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Original Article

Neural correlates of social withdrawal and preference for solitude in adolescence

Matthew Risner[1] and Catherine Stamouls[1,2,*]

[1]Department of Pediatrics, Division of Adolescent and Young Adult Medicine, Boston Children's Hospital, 300 Longwood Avenue, Boston, MA 02115, United States
[2]Department of Pediatrics, Harvard Medical School, 25 Shattuck Street, Boston, MA 02115, United States
*Corresponding author: Catherine Stamouls, Boston Children's Hospital, Department of Pediatrics, 300 Longwood Avenue, Boston, MA 02115, United States. Email: caterina.stamoulis@childrens.harvard.edu

Social isolation during development, especially in adolescence, has detrimental but incompletely understood effects on the brain. This study investigated the neural correlates of preference for solitude and social withdrawal in a sample of 2809 youth [median (IQR) age = 12.0 (1.1) years, 1440 (51.26%) females] from the Adolescent Brain Cognitive Development study. Older youth whose parents had mental health issues more frequently preferred solitude and/or were socially withdrawn ($\beta = 0.04$ to 0.14, CI = [0.002, 0.19], $P < 0.05$), both of which were associated with internalizing and externalizing behaviors, depression, and anxiety ($\beta = 0.25$ to 0.45, CI = [0.20, 0.49], $P < 0.05$). Youth who preferred solitude and/or were socially withdrawn had lower cortical thickness in regions involved in social function (cuneus, insula, anterior cingulate, and superior temporal gyri) and/or mental health ($\beta = -0.09$ to -0.02, CI = [−0.14, −0.003], $P < 0.05$), and higher amygdala, entorhinal cortex, parahippocampal gyrus, and basal ganglia volume ($\beta = 2.62$ to 668.10, CI = [0.13, 668.10], $P < 0.05$). Youth who often preferred solitude had more topologically segregated dorsal attention, temporoparietal, and social networks ($\beta = 0.07$ to 0.10, CI = [0.02, 0.14], $P \leq 0.03$). Socially withdrawn youth had a less topologically robust and efficient ($\beta = -0.05$ to -0.80, CI = [−1.34,−0.01], $P < 0.03$) and more fragile cerebellum ($\beta = 0.04$, CI = [0.01, 0.07], $P < 0.05$). These findings suggest that social isolation in adolescence may be a risk factor for widespread alterations in brain regions supporting social function and mental health.

Keywords: adolescent brain; brain structures; preference for solitude; resting-state brain networks; social withdrawal.

Introduction

Adolescence is a period of heightened neural maturation and circuit rewiring, as the brain's neural architecture is progressively optimized in order to support increasingly complex cognitive processing (Steinberg and Morris 2001; Rogol et al. 2002; Siervogel et al. 2004; Susman and Rogol 2004; Wigfield et al. 2006; Ashtari et al. 2007; Lenroot et al. 2007; Yurgelun-Todd 2007; Blakemore 2008, 2012; Luna 2009; Klimstra et al. 2010; Peper et al. 2011; Sturman and Moghaddam 2011; Goddings et al. 2014; Wierenga et al. 2014; Blakemore and Mills 2014a; Mills et al. 2016; Özdemir et al. 2016; Vijayakumar et al. 2018; Andrews et al. 2021; Best and Ban 2021; Pfeifer and Allen 2021). In parallel, the youth social world expands and changes, in part due to social reorientation—a shift in the relative importance of peer relationships compared to those with family (Wang et al. 1995; Maxwell 2002; Giordano 2003; Jaccard et al. 2005; Lerner and Steinberg 2009; Albert et al. 2013; Sawyer et al. 2018). Changes in the youth social environment can be overwhelming, sometimes leading to social isolation (Oh et al. 2008; Rubin et al. 2009; Biggs et al. 2012; Barzeva et al. 2019; Porcelli et al. 2019; Wood et al. 2022), which may, in turn, adversely impact brain development and increase risk for mental health and behavioral problems (Costello et al. 2011; Reiss 2013; Bor et al. 2014; Blakemore 2019).

Stressors in the youth's immediate environment increase the risk for social withdrawal, isolation, and loneliness. For example, children whose parents have mental health issues may be at higher risk of behavioral and mental health problems, including social isolation (Cogan et al. 2005; Manning and Gregoire 2009; Van Loon et al. 2014; Matthews et al. 2015; Bosch et al. 2017; Dam et al. 2018; Reupert et al. 2021). Relationships with peers are similarly influential, and peer rejection, victimization, lacking friends, and low friendship quality also contribute to social withdrawal and loneliness (Cassidy and Asher 1992; Cheng and Furnham 2002; Asher and Paquette 2003; Woodhouse et al. 2012; Vanhalst et al. 2014; Lodder et al. 2017; Schwartz-Mette et al. 2020). These relationships are, however, bidirectional since social withdrawal may worsen the quality and/or depth of friendships (Rubin et al. 2006; Biggs et al. 2012; Coplan et al. 2018; Barzeva et al. 2022). Social exclusion at school may also lead to social withdrawal and loneliness (Patton et al. 2006; Ford et al. 2018; Arslan and Gökmen. 2021; Arslan et al. 2023). In contrast, a sense of school connectedness may mitigate the adverse psychological effects of social isolation (Hall-Lande et al. 2007; Foster et al. 2017; Marraccini and Brier 2017; London and Ingram 2018; Preston and Rew 2022). Again, these relationships are complex and bidirectional, since socially withdrawn children often encounter difficulties in school, including poor relationships with teachers, academic struggles, and possibly avoiding school altogether. These challenges further reinforce their social isolation and limit opportunities for meaningful social engagement (Rubin et al. 2009; Coplan et al. 2018; Stenseng et al. 2022).

Social isolation and loneliness have been associated with physical health problems in adolescents and young adults, including increased risk for cancer, obesity, diabetes, asthma,

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migraine, hypertension, and back pain (de L. Almeida et al. 2021; Christiansen et al. 2021; Goosby et al. 2013; Mahon et al. 1993; Mushtaq et al. 2014; von Soest et al. 2020), and longer-term cardiovascular problems, inflammation, and impaired immunoregulation (Caspi et al. 2006; Danese et al. 2009; Hawkley et al. 2010; Hawkley and Cacioppo 2010; Patterson and Veenstra 2010; Goosby et al. 2013; Lacey et al. 2014; Matthews et al. 2024).

Common mental health disorders often emerge in adolescence (Paus et al. 2008; de Girolamo et al. 2012; Blakemore 2019), and social isolation may significantly increase their risk of occurrence. Specifically, it has been linked to anxiety, depression, internalizing problems, and suicidal ideation and self-harm (Cacioppo et al. 2006; Rubin et al. 2009; Costello et al. 2011; Jones et al. 2011; Schinka et al. 2012; Reiss 2013; Bor et al. 2014; Gallagher et al. 2014; Endo et al. 2017; Blakemore 2019; McClelland et al. 2020; Harman et al. 2021). Social isolation has also been associated with cognitive problems and deficits, including worse academic performance and impaired reward processing and language skills (de L. Almeida et al. 2021; Jefferson et al. 2023a; 2023b; Matthews et al. 2023; Rubin et al. 2009; Tomova et al. 2022; Stenseng et al. 2022) and impaired memory (Fuhrmann et al. 2019). Recent studies focusing on social isolation of youth during the COVID-19 pandemic have reported associations between pandemic-related social isolation and deficits in executive function, attention, and memory (Lavigne-Cerván et al. 2021; Houghton et al. 2022; Murtaza et al. 2023).

The neural correlates of social withdrawal and isolation remain poorly understood. This is a significant gap in knowledge given that adolescence is not only a formative period for the establishment of social identity and mental health outcomes but also a vulnerable period for social development (Meeus 1996; Kroger 2004; Fergusson et al. 2005; Kessler et al. 2005; Paus et al. 2008; Blakemore and Mills 2014; Blakemore 2019; Branje et al. 2021; Schlack et al. 2021). Adult studies have shown that loneliness and social withdrawal are associated with lower gray matter volume in the posterior superior temporal gyrus, the amygdala, the hippocampus, and the cerebellum (Kanai et al. 2012; Koolschijn et al. 2013; Düzel et al. 2019; Lind et al. 2020), disrupted white matter integrity in the salience network (Tian et al. 2014), and lower white matter density in the inferior parietal lobule and anterior insula (Nakagawa et al. 2015; Lam et al. 2021). It has also been associated with structural changes in the dorsolateral prefrontal cortex, and impaired community between the amygdala and the orbitofrontal cortex, which may, in turn, lead to emotional dysregulation (Kong et al. 2015; Liu et al. 2016; Goetschius et al. 2020; Zheng et al. 2023). Together, these findings suggest that social isolation adversely impacts the structural integrity of brain regions that play critical roles in social perception, cognitive control, and emotional processing.

Beyond its impact on brain structure, social withdrawal, isolation, and loneliness in young adults have been linked to higher resting-state functional connectivity in the right central operculum, supramarginal gyrus, and circuits involved in sustained attention (Layden et al. 2017), and weaker connections between dorsal attention and salience networks, as well as within and between temporal, limbic, and prefrontal networks (Tian et al. 2017; Feng et al. 2019; McIver et al. 2019). In adolescents, social withdrawal has been associated with stronger connections between the amygdala and regions of the dorsal attention, frontoparietal control, and auditory networks and between the prefrontal and limbic networks (Thomas et al. 2024). Loneliness has been associated with lower activation of the ventromedial prefrontal cortex (Golde et al. 2019) and higher functional connectivity in visual attention networks (Brilliant et al. 2022).

Despite valuable insights provided by prior studies, the brain correlates of social withdrawal and/or preference for solitude in adolescence remain incompletely understood and have not been systematically characterized. A significant barrier to robust investigations is the heterogeneity of adolescent brain and social development, and the complexity of associations between social behaviors, environmental factors, and the brain. However, the availability of multimodal (including neuroimaging) data from the Adolescent Brain Cognitive Development (ABCD) study, a historically large (∼12,000 youth) investigation of adolescent brain development (Casey et al. 2018) provides a unique opportunity to bridge this gap in knowledge.

The present study leveraged the ABCD structural MRI and resting-state functional Magnetic Resonance Imaging (fMRI) data, mental health assessments, and survey data on social behaviors and environmental factors in order to investigate associations between preference for solitude and social withdrawal (both leading to social isolation), the organization of intrinsically coordinated brain networks, and their structural correlates in almost 3,000 adolescents (ages 10 to 13 years), who at this age may be at higher risk of mental health disorders and maladaptive social behaviors (Kessler et al. 2005). The two measures were analyzed separately (secondary analyses also analyzed a composite measure). Although preference for solitude and social withdrawal both involve spending time alone, they are different behaviors and may be differentially motivated (Galanaki 2004; Coplan et al. 2021; Weinstein et al. 2023). Preference for solitude may be intentional and driven by positive factors, such as a need for introspection, creative thinking, and personal growth (Long and Averill 2003; Nguyen et al. 2018). Recent studies have shown that as the adolescent social world evolves, youth try to balance social engagement with the need for independence, and preference for solitude increases with age (Goossens 2014; Borg and Willoughby 2022; Chen et al. 2023). However, despite potential positive effects, frequent preference for solitude may lead to social isolation, with similar negative implications for brain development and mental health as social withdrawal. The latter may result from social stressors, social anxiety, depression, and negative emotions (Rubin et al. 2009; Barzeva et al. 2019; Rubin and Chronis-Tuscano 2021) and is thus driven by negative endogenous and exogenous factors. The study hypothesized that although occasional preference for solitude may have a positive effect on the adolescent brain, frequent preference for solitude and social withdrawal are in part driven by negative factors in the youth social environment and are associated with widespread structural and functional brain changes, especially in underdeveloped regions supporting social function.

Materials and methods

This study was approved by the Boston Children's Hospital Institutional Revew Board. It analyzed publicly available and thus anonymized data, and thus, informed consent was not required.

Participants

A sample of $n = 2{,}809$ youth from the 2-year follow-up cohort in the ABCD study was analyzed. The primary criterion for inclusion was availability of at least one high-quality (≤10% of frames censored for motion) 5-min resting-state fMRI run that had been collected prior to the onset of the COVID-19 pandemic (assumed to

Table 1. Demographic and other individual characteristics ($n = 2809$).

Age (years)	Median (IQR)	12.00 (1.08)
Sex	**Male**	1366 (48.63%)
	Female	1440 (51.26%)
	Missing	3 (0.11%)
Race/Ethnicity	**White Non-Hispanic**	1488 (52.97%)
	Black Non-Hispanic	363 (12.92%)
	Asian Non-Hispanic	645 (22.96%)
	Other (including mixed race) Non-Hispanic	61 (2.17%)
	Hispanic	243 (8.66%)
	Missing	9 (0.32%)
Family Income ($)	**<25,000**	266 (9.47%)
	25,000 to **49,999**	331 (11.78%)
	50,000 to **74,999**	355 (12.64%)
	75,000 to **99,999**	361 (12.85%)
	100,000 to **199,999**	883 (31.43%)
	≥200,000	405 (14.42%)
	Missing	208 (7.41%)
BMI Z-Score	**Median (IQR)**	-0.31 (1.138)
	Missing	17 (0.61%)
Pubertal Stage	**Prepuberty**	515 (18.33%)
	Early puberty	609 (21.68%)
	Mid-puberty	918 (32.68%)
	Late/Postpuberty	622 (22.15%)
	Missing	145 (5.16%)

be 2020 March 11, when the World Health Organization declared it as such). Youth measured during the pandemic were excluded to eliminate its potential confounding effects on the brain and social behaviors. Although studying the effects of social isolation during the pandemic on the brain is critical, it was outside the scope of the present study. In addition, participants with clinical MRI findings and neuropsychiatric or neurodevelopmental disorders were also excluded, since they may independently affect brain morphology and the organization of neural circuits (Brooks et al. 2021, 2022, 2023). The final analytic sample included 1,366 boys (48.63%) and 1,440 girls (51.26%), with a median age of 12.0 years (interquartile range [IQR] = 1.1 years). Over half of youth were white non-Hispanic (1488 [53.0%]), 1069 (38.1%) were non-Hispanic racial minorities, and 243 (8.7%) were Hispanic. Socioeconomic status was assessed based on annual household income, with a median income $75,000 to $99,999. The sample included 515 (18.3%) youth in prepuberty, 609 (21.7%) in early puberty, 918 (32.7%) in mid-puberty, and 622 (22.1%) in late/postpuberty. Detailed demographic and other participant characteristics are provided in Table 1.

Measures of social withdrawal

Two measures directly assessing social withdrawal and preference for solitude were extracted from the Child Behavior Checklist (CBCL), completed by parents: *"withdrawn, doesn't get involved with others"* and *"would rather be alone than with others."* Both were measured on a Likert scale from not true (0) to very/often true (2). Secondary analyses also explored a composite social withdrawal measure (the sum of the two items [in a scale of 0 to 4]).

Measures of mental health

Data on anxiety, depression, internalizing, and externalizing behaviors (all *t*-scores), were extracted from the CBCL. Additional information on social anxiety disorder and anhedonia was extracted from the Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS), also completed by parents. For each mental health factor from the K-SADS, responses to two yes/no questions about past and present diagnoses or symptoms were combined into a single binary variable based on any positive responses.

Environmental factors

Multiple aspects of the youth social environment were investigated. Parental mental health was based on the Adult Behavior Checklist (ABCL) and was measured as a *t*-score of critical items related to depression, self-harm, substance use, mood swings, and suicidal thoughts. Family dynamics were assessed based on the parent-reported Family Environment Scale. Conflict and cohesion were measured on continuous scales by aggregating responses from multiple survey items designed to assess specific aspects of the family's organizational structure. In addition, parent responses to one question from the Mexican American Cultural Values Scale were extracted, providing a measure for how strongly they believed that family members should show love and affection to one another. Responses were measured on a Likert scale from not at all (1) to completely (5). Prior work has identified associations between this parental belief and youth prosocial behaviors (Smith and Stamoulis 2023).

Questions on peer relations were: (i) the number of close friends (from the Other Resilience survey); (ii) regular group of friends (binary variable, from the KSAD-S); and (iii) bullying, represented as a binary variable based on questions on whether a child had been bullied in any social setting (from a parent-reported K-SADS question) or had been cyberbullied (from the youth-reported Cyber-bullying instrument). The Discrimination Measure, reported by youth, assessed experiences of perceived discrimination in four domains: race/ethnicity/color, being from another country, sexual orientation, and/or weight. Given small samples with positive responses in each domain, responses were combined into a single binary variable for analysis, indicating any type of discrimination.

Youth responses on whether they got along with their teacher and liked school (from the School Risk and Protective Factors survey) were also examined. Responses were measured on a Likert scale from definitely not true (1) to definitely true (4).

Additional characteristics

Other assessments of youth social behaviors were extracted from the Early Adolescent Temperament Questionnaire (completed by the parents) and included *"Is energized by being in large crowds of people," "Wants to have close relationships with other people," "Is shy,"* and *"Feels shy about meeting new people,"* all on a 5-point scale [almost always untrue (1) to almost always true (5)]. Another question from the same instrument asked if the child *"Likes meeting new people,"* and was reverse-coded by the ABCD, with higher values indicating less frequent social engagement. Two questions on past or present symptoms of a fear of social situations were extracted from the KSAD-S and combined into a binary variable with 1 corresponding to a "true" response to either or both questions, and 0 otherwise. Another question from the CBCL asked parents if their child was *"self-conscious or easily embarrassed"* and was coded on a Likert scale from not true (0) to very/often true (2).

Neuroimaging data analysis

Resting-state fMRI processing and topological property estimation

Structural MRI and resting-state fMRI (rs-fMRI; participants completed up to four 5-min runs) underwent initial preprocessing by the ABCD study's Data Analysis, Informatics and Resource Center (DAIRC) to correct for bias fields, B0 distortion, grad warp, and motion in the scanner (Hagler et al. 2019). Additional processing was necessary to further suppress motion-related and other artifacts, harmonize the data across scanners (across the 21 ABCD sites, data were collected with a 3T GE, Siemens, or Philips scanner), and downsample the voxel-level time series. The custom Next Generation Neural Data Analysis (NGNDA) pipeline was used for this purpose (Next-Generation Neural Data Analysis (NGNDA) 2020). Following segmentation of each participant's structural MRI (sMRI), coregistration of their fMRI to the sMRI, and normalization to the common MNI152 space, fMRI signals were further processed to improve their quality. This process included removal of initial frames, correction for motion, and denoising using signal decomposition to eliminate signal components likely associated with cardiorespiratory and other artifacts (Brooks et al. 2021). Voxel-level time series were then downsampled using three atlases for parcellating cortical and subcortical structures and the cerebellum, resulting in 1088 parcel signals (Diedrichsen et al. 2009; Schaefer et al. 2018; Tian et al. 2020). Only fMRI runs with ≤10% motion-censored frames were retained for further analysis, based on a displacement threshold of 0.3 mm. Each participant's best-quality run, based on the lowest median connectivity (given that the brain at rest is overall weakly coordinated), and typically also the lowest number of frames censored for motion) was first analyzed. For replication purposes, the second-best-quality run was selected from a subsample of participants [$n = 2,160$ (∼77% of the sample)] who had more than one run of adequate quality for analysis. Median (IQR) percent of frames censored for motion was 1.07% (IQR = 4.00%) in the best-quality run and 1.07% (IQR = 3.73%) in the second run. Since two runs were analyzed, associations between resting-state topological properties and measures of social withdrawal that were reproducible across runs are reported in primary analyses and tables. Additional associations based on the best-quality run (and also larger sample) are reported in secondary analyses and supplemental tables.

Resting-state connectivity was calculated as the peak cross-correlation between pairs of fMRI signals, resulting in 1088 × 1088 full and symmetric matrices. To obtain corresponding adjacency matrices used in the calculation of topological properties, statistical thresholds were estimated from the entire cohort and all available runs, as outlined in Brooks et al. (2021). A conservative threshold, equal to the bootstrapped moderate outlying peak cross-correlation value (median + 1.5∗IQR) was then applied to obtain adjacency matrices. Topological properties were estimated at multiple spatial scales: (i) brain regions (network nodes), (ii) large-scale resting-state networks (Yeo et al. 2011) that also included the reward (Haber and Knutson 2010), and social (Blakemore 2008) networks, and (iii) the entire brain connectome. Topological properties at the network and connectome levels included modularity, global clustering, global efficiency, topological robustness, median connectivity (within and between networks), fragility, topological stability, and segregation. The latter was calculated as the ratio of within-network over out-of-network median connectivity. Node properties included degree, local clustering, and eigenvector centrality. Detailed descriptions of each of these properties are provided elsewhere (Rubinov and Sporns 2010; Wu et al. 2011; Pasqualetti et al. 2020; Brooks et al. 2021).

Structural parameters

Morphometric brain properties (estimated from structural MRIs by the ABCD) were analyzed. They were based on a parcellation using the Desikan–Killiany atlas, which segments the cortex into 68 regions based on anatomical landmarks (Desikan et al. 2006). Subcortical voxels were parcellated into 30 regions using a probabilistic approach (Fischl et al. 2002). Properties of 98 regions were analyzed, including cortical thickness and white matter intensity, and cortical and subcortical volume (Hagler et al. 2019). White matter intensity was examined as a potentially sensitive cortical marker of brain development (Westlye et al. 2009; Lewis et al. 2018; Hagler et al. 2019). To compare structural and functional findings, the 1,088 cortical and subcortical resting-state network nodes were mapped to 98 structures based on their anatomical overlap.

Statistical analysis

All relationships of interest were investigated using linear mixed-effects regression models that included a random intercept and slope for each of the 21 ABCD sites, to account for potential site effects. All models included age, pubertal stage, sex, race-ethnicity, family income, and BMI z-score stratified by sex [which has been previously linked to differences in topological properties in the ABCD cohort (Brooks et al. 2023)]. All analyses accounted for potential bias associated with sampling differences at the 21 sites using the ABCD-provided propensity scores. Given limited statistical power to study social withdrawal in individual race/ethnic groups, race-ethnicity was coded as a binary variable representing white non-Hispanic participants (0) and racioethnic minorities (1). Pubertal stage was coded as an ordinal variable in the range 1 (prepuberty) to 4 (late/postpuberty).

Two broad sets of analyses were conducted to investigate (i) associations between social withdrawal and brain structure and circuit organization and (ii) associations between environmental factors and social withdrawal. In the first set of analyses, models that included brain parameters (the dependent variables), social withdrawal, preference for solitude, and the composite measure were the independent variables of interest. These models were also adjusted for internalizing behavior scores, a variable that was consistently significant across analyses. In the second set of analyses, models that examined associations between social isolation and environmental, mental health, and other behavioral factors, social withdrawal, and preference for solitude were the dependent variables. Models that included resting-state brain network parameters were also adjusted for percent of frames censored for motion and scan time of day participants (0 to 23 h) as additional variables (Brooks et al. 2021; Vaisvilaite et al. 2022; Hu et al. 2023). Variations of models were also developed to assess pairwise comparisons between specific response categories of the social withdrawal measures, focusing on two categories at a time or treating these measures as binary variables.

The significance level was set at $\alpha = 0.05$. All parameter P-values were adjusted for the false discovery rate (FDR), using a well-established method (Benjamini and Hochberg 1995). In analyses focusing on topological properties of the entire brain, the FDR correction was done over topological properties (the only available dimension). Networks were assumed to be independent from each other, and P-values were corrected for FDR across 9 properties estimated for each network. In analyses focusing on regional (node) properties, the FDR correction was done over all nodes within a particular network (each large-scale resting-state network typically includes a relatively large number of nodes). In structural models, P-values were adjusted over regional morphometric properties. Associations were considered significant if the model intercept, parameter of interest, and model P-value were all significant. Model cross-validation was performed by randomly dividing the data into training and testing sets (75:25) 100 times. The coefficient of variation of the root-mean-squared error (CV[RMSE]) between predicted and observed responses was used to assess each model's predictive power. Reported results are based on models with good predictive power, ie CV[RMSE] ≤ 0.20 All data were analyzed in the Harvard Medical School high-performance cluster using the software MATLAB (release R2023a, Mathworks, Inc).

Results

Across the cohort, 455 (17.9%) youth sometimes or often preferred solitude, and 170 (6.0%) were sometimes or often socially withdrawn. Less than 10% reported past or present anhedonia [264 (9.4%)] and 40 (1.4%) were diagnosed with social anxiety disorder. Median (IQR) *t*-scores for other mental health measures were 51.0 (2.0) for anxiety, 50.0 (4.0) for depression, 41.0 (16.0) for externalizing behaviors, and 46.0 (14.0) for internalizing behaviors.

Median (IQR) parent mental health score was 51.0 (4.0). Almost 90% of parents said that it was important for the family to show love and affection toward each other. Median family cohesion was 8.0 (2.0), whereas median family conflict was 2.0 (2.0). Median (IQR) family size was 4 (1). Participants had, on average, 5 close friends, and almost 90% had a regular group of kids to hang out with. About 10% reported being discriminated against [302 (10.7%)], and 519 (18.5%) had been bullied. Almost 95% reported having good relationships with teachers, and ~70% said that they liked school a lot [1991 (70.9%)]. Summary statistics for social environmental factors are provided in Table 2.

Almost 70% of parents reported that their child wanted close relationships with other people [1,938 (69.0%)], ~60% of youth were not self-conscious or easily embarrassed [1,717 (61.%)], and liked to meet new people [1,654 (58.9%)], and almost 30% were energized by large crowds [813 (28.9%)]. About a quarter were shy [552 (26.4%)], fewer were specifically shy about meeting new people [466 (16.6%)], and even fewer were afraid of social situations [150 (5.3%)]. Detailed distributions of responses are provided in Table S1.

Table 2. Distribution of social environmental factors in the cohort.

PARENTAL FACTORS		
Parental mental health (T-score)	**Median (IQR)**	51 (4)
	Missing	378 (13.46%)
Parental belief that family members should show love and affection to one another	**Not at all**	15 (0.53%)
	A little	23 (0.82%)
	Somewhat	254 (9.04%)
	Very much	1237 (44.04%)
	Completely	1279 (45.53%)
	Missing	1 (0.04%)
FAMILY ENVIRONMENT		
Family conflict Scale: 0 to 9	**Median (IQR)**	2 (2)
	Missing	1 (0.04%)
Family cohesion Scale: 0 to 9	**Median (IQR)**	8 (2)
	Missing	1 (0.04%)
Family size	**Median (IQR)**	4 (1)
	Missing	36 (1.28%)
PEER RELATIONSHIPS		
Number of close friends	**Median (IQR)**	5 (5)
	Missing	6 (0.21%)
Has a regular group of kids to hang out with at school/neighborhood	**No**	276 (9.83%)
	Yes	2427 (86.40%)
	Missing	106 (3.77%)
Faced discrimination in the past 12 months	**No**	2507 (89.25%)
	Yes	302 (10.75%)
	Missing	0 (0%)
Problems with bullying at school/neighborhood OR cyberbullying	**No**	2276 (81.03%)
	Yes	519 (18.48%)
	Missing	14 (0.50%)
SCHOOL		
Gets along with their teachers	**Strongly disagree**	25 (0.89%)
	Disagree	120 (4.27%)
	Agree	1188 (42.29%)
	Strongly agree	1471 (52.37%)
	Missing	5 (0.18%)
Likes school a lot	**Strongly disagree**	259 (9.22%)
	Disagree	554 (19.72%)
	Agree	1204 (42.86%)
	Strongly agree	787 (28.02%)
	Missing	5 (0.18%)

Associations between individual and environmental factors and social

Older participants and at more advanced pubertal stages were more frequently socially isolated ($\beta = 0.04$ to 0.07, CI = [0.002, 0.13], $P < 0.05$). Parental mental health issues were positively associated with frequency of youth preferring solitude and social withdrawal ($\beta = 0.14$, CI = [0.10, 0.19], $P < 0.01$, and $\beta = 0.13$, CI = [0.09, 0.17], $P < 0.01$), respectively). In contrast, being energized by large crowds of people was negatively associated with preferring solitude ($\beta = -0.23$, CI = [−0.27, −0.19], $P < 0.01$). When participants who often preferred solitude were excluded [due to their small sample size ($n = 48$)], and only participants who sometimes preferred solitude were compared to those who did not, additional positive associations were identified with being shy ($\beta = 0.45$, CI = [0.34, 0.55], $P < 0.01$) and not liking to meet new people ($\beta = 0.58$, CI = [0.46, 0.70], $P < 0.01$). Social withdrawal was also associated with being shy ($\beta = 0.21$, CI = [0.16, 0.25], $P < 0.01$), not liking to meet new people ($\beta = 0.21$, CI = [0.17, 0.25], $P < 0.01$), and feeling shy about meeting new people ($\beta = 0.19$, CI = [0.15, 0.23], $P < 0.01$).

Associations between social isolation and mental health outcomes

More frequent reference for solitude was associated with higher internalizing behaviors ($\beta = 0.45$, CI = [0.42, 0.49], $P < 0.01$), externalizing behaviors ($\beta = 0.23$, CI = [0.20, 0.27], $P < 0.01$), depression ($\beta = 0.39$, CI = [0.35, 0.42], $P < 0.01$), and anxiety ($\beta = 0.29$, CI = [0.26, 0.33], $P < 0.01$). Similarly, more frequent social withdrawal was associated with higher internalizing behavior ($\beta = 0.41$, CI = [0.37, 0.45], $P < 0.01$), externalizing behaviors ($\beta = 0.25$, CI = [0.21, 0.29], $P < 0.01$), depression ($\beta = 0.45$, CI = [0.42, 0.49], $P < 0.01$), and anxiety ($\beta = 0.35$, CI = [0.31, 0.39], $P < 0.01$).

Associations between social isolation and resting-state brain network properties

Whole-brain topology

In the full cohort, there were no consistent associations across both fMRI runs. However, within-group comparisons based on frequency of preference for solitude identified negative correlations between preference for solitude and connectome efficiency and global clustering ($\beta = -0.03$ to −0.02, CI = [−0.05, −0.01], $P \leq 0.04$). Statistics of models based only on the best run, and those based on the composite measure, are summarized in Table S2.

Network topology

More frequent preference for solitude was associated with higher segregation (more locally-connected communities) of the right

Table 3. Statistics of mixed-effect models testing associations between preferring solitude, social withdrawal, and topological properties of individual networks. All reported P-values have been adjusted for the false discovery rate. Regression coefficients in models comparing pairs of groups were not standardized. ∗NS: nonsignificant; CI: confidence interval.

Would rather be alone than with others								
Property	Network	Sample comparison	Beta	95th % CI*	P-value	Beta	95th % CI	P-value
			Left hemisphere			Right hemisphere		
Segregation	Dorsal attention	Entire sample	NS*			0.066	[0.022, 0.110]	0.034
	Social	Entire sample	NS			0.085	[0.042, 0.128]	0.001
		Somewhat vs Very True	NS			0.008	[0.003, 0.013]	0.037
	Temporoparietal	Entire sample	NS			0.095	[0.051, 0.139]	<0.001
Global efficiency	Cerebellum	Somewhat vs Very True	−0.089	[−0.133, −0.045]	<0.001	NS		

Withdrawn, does not get involved with others								
Property	Network	Sample comparison	Beta	95th % CI	P-value	Beta	95th % CI	P-value
			Left hemisphere			Right hemisphere		
Topological robustness	Cerebellum	Somewhat vs Very True	−0.781	[−1.342, −0.220]	0.021	NS		
Topological stability	Cerebellum	Somewhat vs Very True	−0.670	[−1.151, −0.189]	0.021	NS		
Fragility	Cerebellum	Somewhat vs Very True	0.039	[0.005, 0.073]	0.047	NS		

dorsal attention, temporoparietal, and social networks ($\beta = 0.07$ to 0.10, CI = [0.02, 0.14], $P < 0.04$). Within-group comparisons also identified associations between preference for solitude and higher segregation of the right social network ($\beta = 0.01$, CI = [0.003, 0.01], $P = 0.04$) but lower global efficiency of the left cerebellum ($\beta = -0.09$, CI = [−0.13, −0.05], $P < 0.01$). In addition, frequency of social withdrawal was associated with lower topological robustness and stability ($\beta = -0.78$ to −0.67, CI = [−1.34, −0.19], $P < 0.03$) and higher fragility ($\beta = 0.04$, CI = [0.01, 0.07], $P < 0.05$) of the left cerebellum. Model statistics are summarized in Table 3. Results based on the larger sample with one best-quality run, and those based on the composite score are summarized in Table S3.

Detailed results and model statistics are provided in Table S3. Finally, there were no consistent associations between any social isolation measures and node properties across both fMRI runs.

Associations between social withdrawal and structural brain properties

Frequent social withdrawal was associated with higher white matter intensity in the right isthmus of the cingulate gyrus ($\beta = 0.03$, CI = [0.01, 0.05], $P = 0.04$). Frequent preference for solitude was associated with lower thickness of the left superior temporal gyrus, right caudal anterior cingulate gyrus, right insula, and the left cuneus and pars opercularis ($\beta = -0.09$ to −0.05, CI = [−0.14, −0.01], $P < 0.05$), and lower white matter intensity but higher volume of the right parahippocampal gyrus ($\beta = -0.02$, CI = [−0.04, −0.002], $P < 0.05$, and $\beta = 0.06$, CI = [0.01, 0.10], $P < 0.05$, respectively).

Youth who often preferred solitude versus those who did not had lower thickness of the left cuneus, and left superior temporal gyrus, right caudal anterior cingulate gyrus, and right insula ($\beta = -0.04$ to −0.02, CI = [−0.07, −0.003], $P < 0.05$), lower volume of the left cuneus and right fusiform gyrus ($\beta = -264.31$ to −109.54, CI = [−474.51, −11.40], $P = 0.04$), and lower white matter intensity of the right parahippocampal gyrus ($\beta = -0.23$, CI = [−0.42, −0.05], $P = 0.04$). Frequent social withdrawal was associated with higher volume of the right pallidum ($\beta = 81.06$, CI = [12.50, 149.62], $P = 0.02$); lower thickness of the right cuneus, right insula, and lingual gyrus ($\beta = -0.06$, CI = [−0.09, −0.01], $P \leq 0.04$); and lower volume of the right cuneus ($\beta = -333.56$, CI = [−529.69, −137.44], $P < 0.01$) and right lingual gyrus ($\beta = -492.48$, CI = [−848.47, −136.49], $P = 0.02$).

Ingroup comparisons, preference for solitude was associated with lower white matter intensity in the right inferior temporal gyrus ($\beta = -0.39$, CI = [−0.68, −0.10], $P = 0.03$), and social withdrawal was associated with higher volume of left caudate nucleus, right pallidum and the putamen ($\beta = 231.75$ to 369.01, CI = [2.68, 668.10], $P < 0.05$), lower thickness of the right cuneus ($\beta = -0.15$, CI = [−0.23, −0.06], $P < 0.01$) and right lingual gyrus ($\beta = -0.09$, CI = [−0.17, −0.01], $P = 0.04$), and lower volume of the right cuneus ($\beta = -723.26$, CI = [−1185.41, −261.12], $P < 0.01$).

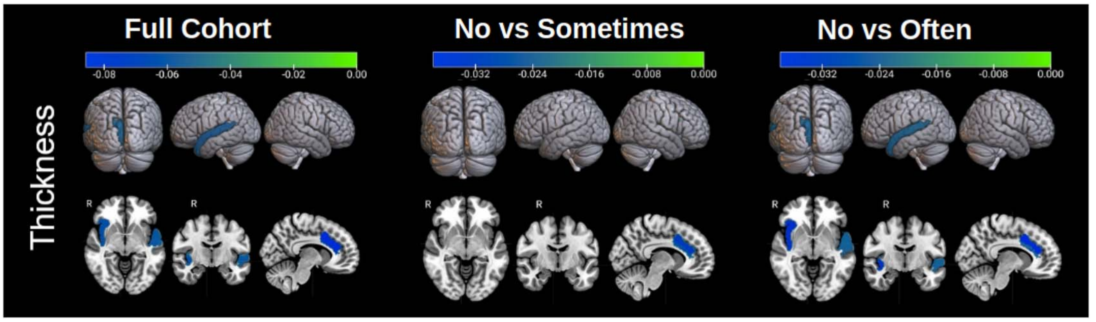
Comparisons of those who somewhat preferred solitude versus those who did not also identified associations between preference for solitude and higher volume of the left amygdala, and right entorhinal and parahippocampal gyri ($\beta = 25.72$ to 61.62, CI = [0.13, 106.57], $P < 0.05$), and lower thickness of the right pars opercularis and right caudal anterior cingulate gyrus ($\beta = -0.03$, CI = [−0.06, −0.003], $P < 0.05$). Similar comparisons of those who were somewhat socially withdrawn to those who were not identified a negative association between social withdrawal and volume in the right caudal middle frontal gyrus ($\beta = -319.88$, CI = [−579.79, −59.97], $P < 0.05$). Model statistics are summarized in Table 4. Negative associations between preference for solitude and cortical thickness, which were more consistent across group comparisons (especially in the caudal anterior cingulate cortex) are shown in Fig. 1.

Table 4. Statistics of mixed-effect models testing associations between preferring solitude and morphological properties. All reported *P*-values have been adjusted for the false discovery rate. Regression coefficients in models comparing only 2 response options were not standardized. *NS: nonsignificant; *CI: confidence interval.

Would rather be alone than with others								
Property	**Structure**	**Sample comparison**	**Beta**	**95th % CI***	**P-value**	**Beta**	**95th % CI**	**P-value**
			Left hemisphere			**Right hemisphere**		
Cortical Thickness	**Cuneus**	**Entire sample**	−0.054	[−0.096, −0.011]	0.039	NS*		
		Not vs Very True	−0.024	[−0.044, −0.004]	0.043	NS		
	Superior temporal gyrus	**Entire sample**	−0.058	[−0.100, −0.016]	0.019	NS		
		Not vs Very True	−0.024	[−0.045, −0.003]	0.0496	NS		
	Caudal anterior cingulate gyrus	**Entire sample**	NS			−0.086	[−0.137, −0.034]	0.003
		Not vs Somewhat True	NS			−0.032	[−0.056, −0.008]	0.030
		Not vs Very True	NS			−0.038	[−0.066, −0.010]	0.023
	Pars opercularis	**Entire sample**	NS			−0.053	[−0.096, −0.010]	0.047
		Not vs Somewhat True	NS			−0.018	[−0.033, −0.003]	0.050
	Insula	**Entire sample**	NS			−0.062	[−0.104, −0.020]	0.012
		Not vs Very True	NS			−0.035	[−0.056, −0.013]	0.023
Volume	**Amygdala**	**Not vs Somewhat True**	25.718	[0.128, 51.308]	0.049	ND		
	Cuneus	**Not vs Very True**	−109.540	[−207.7, −11.4]	0.043	ND		
	Entorhinal	**Not vs Somewhat True**	NS			61.62	[16.67, 106.57]	0.022
	Fusiform	**Not vs Very True**	NS			−264.3	[−474.5, −54.1]	0.041
	Parahippocampal gyrus	**Entire sample**	NS			0.055	[0.011, 0.100]	0.046
		Not vs Somewhat True	NS			53.95	[20.05, 87.84]	0.005
	Supramarginal gyrus	**Somewhat vs Very True**	−1044.6	[−1851, −248]	0.031	NS		
Cortical white matter intensity	**Parahippocampal gyrus**	**Entire sample**	NS			−0.020	[−0.039, −0.002]	0.0496
		Not vs Very True	NS			−0.234	[−0.420, −0.048]	0.041
	Inferior temporal gyrus	**Somewhat vs Very True**	NS			−0.389	[−0.682, −0.095]	0.029

Withdrawn, does not get involved with others								
Property	**Structure**	**Sample comparison**	**Beta**	**95th % CI***	**P-value**	**Beta**	**95th % CI**	**P-value**
			Left hemisphere			**Right hemisphere**		
Cortical thickness	**Cuneus**	**Not vs Very True**	NS			−0.055	[−0.093, −0.017]	0.006
		Somewhat vs Very True	NS			−0.146	[−0.229, −0.063]	0.002
	Insula	**Not vs Very True**	NS			−0.057	[−0.098, −0.016]	0.021
	Lingual gyrus	**Not vs Very True**	NS			−0.040	[−0.074, −0.005]	0.038
		Somewhat vs Very True	NS			−0.090	[−0.170, −0.010]	0.043
Cortical volume	**Caudal middle frontal gyrus**	**Not vs Somewhat True**	NS			−319.9	[−579.8, −60.0]	0.048
	Caudate nucleus	**Somewhat vs Very True**	308.498	[2.68, 614.31]	0.048	NS		
	Cuneus	**Not vs Very True**	NS			−333.6	[−529.7, −137.4]	0.003
		Somewhat vs Very True	NS			−723.3	[−1185, −261]	0.004
	Lingual gyrus	**Not vs Very True**	NS			−492.5	[−848.5, −136.5]	0.020
	Pallidum	**Not vs Very True**	NS			81.06	[12.50, 149.62]	0.021
		Somewhat vs Very True	NS			231.7	[96.85, 366.6]	<0.001
	Putamen	**Somewhat vs Very True**	NS			369.0	[69.92, 668.10]	0.016
White matter intensity	**Isthmus of cingulate cortex**	**Entire sample**	NS			0.026	[0.005, 0.047]	0.042

NS, nonsignificant.



Fig; 1. Associations between preferring solitude and cortical thickness. The left panel shows associations in the entire cohort. In the middle panel, youth who sometimes prefer solitude are compared to those who do not. In the right panel, youth who often prefer solitude are compared to those who sometimes do. Colors represent the regression coefficients associated with cortical thickness.

Mappings between functional and structural correlates of preference for solitude

Segregation of the right dorsal attention network was positively associated with morphometric properties of the right pars opercularis ($\beta = 0.06$, CI = [0.02, 0.11], $P < 0.02$) and the right inferior temporal gyrus ($\beta = -0.06$, CI = [−0.12, 0.01], $P < 0.04$), which both overlap with this network and were negatively associated with preference for solitude. Similarly, segregation of the right social network was positively associated with morphometric properties of the overlapping right insula ($\beta = 0.08$, CI = [0.02, 0.13], $P < 0.03$), and preference for solitude was associated with higher segregation of the network and lower thickness of the region.

Discussion

In a large cohort of almost 3,000 adolescents, we have systematically investigated the neural correlates of preference for solitude and social withdrawal, especially hallmark structural and topological characteristics of large-scale networks that play critical roles in cognitive (including social) function. Social isolation in adolescence, a sensitive period of brain and social development, can lead to neural miswiring, increased risk of cognitive delays and deficits, maladaptive behaviors, and mental health problems across the lifespan. In this study's cohort, about 18% of youth sometimes or often preferred solitude, and 6% were socially withdrawn. Older youth whose parents had mental health issues more frequently preferred solitude and/or were socially withdrawn. These findings are in agreement with prior studies that have shown that parental behaviors and mental health issues are significant risk factors for youth loneliness, social withdrawal, and isolation (Matthews et al. 2015; de L. Almeida et al. 2021) as early as infancy (Mäntymaa et al. 2008).

As their social world expands beyond the family, adolescents may not only seek solitude, as part of their growing independence and autonomy, but also become increasingly exposed to social stressors (such as peer rejection and victimization), which may, in turn, lead to social withdrawal and isolation. In this cohort, almost 90% had a regular group of friends, only ~10% had experienced discrimination (or any form), and ~20% had been bullied. Neither overall discrimination nor bullying was statistically associated with an increased likelihood of social isolation. However, unmeasured (by the ABCD) granular aspects of peer relationships and their quality and other latent factors in the youth environment that change with age could contribute to social isolation. Frequent preference for solitude and social withdrawal were also associated with youth depression, anxiety, and internalizing and externalizing behaviors, in agreement with prior work that has identified extensive links between social isolation and mental health issues in youth (Rubin et al. 2009; Rubin and Lollis 2015; Orben et al. 2020; Christiansen et al. 2021).

Preference for solitude and social withdrawal had overlapping structural but distinct topological brain correlates. Both were associated with lower thickness of the cuneus and insula. Frequent reference for solitude was also associated with lower thickness of the superior temporal and caudal anterior cingulate gyri and the pars opercularis, and social withdrawal with lower thickness of the lingual gyrus. The cuneus is a structural brain hub (Oldham and Fornito 2019), ie a brain region where multimodal information is integrated, and has been implicated both in emotional processing and social function (Riedel et al. 2018; Eslinger et al. 2021), but also loneliness (Lam et al. 2021; Wong et al. 2022). The insular cortex is another structural hub that supports interoception but is also involved in (social) emotional processing and maladaptive social behaviors (Lamm and Singer 2010; Terasawa et al. 2013; Emmerling et al. 2016; Gogolla 2017). The superior temporal gyrus is considered a "hub" of the social brain and plays a central role in social perception and processing (Blakemore 2008; Pelphrey and Carter 2008; Lahnakoski et al. 2012; Beauchamp 2015). Decreased thickness of the cuneus, insula, and superior temporal gyrus has been associated with not only cognitive deficits but also mental health issues, both in adults and adolescents (van Tol et al. 2014; Pan et al. 2015; Sheffield et al. 2021). The anterior cingulate cortex has distributed connections with frontal and limbic regions and plays a ubiquitous role in cognitive function, including decision-making, cognitive control, and emotion and reward processing and regulation, and is also involved in social cognition (Devinsky et al. 1995; Vogt 2005; Apps et al. 2016). The caudal part of the anterior cingulate cortex is involved in cognitive control, and decreased thickness of this region has been associated with depression and developmental disorders affecting social function, such as autism spectrum disorders (ASDs) (Laidi et al. 2019; Mertse et al. 2022). Finally, the pars opercularis and lingual gyrus are both involved in speech and language processing (Palejwala et al. 2021; Zaccarella and Friederici 2015). Morphological anomalies in these regions have been associated with both linguistic deficits but more broadly impaired social communication and mental health issues, including depression and internalizing symptoms (Jensen et al. 2015; Rosada et al. 2023).

Preference for solitude and social withdrawal was also associated with other structural differences in some of the same areas, including not only lower volume of the cuneus and the lingual gyrus but also higher volume of the entorhinal and parahippocampal gyri, amygdala, and basal ganglia structures, including the caudate, pallidum, and putamen. These findings are in agreement with those of prior studies that have associated social isolation and loneliness with higher amygdala volume (Xiong et al. 2023), potentially as a result of higher emotional sensitivity, but also distress in social settings (Lam et al. 2021; Vitale and Smith 2022) and mental health issues (Espinoza Oyarce et al. 2020; Suor et al. 2020). Specifically in children and adolescents, it has been associated with anxiety, negative affect, and behavioral issues (Merz et al. 2018; Liu et al. 2024; Pereira Camejo et al. 2024). In addition, higher putamen volume has been associated with disorders affecting social function, such as ASD (Sato et al. 2014), and higher caudate volume with behavioral dysregulation, impulsivity, and risk for developmental disorders such as ASD (Voelbel et al. 2006). Together, these findings suggest that social isolation is associated with extensive morphological alterations in the adolescent brain in regions that support social function and are also implicated in mental health disorders, social dysfunction, and developmental disorders impacting social communication. In addition, cortical thinning and increased structural volume are hallmark characteristics of brain development. It is possible that social isolation may be associated with accelerated neural maturation in selective regions, which, in turn, increases the risk for mental health and behavioral problems. A recent study on adolescents during the COVID-19 pandemic reported accelerated brain maturation partly as a result of social isolation due to lockdowns and social distancing (Corrigan et al. 2024).

More frequent preference for solitude was also associated with higher topological segregation (modularity) of the dorsal attention and temporoparietal networks, and an overlapping distributed network representing the social brain (Blakemore 2008). Increased structural and functional network modularity is also a fundamental characteristic of brain and cognitive development (Baum et al. 2017; Tooley et al. 2022); however, in socially isolated youth, it may reflect aberrantly accelerated neural maturation. Higher modularity has also been associated with mental health issues (Gao et al. 2023). Furthermore, more frequent social withdrawal was associated with topological changes in the cerebellum, including lower robustness and efficiency and higher fragility. A number of studies have shown that the cerebellum, which has extensive cortical and subcortical connections with brain regions supporting social function, plays an important role in social development, perception and prediction, and emotional processing (Van Overwalle et al. 2020; Van Overwalle 2024; Turrini and Avenanti 2024). Abnormal structural changes in the cerebellum have been associated with developmental and mental health disorders, including those directing affecting social function (Fett et al. 2015; Jack and Morris 2014; Phillips et al. 2015; Zhu and Qiu 2022; Olivito et al. 2023; Wang et al. 2023). Together, these findings suggest that social isolation during adolescence may have profound detrimental impacts on large-scale networks and their constituent structures that play ubiquitous roles in cognitive and specifically social functions and are abnormally modulated by mental health disorders.

Despite its strengths, including the large sample that captures the heterogeneity of adolescent brain development, comprehensive assessment of topological properties of resting-state networks, concurrent investigation of morphological and functional brain characteristics, and examination of environmental correlates of youth social isolation, this study also had some limitations. First, assessments of social withdrawal and preference for solitude were based on parent reports. When possible, youth surveys were analyzed, but across surveys measuring the youth environment and mental health/behavioral assessments, parent reports were, in general, more complete and reliable or the only available reports (ie corresponding youth ones were not available). Second, as is the case with any retrospective investigation, analyses were limited by the experimental decisions made by the ABCD investigators. Thus, more granular assessments of the youth social environment and related behaviors were not available. Nevertheless, the ABCD is the only investigation that extensively samples the youth social world and relationships with parents, family, teachers, and peers. The present study leveraged data on these relationships in order to examine their associations with social isolation.

This study makes a significant scientific contribution and provides novel insights into the detrimental effects of social isolation on the developing adolescent brain and its maturating and thus vulnerable to miswiring neural circuitry. It has identified widespread morphological and topological brain alterations in youth who often prefer to be alone and/or are socially withdrawn, several of which have not been previously related directly to social isolation, but to disorders affecting social communication. It has also associated preference for not only solitude and social withdrawal with parental mental health but also common youth mental health issues. Adolescence is a sensitive period for mental health. Many identified brain alterations were in regions that support social function but have also been implicated in mental health disorders. In addition, lower cortical thickness and higher subcortical volume and increased modularity of several large-scale networks also suggest potential accelerated maturation of the socially isolated brain, which has also been associated with mental health issues. The ABCD follows youth longitudinally, thus future investigations could specifically examine the hypothesis of accelerated neural maturation and track the emergence of mental health issues as a function of age in socially withdrawn youth.

Author contributions

Catherine Stamoulis (Conceptualization, Funding acquisition, Resources, Investigation, Supervision, Project administration, Methodology, Writing—original draft, Writing—review and editing) and Matthew Risner (Data curation, Formal analysis, Investigation, Software, Validation, Visualization, Writing—original draft, Writing—review and editing).

Supplementary material

Supplementary material is available at *Cerebral Cortex* online.

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Conflict of interest statement: None declared.

Data availability

The data underlying this article are available in National Institute of Mental Health Data Archive (NDA). https://nda.nih.gov/. *The codes associated with neuroimaging data analysis are available at:* https://github.com/cstamoulis1/Next-Generation-Neural-Data-

Analysis-NGNDA. *The codes associated with the statistical analysis are available at:* https://github.com/cstamoulis1/Brain_Social_Isolation.

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