the study and/or provided data but did not necessarily participate in the analysis or writing of this report. The views expressed in this paper are those of the authors and do not necessarily reflect the official views of the National Institutes of Health, the Department of Health and Human Services, the US federal government or ABCD consortium investigators.

Author contributions

D.R. conceptualized the study and research design, conducted analyses and wrote and revised the first and subsequent drafts of the paper. D.I.T. and T.V. consulted on the analysis plan and provided additional feedback on the paper. K.E.P. and V.P. provided feedback on the analysis plan, critical feedback on the paper and expert guidance and support. All authors approved the final version before submission. All authors have read and agreed to the published version of the paper.

Competing interests

The authors declare no competing interests.

Additional information

Supplementary information The online version contains supplementary material available at <https://doi.org/10.1038/s44220-025-00508-1>.

Correspondence and requests for materials should be addressed to Divyangana Rakesh.

Peer review information *Nature Mental Health* thanks Pilyoung Kim, Genevieve Patterson, Xueyi Shen and the other, anonymous reviewer(s) for their contribution to the peer review of this work.

Reprints and permissions information is available at www.nature.com/reprints.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>.

© The Author(s) 2025

Divyangana Rakesh ¹✉, Dimitris I. Tsomokos ^{1,2}, Teresa Vargas³, Kate E. Pickett ⁴ & Vikram Patel ⁵

¹Department of Neuroimaging, Institute of Psychology, Psychiatry and Neuroscience, King's College London, London, UK. ²UCL Institute of Education, Department of Psychology and Human Development, University College London, London, UK. ³Department of Psychology, Harvard University, Cambridge, MA, USA. ⁴Department of Health Sciences, University of York, York, UK. ⁵Department of Global Health and Social Medicine, Harvard Medical School, Boston, MA, USA. ✉e-mail: divyangana.rakesh@kcl.ac.uk

Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our [Editorial Policies](#) and the [Editorial Policy Checklist](#).

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed
☐	☒ The exact sample size (<i>n</i>) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒ A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒ The statistical test(s) used AND whether they are one- or two-sided <i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i>
☐	☒ A description of all covariates tested
☐	☐ A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒ A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒ For null hypothesis testing, the test statistic (e.g. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>
☒	☐ For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☐	☒ For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☐	☒ Estimates of effect sizes (e.g. Cohen's <i>d</i> , Pearson's <i>r</i>), indicating how they were calculated

Our web collection on [statistics for biologists](#) contains articles on many of the points above.

Software and code

Policy information about [availability of computer code](#)

Data collection	No custom algorithms were written for this project.
Data analysis	All analyses were conducted in R version 4.3.1 using the lmer function from the lme4 package for mixed-effects models, the lmerTest package for significance testing of fixed effects, and the lavaan package for structural equation modeling.

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio [guidelines for submitting code & software](#) for further information.

Data

Policy information about [availability of data](#)

All manuscripts must include a [data availability statement](#). This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our [policy](#)

The ABCD study is a publicly available dataset, access to which is available through a data use agreement.

Research involving human participants, their data, or biological material

Policy information about studies with [human participants or human data](#). See also policy information about [sex, gender \(identity/presentation\), and sexual orientation](#) and [race, ethnicity and racism](#).

Reporting on sex and gender	Biological sex-assigned at birth has been reported in the manuscript. Analyses included both male and female participants.
Reporting on race, ethnicity, or other socially relevant groupings	Race and ethnicity have been reported in the manuscript as part of demographic information. No associations between race/ethnicity and neurobiology were examined.
Population characteristics	See above.
Recruitment	School-based sampling strategy was used to approximate the demographic diversity of the U.S. population. The study enrolled nearly 12,000 children aged 9–10 years at baseline, starting in 2016. Recruitment occurred across 21 research sites in the United States, covering diverse geographic and demographic regions. Researchers used probability sampling of schools (public and private) within selected catchment areas. Schools were randomly invited, and then students and families were invited to participate through presentations, flyers, and follow-up outreach.
Ethics oversight	Institutional Review Board (IRB) at the University of California, San Diego (UCSD)

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☐ Life sciences ☒ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see [nature.com/documents/nr-reporting-summary-flat.pdf](https://www.nature.com/documents/nr-reporting-summary-flat.pdf)

Behavioural & social sciences study design

All studies must disclose on these points even when the disclosure is negative.

Study description	Cross-sectional quantitative study
Research sample	Over 11800 children 9-10 years from 21 sites across 17 states in the US
Sampling strategy	School-based sampling strategy was used to approximate the demographic diversity of the U.S. population. The study enrolled nearly 12,000 children aged 9–10 years at baseline, starting in 2016. Recruitment occurred across 21 research sites in the United States, covering diverse geographic and demographic regions. Researchers used probability sampling of schools (public and private) within selected catchment areas. Schools were randomly invited, and then students and families were invited to participate through presentations, flyers, and follow-up outreach. See Garavat et al. (2018) for details.
Data collection	Imaging scanners, computers
Timing	2016-2018
Data exclusions	Excluded due to poor quality scans
Non-participation	Analyses included individuals with data on variables of interest and usable MRI scans
Randomization	N/A

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☐	☐ Antibodies
☐	☐ Eukaryotic cell lines
☐	☐ Palaeontology and archaeology
☐	☐ Animals and other organisms
☐	☐ Clinical data
☐	☐ Dual use research of concern
☐	☐ Plants

Methods

n/a	Involved in the study
☐	☐ ChIP-seq
☐	☐ Flow cytometry
☐	☒ MRI-based neuroimaging

Antibodies

Antibodies used *Describe all antibodies used in the study; as applicable, provide supplier name, catalog number, clone name, and lot number.*

Validation *Describe the validation of each primary antibody for the species and application, noting any validation statements on the manufacturer's website, relevant citations, antibody profiles in online databases, or data provided in the manuscript.*

Eukaryotic cell lines

Policy information about [cell lines and Sex and Gender in Research](#)

Cell line source(s) *State the source of each cell line used and the sex of all primary cell lines and cells derived from human participants or vertebrate models.*

Authentication *Describe the authentication procedures for each cell line used OR declare that none of the cell lines used were authenticated.*

Mycoplasma contamination *Confirm that all cell lines tested negative for mycoplasma contamination OR describe the results of the testing for mycoplasma contamination OR declare that the cell lines were not tested for mycoplasma contamination.*

Commonly misidentified lines (See [ICLAC](#) register) *Name any commonly misidentified cell lines used in the study and provide a rationale for their use.*

Palaeontology and Archaeology

Specimen provenance *Provide provenance information for specimens and describe permits that were obtained for the work (including the name of the issuing authority, the date of issue, and any identifying information). Permits should encompass collection and, where applicable, export.*

Specimen deposition *Indicate where the specimens have been deposited to permit free access by other researchers.*

Dating methods *If new dates are provided, describe how they were obtained (e.g. collection, storage, sample pretreatment and measurement), where they were obtained (i.e. lab name), the calibration program and the protocol for quality assurance OR state that no new dates are provided.*

☐ Tick this box to confirm that the raw and calibrated dates are available in the paper or in Supplementary Information.

Ethics oversight *Identify the organization(s) that approved or provided guidance on the study protocol, OR state that no ethical approval or guidance was required and explain why not.*

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Animals and other research organisms

Policy information about [studies involving animals](#); [ARRIVE guidelines](#) recommended for reporting animal research, and [Sex and Gender in Research](#)

Laboratory animals *For laboratory animals, report species, strain and age OR state that the study did not involve laboratory animals.*

Wild animals *Provide details on animals observed in or captured in the field; report species and age where possible. Describe how animals were caught and transported and what happened to captive animals after the study (if killed, explain why and describe method; if released, say where and when) OR state that the study did not involve wild animals.*

Reporting on sex *Indicate if findings apply to only one sex; describe whether sex was considered in study design, methods used for assigning sex. Provide data disaggregated for sex where this information has been collected in the source data as appropriate; provide overall*

numbers in this Reporting Summary. Please state if this information has not been collected. Report sex-based analyses where performed, justify reasons for lack of sex-based analysis.

Field-collected samples

For laboratory work with field-collected samples, describe all relevant parameters such as housing, maintenance, temperature, photoperiod and end-of-experiment protocol OR state that the study did not involve samples collected from the field.

Ethics oversight

Identify the organization(s) that approved or provided guidance on the study protocol, OR state that no ethical approval or guidance was required and explain why not.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Clinical data

Policy information about [clinical studies](#)

All manuscripts should comply with the ICMJE [guidelines for publication of clinical research](#) and a completed [CONSORT checklist](#) must be included with all submissions.

Clinical trial registration

Provide the trial registration number from ClinicalTrials.gov or an equivalent agency.

Study protocol

Note where the full trial protocol can be accessed OR if not available, explain why.

Data collection

Describe the settings and locales of data collection, noting the time periods of recruitment and data collection.

Outcomes

Describe how you pre-defined primary and secondary outcome measures and how you assessed these measures.

Dual use research of concern

Policy information about [dual use research of concern](#)

Hazards

Could the accidental, deliberate or reckless misuse of agents or technologies generated in the work, or the application of information presented in the manuscript, pose a threat to:

- | No | Yes | |
|--------------------------|--------------------------|----------------------------|
| ☐ | ☐ | Public health |
| ☐ | ☐ | National security |
| ☐ | ☐ | Crops and/or livestock |
| ☐ | ☐ | Ecosystems |
| ☐ | ☐ | Any other significant area |

Experiments of concern

Does the work involve any of these experiments of concern:

- | No | Yes | |
|--------------------------|--------------------------|---|
| ☐ | ☐ | Demonstrate how to render a vaccine ineffective |
| ☐ | ☐ | Confer resistance to therapeutically useful antibiotics or antiviral agents |
| ☐ | ☐ | Enhance the virulence of a pathogen or render a nonpathogen virulent |
| ☐ | ☐ | Increase transmissibility of a pathogen |
| ☐ | ☐ | Alter the host range of a pathogen |
| ☐ | ☐ | Enable evasion of diagnostic/detection modalities |
| ☐ | ☐ | Enable the weaponization of a biological agent or toxin |
| ☐ | ☐ | Any other potentially harmful combination of experiments and agents |

Plants

Seed stocks	Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.
Novel plant genotypes	Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.
Authentication	Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosaicism, off-target gene editing) were examined.

ChIP-seq

Data deposition

- ☐ Confirm that both raw and final processed data have been deposited in a public database such as [GEO](#).
- ☐ Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

Data access links May remain private before publication.	For "Initial submission" or "Revised version" documents, provide reviewer access links. For your "Final submission" document, provide a link to the deposited data.
Files in database submission	Provide a list of all files available in the database submission.
Genome browser session (e.g. UCSC)	Provide a link to an anonymized genome browser session for "Initial submission" and "Revised version" documents only, to enable peer review. Write "no longer applicable" for "Final submission" documents.

Methodology

Replicates	Describe the experimental replicates, specifying number, type and replicate agreement.
Sequencing depth	Describe the sequencing depth for each experiment, providing the total number of reads, uniquely mapped reads, length of reads and whether they were paired- or single-end.
Antibodies	Describe the antibodies used for the ChIP-seq experiments; as applicable, provide supplier name, catalog number, clone name, and lot number.
Peak calling parameters	Specify the command line program and parameters used for read mapping and peak calling, including the ChIP, control and index files used.
Data quality	Describe the methods used to ensure data quality in full detail, including how many peaks are at FDR 5% and above 5-fold enrichment.
Software	Describe the software used to collect and analyze the ChIP-seq data. For custom code that has been deposited into a community repository, provide accession details.

Flow Cytometry

Plots

Confirm that:

- ☐ The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).
- ☐ The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).
- ☐ All plots are contour plots with outliers or pseudocolor plots.
- ☐ A numerical value for number of cells or percentage (with statistics) is provided.

Methodology

Sample preparation	Describe the sample preparation, detailing the biological source of the cells and any tissue processing steps used.
Instrument	Identify the instrument used for data collection, specifying make and model number.
Software	Describe the software used to collect and analyze the flow cytometry data. For custom code that has been deposited into a community repository, provide accession details.

Cell population abundance

Describe the abundance of the relevant cell populations within post-sort fractions, providing details on the purity of the samples and how it was determined.

Gating strategy

Describe the gating strategy used for all relevant experiments, specifying the preliminary FSC/SSC gates of the starting cell population, indicating where boundaries between "positive" and "negative" staining cell populations are defined.

☐ Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.

Magnetic resonance imaging

Experimental design

Design type

T1 and resting state fMRI

Design specifications

N/A

Behavioral performance measures

N/A

Acquisition

Imaging type(s)

Structural and functional

Field strength

3T

Sequence & imaging parameters

The ABCD study is an openly available dataset with standardised preprocessing pipeline. This study used processed tabulated data, details for which can be found in Casey et al. (see reference below)

Casey, B. J., Cannonier, T., Conley, M. I., Cohen, A. O., Barch, D. M., Heitzeg, M. M., ... & Dale, A. M. (2018). The adolescent brain cognitive development (ABCD) study: imaging acquisition across 21 sites. *Developmental cognitive neuroscience*, 32, 43-54.

Area of acquisition

Whole-brain

Diffusion MRI

☐ Used☒ Not used

Preprocessing

Preprocessing software

The ABCD study is an openly available dataset with standardised preprocessing pipeline. This study used processed tabulated data, details for which can be found in Hagler et al. (see reference below)

Hagler Jr, D. J., Hatton, S., Cornejo, M. D., Makowski, C., Fair, D. A., Dick, A. S., ... & Dale, A. M. (2019). Image processing and analysis methods for the Adolescent Brain Cognitive Development Study. *Neuroimage*, 202, 116091.

Normalization

See above.

Normalization template

See above.

Noise and artifact removal

See above.

Volume censoring

See above.

Statistical modeling & inference

Model type and settings

N/A as not task

Effect(s) tested

N/A as not task

Specify type of analysis: ☐ Whole brain ☐ ROI-based ☐ Both

Statistic type for inference

N/A as not task

(See [Eklund et al. 2016](#))

Correction

N/A as not task

Models & analysis

n/a	Involvement in the study	
☐	☒ Functional and/or effective connectivity	
☐	☐ Graph analysis	
☐	☐ Multivariate modeling or predictive analysis	
Functional and/or effective connectivity		Pearson correlation within and between 12 networks from the Gordon parcellation scheme.
Graph analysis		Report the dependent variable and connectivity measure, specifying weighted graph or binarized graph, subject- or group-level, and the global and/or node summaries used (e.g. clustering coefficient, efficiency, etc.).
Multivariate modeling and predictive analysis		Specify independent variables, features extraction and dimension reduction, model, training and evaluation metrics.