Neural Correlates of Resilience to Trauma During Adolescence: A Multi-Modal Study

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Abstract

Background: Understanding resilience mechanisms is important for advancing early intervention strategies, yet research on the neurobiology of resilience in adolescents is limited. The present study examined the brain structural and resting-state functional connectivity (rsFC) correlates of resilience to internalizing and externalizing symptoms in a large sample of adolescents.

Methods: We analyzed longitudinal data from 8,499 adolescents (baseline mean age 9.92 ± 0.62 years) from the Adolescent Brain Cognitive Development Study. Participants were categorized as resilient, maladaptive, healthy, or vulnerable based on reports of traumatic events and internalizing/externalizing symptoms three years later. We used multinomial regressions to examine associations of brain structure and rsFC with resilience. Sex differences were also investigated.

Results: Increased odds of being resilient (relative to healthy) to both internalizing and externalizing symptoms were associated with rsFC between the dorsal and ventral attention networks and hippocampus. Resilience to internalizing symptoms was associated with rsFC between the cingulo-opercular network and hippocampus. We found the association of fusiform cortical area, and rsFC between cortical networks and hippocampus, with resilient group membership (relative to maladaptive) to be in opposite directions in males and females.

Conclusions: Resilience to internalizing and externalizing symptoms in adolescents may be associated with rsFC of networks involved in salience detection and encoding, with some differences between males and females. However, it is unclear if all findings

reflect resilience specifically, or could be better interpreted as reflecting trauma exposure or psychopathology. This underscores the need for further research into the neurobiological basis of resilience during adolescence.

Keywords: Resilience, brain, adolescence, trauma, mental health

Introduction

Childhood adversity, including experiences of neglect and abuse, is a potent risk factor for mental health problems (Kessler et al., 2010; McLaughlin et al., 2012). This is particularly relevant given the high prevalence of childhood adversity amongst adolescents; population-level studies indicate that more than 50% of children experience some form of adversity (Green et al., 2010; Kessler et al., 2010; WHO, 2020). Neurobiological alterations have been postulated to underpin the association between childhood adversity and later mental health outcomes (Berens, Jensen, & Nelson, 2017). Indeed, reviews and studies have documented the influence of childhood adversity on brain development (McLaughlin, Weissman, & Bitrán, 2019; Teicher, Samson, Anderson, & Ohashi, 2016), and risk for psychopathology (e.g., Barch et al., 2020; Chahal, Kirshenbaum, Ho, Mastrovito, & Gotlib, 2021; Hanson, Hariri, & Williamson, 2015; Whittle et al., 2022). However, while research investigating risk pathways is important (McLaughlin, 2016), this traditional 'risk-focused' approach is limited in its ability to identify factors and mechanisms that may foster resilience. Research on resilience, which is defined as a multisystem process (e.g., biological, psychological, socio-ecological) that allows an individual to successfully adapt to threats or challenges to their survival (Masten, Lucke, Nelson, & Stallworthy, 2021), is needed. Investigating the neurobiological correlates of resilience during adolescence, a period characterized by marked brain development (Fuhrmann, Knoll, & Blakemore, 2015; Rakesh, Dehestani, & Whittle, 2024) as well as the onset of several psychiatric disorders (Kessler et al., 2005; Solmi et al., 2022), is pivotal for characterizing the neurobiological factors that may promote resilience.

Neural correlates of resilience typically refer to brain changes associated with positive outcomes or the absence of negative outcomes in the context of stress or adversity (Ioannidis, Askelund, Kievit, & van Harmelen, 2020). Common methodologies to examine neural correlates of resilience include testing moderating or mediation pathways of brain markers between adversity and positive outcomes (e.g., Callaghan et al., 2019), or identifying differences in brain markers between individuals that share similar risks but differ in outcomes: resilient individuals—those with high adversity without psychopathology— and 'maladaptive' individuals—those with high adversity and psychopathology (e.g., De Bellis et al., 2015; Masten et al., 1999). However, to interpret differences as true indicators of resilience rather than mere absence of psychopathology, other suggest the need to establish an absence of differences between 'healthy' (absence of adversity and psychopathology) and 'vulnerable' (absence of adversity and presence of psychopathology) individuals (Masten et al., 1999; Miller-Lewis, Searle, Sawyer, Baghurst, & Hedley, 2013). This group approach has been widely used in the resilience literature, given its ability to parse resilience effects from general effects of adversity or psychopathology.

While several studies have investigated the neural markers of resilience during childhood and adolescence (Eaton, Cornwell, Hamilton-Giachritsis, & Fairchild, 2022; Feder, Fred-Torres, Southwick, & Charney, 2019; Masten et al., 2021), our recent systematic review of this literature showed mostly mixed findings (Zhang, Rakesh, Cropley, & Whittle, 2023). Nevertheless, there was some preliminary support that resilience to internalizing/post-traumatic Stress Disorder (PTSD) symptoms was associated with greater subcortical (i.e., amygdala and hippocampus) volumes and reduced connectivity between prefrontal and subcortical regions. Notably, most

consistent findings were from studies that leveraged the group approach. For example, adolescents resilient to PTSD symptoms, compared to those with PTSD symptoms, showed reduced connectivity between inferior frontal gyrus (IFG) and hippocampus in two studies (Li et al., 2021; Sheynin et al., 2020). Although limited research has examined the neural correlates of resilience to externalizing symptoms, work from our group suggests that increased resting-state functional connectivity (rsFC) within the salience network may confer resilience against problematic substance use among those with maltreatment experiences (Rakesh, Allen, & Whittle, 2021). Further, resilience to internalizing and externalizing symptoms was associated with increased white matter microstructure integrity in the corpus callosum projecting to frontal areas in another study (Galinowski et al., 2015). Additionally, our review noted various limitations in the literature, including a dearth of research examining sex differences in the neural correlates of resilience. Only one study was identified, which observed resilience to be associated with an opposite pattern of low-frequency fluctuations in the orbitofrontal cortex in males and females (Wang et al., 2019). Given evidence for sex differences in neurodevelopmental trajectories (Lenroot & Giedd, 2010), and in the influence of adversity on the developing brain (Bath, 2020; De Bellis & Keshavan, 2003; Rakesh, Kelly, et al., 2021; Whittle et al., 2017), further research is needed to understand potential sex differences in neural correlates of resilience.

Given the widespread alterations in brain structure, function, and connectivity associated with adversity (McLaughlin et al., 2019; Rakesh & Whittle, 2021), which have been suggested to contribute to mental health outcomes (Rakesh, Kelly, et al., 2021; Whittle, Zhang, & Rakesh, 2024), it is possible that resilience may show similarly widespread patterns. However, few studies have adopted whole-brain approaches, with

most research focusing on the structure or function of specific regions (Zhang et al., 2023). Despite evidence linking both adversity and mental health outcomes with rsFC and white matter microstructure (McLaughlin et al., 2019; Whittle et al., 2024), few studies have examined the neurobiology of resilience using resting-state functional magnetic imaging (rsfMRI) or diffusion tensor imaging (DTI). As such, to better understand the likely complex neural processes associated with resilience, holistic examination of the neural correlates of resilience across different imaging modalities using a whole-brain approach is needed.

To address these gaps in the literature, the present study aimed to examine the neural correlates of resilience to internalizing and externalizing symptoms among adolescents with childhood trauma (a severe form of adversity) by employing a multimodal whole-brain approach. Using data from the Adolescent Brain Cognitive Development (ABCD) study and the conventional group approach, we examined associations between resilience and i) cortical thickness, surface area, and subcortical volume, ii) white matter microstructure as measured by fractional anisotropy (FA), and iii) within and between network rsFC. We also examined sex differences in these associations.

Based on existing literature, we formulated the following broad predictions: i) resilience to internalizing symptoms will be associated with greater amygdala and hippocampal volume, as well as reduced connectivity between cortical and subcortical networks (Zhang et al., 2023); ii) resilience to externalizing symptoms will be associated with greater within-salience network connectivity (Rakesh, Allen, et al., 2021); and iii) resilience to internalizing and externalizing symptoms will be associated with greater FA, particularly in tracts involving frontal regions (Galinowski et al., 2015). Given the

dearth of studies examining sex differences, no specific hypotheses regarding sex differences were made.

Methods

The present study was preregistered on the Open Science Framework (https://osf.io/bauc7). Deviations from the preregistration have been fully described.

Participants

Participants were sampled from the ongoing ABCD Study (https://abcdstudy.org/; release 5.0). The study recruited ~11,800 9–10-year-old children across 21 study sites in the U.S., intending to comprehensively characterize mental health and cognitive development across adolescence. Details of the study protocol and recruitment processes have been previously documented (Barch et al., 2018; Garavan et al., 2018). Ethics approval was obtained from the Institutional Review Board of each study site. Written informed consent was obtained from parents/caregivers and all participants provided assent. All participants with available data for variables of interest (i.e., trauma and imaging data at baseline, and mental health data at three-year follow-up) were included in the present study, leading to a final sample of 8,499 participants.

Behavioral Measures

Trauma

The parent-report Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS) PTSD module was used to assess childhood trauma exposure (Kaufman et al., 1997). Trauma was operationalized as a binary variable of exposed vs. non-exposed; adolescents with any traumatic event endorsed on the K-SADS PTSD module were coded as trauma-exposed. Binarization of trauma experiences was done due to a heavy right-skewed distribution (see Supplementary Material [SM]).

Psychopathology

Adolescent internalizing and externalizing symptoms were assessed using the youth-report Brief Problem Monitor (BPM) scale, a short youth-report version of the Child Behavior Checklist (Achenbach, 1999, 2009). Given that psychopathology symptoms typically emerge later in adolescence (Solmi et al., 2022), and that third-year follow-up data was the last wave of complete data available, symptom data from this wave was used to assess mental health outcomes.

Neuroimaging

Neuroimaging data was acquired across sites using harmonized protocols (see Casey et al., 2018). MRI scanners used included 3T Siemens, Phillips, and General Electric with a 32-channel head coil. Preprocessing of images was performed using a standard pipeline by the ABCD Data Analysis and Informatics Core (see Hagler et al., 2019). Quality control recommendations provided by the ABCD Study were used, and only those that met quality control for the relevant imaging modalities were included in analyses. For further details on imaging acquisition, preprocessing, and quality control see Casey et al. (2018) and Hagler et al. (2019).

Gray matter thickness and surface area of 34 cortical regions and volumes of 7 subcortical regions were obtained using the Desikan-Killiany and ASEG parcellation atlases, respectively, in FreeSurfer version 7.1.1 (Desikan et al., 2006; Fischl et al., 2002). FA of 19 white matter tracts was derived using Atlas Track (Hagler et al., 2009). To allow for comparison with previous work, we examined FA specifically given it is the most commonly investigated metric for white matter microstructure in the literature (Zhang et al., 2023). rsFC (Fisher transformed Pearson correlation) values of 12 predefined

networks based on the Gordon parcellation scheme (Gordon et al., 2016) were extracted. This includes 12 within-network and 66 between-network connectivity metrics. Connectivity between the 12 networks and the amygdala and hippocampus were also extracted as cortical connectivity with these subcortical regions have been implicated in previous work (Zhang et al., 2023). In total, we examined 196 imaging variables (75 gray matter, 19 white matter, and 102 rsFC variables).

Statistical Analyses

Outcome Group Categorization

As preregistered, we first attempted to classify groups based on trauma exposure at baseline and symptoms at the third-year follow-up using Latent Profile Analysis, a data-driven approach to observe characteristically distinct profiles within a sample (Weller, Bowen, & Faubert, 2020). However, groups were unidentifiable due to model convergence issues. Efforts to transform the data to similar scales and reduce skewness did not mitigate these issues. We then followed our preregistered plan and defined our outcome groups using established symptom cut-offs provided for the BPM (i.e., high symptoms = T-score > 65, Achenbach, McConaughy, Ivanova, & Rescorla, 2011) and trauma exposure (exposed vs. non-exposed). Based on previous work that has also adopted the group approach (e.g., Burt et al., 2016), we classified adolescents into profiles of *resilient* (trauma-exposed, low symptoms), *maladaptive* (trauma-exposed, high symptoms), *vulnerable* (trauma non-exposed, high symptoms), and *healthy controls* (trauma non-exposed, low symptoms). Groups were created separately for internalizing and externalizing symptoms (see Table 1 for group Ns).

We acknowledge that certain group labels may carry connotations of deficiency; however, our choice of terminology is intended solely to maintain consistency with the existing literature (e.g., Burt et al., 2016; Masten et al., 1999). These terms are used to describe participants' experience of adversity and mental health within this specific research context and are not meant to reflect their inherent abilities or functioning.

Main Analyses

Multinomial logistic regression models were conducted in R version 4.3.0 (R Core Team, 2022) using the VGAM package version 1.1-8 (Yee, 2010). Given that the VGAM package cannot model random effects, one child per family was randomly selected account for family structure. In addition, scanner was included as a fixed effect in models. Brain variables were standardized and included as the predictor in separate models and the outcome groups (as a categorical variable) were modeled as the response variable. The resilient group was set as the reference group in all models, allowing comparison between the resilient group and every other group (i.e., maladaptive, vulnerable, and healthy). We corrected for multiple comparisons using the false discovery rate (FDR). FDR correction was applied to account for multiple ROIs within each imaging modality (i.e., structural MRI [sMRI], DTI, and rsfMRI) and multiple group comparisons (resilient vs healthy, resilient vs vulnerable, resilient vs maladaptive) (pFDR < .05; 75 comparisons for gray matter, 19 comparisons for white matter, and 102 comparisons for rsFC; Benjamini & Hochberg, 1995). To examine whether neurobiological correlates of resilience differed by sex, analyses were repeated with an additional interaction term between sex and each brain variable with the same FDR correction applied. See SM for model equations.

To examine whether the observed significant results truly reflect resilience-specific effects, additional post-hoc logistic models were conducted to examine differences between all groups. Six post-hoc models were conducted for each significant finding, which examined the difference between maladaptive, vulnerable, and healthy groups (in addition to differences between these groups and the resilient group). No multiple comparison correction was applied for post-hoc analyses.

Our preregistration specified the use of within-sample split-half replication to test the replicability of our results given the power afforded by the ABCD sample (Rakesh, Zalesky, & Whittle, 2021, 2022; Saragosa-Harris et al., 2022). This was not possible due to the small sample sizes of individual groups (e.g., maladaptive group size varied between 47 to 129 for discovery and replication samples). As such, we primarily interpreted the results from analyses using the full sample. We explain the issue in detail in the SM S3 with the split-half replication findings presented for transparency purposes.

Covariates

We covaried for age, sex, socioeconomic status (SES), and scanner type in all models. Age, sex, and SES were taken from baseline demographics data. Household SES was operationalized as average parental education attainment for both caregivers. We chose parental education over other SES indicators (e.g., household income) based on prior research showing that it is associated with resilience in young people (Reiss et al., 2019). Data for one caregiver was used when data for both was unavailable. In addition, framewise displacement was covaried for in models that included rsFC variables, and

total brain volume was covaried for in models that analyzed subcortical volume and cortical surface area (Mills et al., 2016; Parkes, Fulcher, Yücel, & Fornito, 2018).

Sensitivity Analyses

Preregistered sensitivity analyses with site and race added as additional covariates were not conducted due to the following reasons. First, prior work has shown that race associated brain differences in the ABCD study may be accounted for by childhood adversity, including trauma exposure (Dumornay, Lebois, Ressler, & Harnett, 2023). Given the confounding nature of race and childhood adversity in the ABCD sample, including race in models makes it challenging to disentangle the effects of resilience from race. Second, studies show a high overlap between site and scanner type in the ABCD study, and covarying for site explained minimal additional variance when scanner type has been accounted for (Rakesh et al., 2022; Taylor, Cooper, Jackson, & Barch, 2020). As such, analyses were conducted with scanner type (an important covariate for imaging analyses), but not site, as a covariate. Following prior recommendations to report adjusted and unadjusted models, we conducted analyses without the inclusion of SES as a covariate (Hyatt et al., 2020).

Results

Demographic Information

8,499 unique participants were included in analyses, with sample sizes varying between modalities: gray matter (n = 7,526), white matter (n = 6,959), and rsFC (n = 6,485). See Table 1 for sample demographic information. Notably, there was considerable overlap between the internalizing and externalizing groups, with 91% of those resilient to internalizing symptoms also showing resilience to externalizing symptoms.

Main Analyses

Gray or white matter structure did not significantly predict resilient group membership. Increased predicted odds of being resilient relative to being healthy to internalizing symptoms were associated with i) increased connectivity between the dorsal attention network (DAN) and ventral attention network (VAN), ii) decreased connectivity between the cingulo-opercular network (CON) and hippocampus, and iii) decreased connectivity between the VAN and hippocampus. Similarly, increased predicted odds of being resilient relative to being healthy for externalizing symptoms were also associated with increased DAN – VAN connectivity, and decreased VAN – hippocampus connectivity. See Table 2 for relevant statistics.

Post-hoc model results showed that there were no additional group differences (i.e., healthy vs maladaptive, healthy vs vulnerable, maladaptive vs vulnerable) for any of the previously implicated brain variables (see Figure 1). Of note, in these uncorrected analyses, increased DAN – VAN connectivity was associated with increased predicted odds of being resilient relative to being vulnerable to internalizing symptoms.

Sex moderated the association between several brain variables and resilient group membership for internalizing but not externalizing symptoms, and only in models that predicted maladaptive relative to resilient group membership (see Table 2). Specifically, we observed significant interaction effects between sex and i) fusiform surface area, ii) connectivity between the sensorimotor hand network (SMN [H]) and the visual network (VN), and iii) connectivity between the retrosplenial temporal network (RTN) and the hippocampus. Post-hoc models were run in males and females separately to interpret the sex difference (see Table 3). Notably, the direction of effect was opposite in males and females for all results. For example, increased fusiform surface area and increased RTN – hippocampus connectivity was associated with higher odds of being resilient relative to being maladaptive in males, but lower odds in females. For most implicated brain variables, there were no differences between the vulnerable and healthy groups, except for the SMN (H) – VN connectivity in females (see SM Table 5).

For detailed results of non-significant findings, see SM Tables S7-8.

Sensitivity Analyses

Significant results from the main analysis remained stable without SES as a covariate. Moreover, we observed additional statistically significant findings for the prediction of resilient group membership (for both internalizing and externalizing groups) when SES was not included (see SM S9-10). Note that when main and sensitivity analyses were conducted across discovery and replication samples, no findings were replicated, potentially due to the small sample size in some outcome groups as discussed.

Discussion

This preregistered study leveraged a large sample and multimodal neuroimaging to examine the neural correlates of resilience to trauma-related internalizing and externalizing symptoms among adolescents. Additionally, we explored potential sex differences in these associations. Hypotheses were partially supported. We found resilience to be associated with rsFC but not gray or white matter structure. Specifically, we found higher predicted odds of being resilient to both internalizing and externalizing symptoms (relative to being healthy) to be associated with increased DAN – VAN connectivity and decreased VAN – hippocampus connectivity. Increased predicted odds of being resilient to internalizing symptoms (relative to being healthy) were additionally associated with decreased CON – hippocampus connectivity. However, post-hoc analyses suggest that these associations may not reflect resilience-specific markers. Moreover, we observed several sex differences in the neural correlates of resilience to internalizing symptoms. Specifically, the direction of the association of fusiform cortical area, SMN (H) – VN connectivity, and RTN – hippocampus connectivity with resilience relative to maladaptive was opposite in males and females. These associations, aside from the SMN (H) – VN connectivity in females, may reflect resilience specific sex effects given the lack of differences between vulnerable and healthy control groups.

Contrary to hypotheses, we did not find evidence for associations of resilience with amygdala and hippocampal volume, nor with white matter microstructure or brain structure more generally. Of note, previous studies reporting associations between resilience and larger amygdala and hippocampal volume (Li et al., 2021; Morey, Haswell, Hooper, & De Bellis, 2016; Ross et al., 2021) examined resilience specifically to PTSD, which may explain our discrepant findings and suggest that increased amygdala and

hippocampal volume is a marker for resilience to PTSD symptoms specifically. Outside of the amygdala and hippocampus, evidence on structure correlates of resilience is mixed, with some studies reporting similar null results for gray and white matter structure in adolescents (Keding et al., 2021; Kim, Farber, Knodt, & Hariri, 2019; Lu et al., 2017). These mixed findings underscore the need for studies to further investigate resilience in association with brain structure.

Our connectivity findings provide preliminary insights into the possible neural correlates of resilience. These findings are partially consistent with our hypotheses and findings from our review, which highlighted an association between resilience to PTSD symptoms and decreased rsFC between the IFG (a part of the VAN) and hippocampus (Zhang et al., 2023). This finding was postulated to reflect a reduced need to regulate fear responses or an intact ability to orient attention (Li et al., 2021; Sheynin et al., 2020). As such, our findings may suggest a possible role for this circuitry, important for attention regulation and salience detection/encoding (Preston & Eichenbaum, 2013; Sheynin et al., 2020; Vossel, Geng, & Fink, 2014), in adolescent resilience to psychopathology more generally.

Importantly, however, it is unclear whether these findings are specific to resilience or driven by other factors such as trauma or differences in symptoms. To conclude an effect is specific to resilience, differences between resilient and maladaptive groups and no differences between healthy and vulnerable groups are necessary (Masten et al., 1999; Miller-Lewis et al., 2013). However, our post-hoc analyses showed that connectivity did not differ between resilient and maladaptive groups. This limits our ability to interpret the observed effects as being resilience specific. For example, previous studies have also

shown a negative association between childhood adversity and hippocampus – PFC connectivity (McLaughlin et al., 2019). Our findings may therefore reflect neural correlates of childhood trauma as opposed to resilience. Future studies should examine differences in trauma exposed versus non-exposed groups to clarify this. It should be noted that our inability to detect differences between the resilient and maladaptive groups may be due to the relatively small sample size of the maladaptive group (i.e., 94 to 116 individuals for externalizing outcomes and 228 to 258 for internalizing outcomes). Larger sample sizes in the maladaptive group will be needed to investigate these associations further.

Additionally, we observed significant overlap between the brain variables related to resilience against externalizing and internalizing symptoms. This is unsurprising given that 91% of individuals that were resilient to internalizing symptoms were also resilient to externalizing symptoms. This high overlap precludes us from commenting on the specificity of the findings to internalizing, externalizing, or comorbid presentations of internalizing and externalizing symptoms. Future work with lower overlap between resilience groups is needed to explore this further. Nevertheless, the high overlap between groups provides evidence that supports the idea that resilience is unlikely to be disorder specific (van Rooij et al., 2024; Walsh, Dawson, & Mattingly, 2010).

The present study also highlighted possible sex differences in the neural correlates of resilience to internalizing symptoms. Specifically, we noted that the association of fusiform surface area, SMN (H) – VN connectivity, and RTN – hippocampus connectivity with resilience (relative to being maladaptive) in males and females were in opposite directions. Importantly, given we did not observe differences between the healthy and

vulnerable group (except for the SMN (H) - VN connectivity), these findings may reflect sex differences in the neural correlates of resilience to trauma. Considering the roles of the implicated regions/networks in processing and responding to visual/environmental cues as well as memory formation (Hunsaker & Kesner, 2018; Uddin, Yeo, & Spreng, 2019), we speculate that resilience to internalizing symptoms may entail different patterns of involvement of these processes between females and males. These regions/networks were not associated with resilience in the whole sample. As such, these findings may reflect distinct neural underpinnings of resilience in males and females during adolescence. Our findings underscore the need for future work to consider the role of sex when investigating the neurobiology of resilience during adolescence.

Although we observed additional neural features that may be associated with resilience in sensitivity analyses not adjusting for SES, we do not interpret these findings for the following reasons. SES is a confounder (Wysocki, Lawson, & Rhemtulla, 2022) as it influences both resilience (Qiu et al., 2021; Reiss et al., 2019) and brain structure and function (Buthmann et al., 2024; Michael et al., 2023; Rakesh & Whittle, 2021; Rakesh, Zalesky, et al., 2021; Rakesh et al., 2022; Taylor et al., 2020). Models that account for SES as a confounder can therefore provide more accurate estimates of the association of brain structure and connectivity with resilience.

While this study has several strengths, including a large sample size and the use of multimodal neuroimaging, interpretations must be considered in light of limitations. First, we used a single approach to operationalize resilience. While the utilized group approach is common in the literature, and allows for parsing of resilience from

trauma/psychopathology effecs, this method does not allow exploration of individual differences (Kalisch et al., 2021; Miller-Lewis et al., 2013). Second, the present study focused on resilience to poor mental health outcomes and did not examine other social, academic, and cognitive domains of functioning. Recent work has highlighted that resilience may be present across various functioning domains (Miller-Graff, 2022). Given that past work on the neural correlates of resilience has yielded different findings when examining cross-domain resilience (e.g., Burt et al., 2016) versus domain-specific resilience (e.g., studies reviewed in Zhang et al., 2023), future work is therefore needed to further explore the domain specificity of the neural correlates of resilience beyond mental health. Third, the dichotomous approach for trauma exposure and mental health symptoms undermined our ability to examine more nuanced relationships between adversity, brain, and mental health outcomes. For example, it limited our ability to examine the association of type, intensity, and number of traumatic experiences with resilience, which have been suggested as important factors to consider for adversity research (see McLaughlin et al., 2019). Further, the low incidence of several of the trauma types and clinically high symptoms in the ABCD sample resulted in relatively small sample sizes of the maladaptive and vulnerable groups. This additionally constrained our ability to ascertain whether the observed effects truly reflect resilience. Future research may benefit from more targeted recruitment of 'maladaptive' and 'vulnerable' individuals. Finally, we examined the independent contribution of individual brain features to resilience. Such an approach overlooks potential interactions and interdependencies among different brain features that may jointly contribute to resilience. Future investigations should use multivariate methodologies that allow for interactions and non-linear relationships to elucidate the neural correlates of resilience.

Conclusions

In sum, the present study comprehensively examined the neural correlates of resilience to both internalizing and externalizing symptoms, across ~200 brain features and three imaging modalities. We found preliminary support for rsFC of the DAN, VAN, CON, and hippocampus being implicated in resilience. However, given the lack of differences between the resilient and maladaptive groups, it is unclear whether the neural findings truly reflect resilience versus markers of trauma exposure or psychopathology. Importantly, we observed potential sex differences in structural and rsFC neural markers that may specifically reflect resilience. Future work that leverages complex multivariate methods may be beneficial in uncovering the intricate relationship between neural properties and resilience during adolescence, as well as related sex differences.

References

Achenbach, T. M. (1999). The Child Behavior Checklist and related instruments. *The use of psychological testing for treatment planning and outcomes assessment, 2nd ed.* (pp. 429–466). Mahwah, NJ, US: Lawrence Erlbaum Associates Publishers.

Achenbach, T. M. (2009). *The Achenbach System of Empirically Based Assessemnt (ASEBA): Development, Findings, Theory, and Applications.* Burlington, VT: University of Vermont Research Center for Children, Youth, & Families.

Achenbach, T. M., McConaughy, S. H., Ivanova, M. Y., & Rescorla, L. A. (2011). Manual for the ASEBA Brief Problem Monitor™ (BPM).

Barch, D. M., Albaugh, M. D., Avenevoli, S., Chang, L., Clark, D. B., Glantz, M. D., Hudziak, J. J., et al. (2018). Demographic, physical and mental health assessments in the adolescent brain and cognitive development study: Rationale and description. *Developmental Cognitive Neuroscience*, The Adolescent Brain Cognitive Development (ABCD) Consortium: Rationale, Aims, and Assessment Strategy, *32*, 55–66.

Barch, D. M., Shirtcliff, E. A., Elsayed, N. M., Whalen, D., Gilbert, K., Vogel, A. C., Tillman, R., et al. (2020). Testosterone and hippocampal trajectories mediate relationship of poverty to emotion dysregulation and depression. *Proceedings of the National Academy of Sciences of the United States of America*, *117*(36), 22015–22023. NLM (Medline).

Bath, K. G. (2020). Synthesizing Views to Understand Sex Differences in Response to Early Life Adversity. *Trends in Neurosciences*, *43*(5), 300–310.

Benjamini, Y., & Hochberg, Y. (1995). Controlling the False Discovery Rate: A Practical and Powerful Approach to Multiple Testing. *Journal of the Royal Statistical Society: Series B (Methodological)*, *57*(1), 289–300.

Berens, A. E., Jensen, S. K. G., & Nelson, C. A. (2017). Biological embedding of childhood adversity: From physiological mechanisms to clinical implications. *BMC Medicine*, *15*(1), 1–12. BioMed Central Ltd.

Burt, K. B., Whelan, R., Conrod, P. J., Banaschewski, T., Barker, G. J., Bokde, A. L. W., Bromberg, U., et al. (2016). Structural brain correlates of adolescent resilience. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *57*(11), 1287–1296. John Wiley & Sons, Ltd.

Buthmann, J. L., Uy, J. P., Miller, J. G., Yuan, J. P., Coury, S. M., Ho, T. C., & Gotlib, I. H. (2024). Neighborhood disadvantage and parenting predict longitudinal clustering of uncinate fasciculus microstructural integrity and clinical symptomatology in adolescents. *Developmental Cognitive Neuroscience*, *66*.

Callaghan, B. L., Gee, D. G., Gabard-Durnam, L., Telzer, E. H., Humphreys, K. L., Goff, B., Shapiro, M., et al. (2019). Decreased Amygdala Reactivity to Parent Cues Protects Against Anxiety Following Early Adversity: An Examination Across 3 Years. *Biological psychiatry. Cognitive neuroscience and neuroimaging*, *4*(7), 664–671. United States.

Casey, B. J., Cannonier, T., Conley, M. I., Cohen, A. O., Barch, D. M., Heitzeg, M. M., Soules, M. E., et al. (2018). The Adolescent Brain Cognitive Development (ABCD) study: Imaging acquisition across 21 sites. *Developmental Cognitive Neuroscience*, *32*, 43–54. Elsevier.

Chahal, R., Kirshenbaum, J. S., Ho, T. C., Mastrovito, D., & Gotlib, I. H. (2021). Greater age-related changes in white matter morphometry following early life stress: Associations with internalizing problems in adolescence. *Developmental Cognitive Neuroscience*, *47*.

De Bellis, M. D., Hooper, S. R., Chen, S. D., Provenzale, J. M., Boyd, B. D., Glessner, C. E., Macfall, J. R., et al. (2015). Posterior structural brain volumes differ in maltreated youth with and without chronic posttraumatic stress disorder. *Development and Psychopathology*, *27*(4), 1555–1576. Cambridge University Press.

De Bellis, M. D., & Keshavan, M. S. (2003). Sex differences in brain maturation in maltreatment-related pediatric posttraumatic stress disorder. *Neuroscience & Biobehavioral Reviews*, *27*(1–2), 103–117.

Desikan, R. S., Ségonne, F., Fischl, B., Quinn, B. T., Dickerson, B. C., Blacker, D., Buckner, R. L., et al. (2006). An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. *NeuroImage*, *31*(3), 968–980.

Dumornay, N. M., Lebois, L. A. M., Ressler, K. J., & Harnett, N. G. (2023). Racial Disparities in Adversity During Childhood and the False Appearance of Race-Related Differences in Brain Structure. *American Journal of Psychiatry*, *180*(2), 127–138. American Psychiatric Publishing.

Eaton, S., Cornwell, H., Hamilton-Giachritsis, C., & Fairchild, G. (2022). Resilience and young people's brain structure, function and connectivity: A systematic review. *Neuroscience and Biobehavioral Reviews*, *132*, 936–956.

Feder, A., Fred-Torres, S., Southwick, S. M., & Charney, D. S. (2019). The Biology of Human Resilience: Opportunities for Enhancing Resilience Across the Life Span. *Biological psychiatry*, *86*(6), 443–453. United States.

Fischl, B., Salat, D. H., Busa, E., Albert, M., Dieterich, M., Haselgrove, C., Van Der Kouwe, A., et al. (2002). Whole Brain Segmentation: Automated Labeling of Neuroanatomical Structures in the Human Brain. *Neuron*, *33*(3), 341–355.

Fuhrmann, D., Knoll, L. J., & Blakemore, S. J. (2015). Adolescence as a Sensitive Period of Brain Development. *Trends in Cognitive Sciences*, *19*(10), 558–566. Elsevier Current Trends.

Galinowski, A., Miranda, R., Lemaitre, H., Paillère Martinot, M. L., Artiges, E., Vulser, H., Goodman, R., et al. (2015). Resilience and corpus callosum microstructure in adolescence. *Psychological Medicine*, *45*(11), 2285–2294. Cambridge University Press.

Garavan, H., Bartsch, H., Conway, K., Decastro, A., Goldstein, R. Z., Heeringa, S., Jernigan, T., et al. (2018). Recruiting the ABCD sample: Design considerations and procedures. *Developmental Cognitive Neuroscience*, *32*, 16–22. Elsevier.

Gordon, E. M., Laumann, T. O., Adeyemo, B., Huckins, J. F., Kelley, W. M., & Petersen, S. E. (2016). Generation and Evaluation of a Cortical Area Parcellation from Resting-State Correlations. *Cerebral Cortex*, *26*(1), 288–303.

Green, J. G., Mclaughlin, K. A., Berglund, P. A., Gruber, M. J., Sampson, N. A., Zaslavsky, A. M., & Kessler, R. C. (2010). Childhood Adversities and Adult Psychiatric Disorders in the National Comorbidity Survey Replication I Associations With First Onset of DSM-IV Disorders. *Arch Gen Psychiatry*, *67*(2), 113–123.

Hagler, D. J., Ahmadi, M. E., Kuperman, J., Holland, D., McDonald, C. R., Halgren, E., & Dale, A. M. (2009). Automated white-matter tractography using a probabilistic diffusion tensor atlas: Application to temporal lobe epilepsy. *Human Brain Mapping*, *30*(5), 1535–1547.

Hagler, D. J., Hatton, SeanN., Cornejo, M. D., Makowski, C., Fair, D. A., Dick, A. S., Sutherland, M. T., et al. (2019). Image processing and analysis methods for the Adolescent Brain Cognitive Development Study. *NeuroImage*, *202*, 116091.

Hanson, J. L., Hariri, A. R., & Williamson, D. E. (2015). Blunted ventral striatum development in adolescence reflects emotional neglect and predicts depressive symptoms. *Biological psychiatry*, *78*(9), 598–605.

Hunsaker, M. R., & Kesner, R. P. (2018). Unfolding the cognitive map: The role of hippocampal and extra-hippocampal substrates based on a systems analysis of spatial processing. *Neurobiology of Learning and Memory*, *147*, 90–119.

Hyatt, C. S., Owens, M. M., Crowe, M. L., Carter, N. T., Lynam, D. R., & Miller, J. D. (2020). The quandary of covarying: A brief review and empirical examination of covariate use in structural neuroimaging studies on psychological variables. *NeuroImage*, *205*, 116225.

Ioannidis, K., Askelund, A. D., Kievit, R. A., & van Harmelen, A.-L. (2020). The complex neurobiology of resilient functioning after childhood maltreatment. *BMC medicine*, *18*(1), 32.

Kalisch, R., Köber, G., Binder, H., Ahrens, K. F., Basten, U., Chmitorz, A., Choi, K. W., et al. (2021). The Frequent Stressor and Mental Health Monitoring-Paradigm: A Proposal for the Operationalization and Measurement of Resilience and the Identification of Resilience Processes in Longitudinal Observational Studies. *Frontiers in Psychology*, *12*.

Kaufman, J., Birmaher, B., Brent, D., Rao, U., Flynn, C., Moreci, P., Williamson, D., et al. (1997). Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL): Initial reliability and validity data. *Journal of the American Academy of Child and Adolescent Psychiatry*, *36*(7), 980–988.

Keding, T. J., Heyn, S. A., Russell, J. D., Zhu, X., Cisler, J., McLaughlin, K. A., & Herringa, R. J. (2021). Differential Patterns of Delayed Emotion Circuit Maturation in Abused Girls

With and Without Internalizing Psychopathology. *The American Journal of Psychiatry*, *178*(11), 1026–1036. American Psychiatric Association Washington, DC.

Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005). Lifetime Prevalence and Age-of-Onset Distributions of. *Arch Gen Psychiatry*, *62*(June), 593–602.

Kessler, R. C., McLaughlin, K. A., Green, J. G., Gruber, M. J., Sampson, N. A., Zaslavsky, A. M., Aguilar-Gaxiola, S., et al. (2010). Childhood adversities and adult psychopathology in the WHO World Mental Health Surveys. *The British Journal of Psychiatry*, *197*(5), 378. Royal College of Psychiatrists.

Kim, M. J., Farber, M. J., Knodt, A. R., & Hariri, A. R. (2019). Corticolimbic circuit structure moderates an association between early life stress and later trait anxiety. *NeuroImage. Clinical*, *24*, 102050. Netherlands.

Lenroot, R. K., & Giedd, J. N. (2010). Sex differences in the adolescent brain. *Brain and cognition*, *72*(1), 46. NIH Public Access.

Li, L., Pan, N., Zhang, L., Lui, S., Huang, X., Xu, X., Wang, S., et al. (2021). Hippocampal subfield alterations in pediatric patients with post-traumatic stress disorder. *Social cognitive and affective neuroscience*, *16*(3), 334–344. England.

Lu, S., Gao, W., Wei, Z., Wang, D., Hu, S., Huang, M., Xu, Y., et al. (2017). Intrinsic brain abnormalities in young healthy adults with childhood trauma: A resting-state functional magnetic resonance imaging study of regional homogeneity and functional connectivity. *Australian and New Zealand Journal of Psychiatry*, *51*(6), 614–623.

Masten, A. S., Hubbard, J. J., Gest, S. D., Tellegen, A., Garmezy, N., & Ramirez, M. (1999). Competence in the context of adversity: Pathways to resilience and maladaptation

from childhood to late adolescence. *Development and Psychopathology*, *11*(1), 143–169. Cambridge University Press.

Masten, A. S., Lucke, C. M., Nelson, K. M., & Stallworthy, I. C. (2021). Resilience in Development and Psychopathology: Multisystem Perspectives. *Annual Review of Clinical Psychology*, *17*, 521–549.

McLaughlin, K. A. (2016). Future Directions in Childhood Adversity and Youth Psychopathology. *Journal of Clinical Child & Adolescent Psychology*, *45*(3), 361–382. Routledge.

McLaughlin, K. A., Greif Green, J., Gruber, M. J., Sampson, N. A., Zaslavsky, A. M., & Kessler, R. C. (2012). Childhood adversities and first onset of psychiatric disorders in a national sample of US adolescents. *Archives of General Psychiatry*, *69*(11), 1151–1160.

McLaughlin, K. A., Weissman, D., & Bitrán, D. (2019). Childhood Adversity and Neural Development: A Systematic Review. *Annual Review of Developmental Psychology*, *1*(1), 277–312.

Michael, C., Tillem, S., Sripada, C. S., Burt, S. A., Klump, K. L., & Hyde, L. W. (2023). Neighborhood poverty during childhood prospectively predicts adolescent functional brain network architecture. *Developmental Cognitive Neuroscience*, *64*.

Miller-Graff, L. E. (2022). The Multidimensional Taxonomy of Individual Resilience. *Trauma, Violence, & Abuse*, *23*(2), 660–675.

Miller-Lewis, L. R., Searle, A. K., Sawyer, M. G., Baghurst, P. A., & Hedley, D. (2013). Resource factors for mental health resilience in early childhood: An analysis with multiple methodologies. *Child and Adolescent Psychiatry and Mental Health*, *7*(1), 1–23. BioMed Central.

Mills, K. L., Goddings, A.-L., Herting, M. M., Meuwese, R., Blakemore, S.-J., Crone, E. A., Dahl, R. E., et al. (2016). Structural brain development between childhood and adulthood: Convergence across four longitudinal samples. *NeuroImage*, *141*, 273–281.

Morey, R. A., Haswell, C. C., Hooper, S. R., & De Bellis, M. D. (2016). Amygdala, hippocampus, and ventral medial prefrontal cortex volumes differ in maltreated youth with and without chronic posttraumatic stress disorder. *Neuropsychopharmacology*, *41*(3), 791–801.

Parkes, L., Fulcher, B., Yücel, M., & Fornito, A. (2018). An evaluation of the efficacy, reliability, and sensitivity of motion correction strategies for resting-state functional MRI. *NeuroImage*, *171*, 415–436.

Preston, A. R., & Eichenbaum, H. (2013). Interplay of Hippocampus and Prefrontal Cortex in Memory. *Current Biology*, *23*(17), 764–773. Cell Press.

Qiu, Y., Huang, Y., Wang, Y., Ren, L., Jiang, H., Zhang, L., & Dong, C. (2021). The Role of Socioeconomic Status, Family Resilience, and Social Support in Predicting Psychological Resilience Among Chinese Maintenance Hemodialysis Patients. *Frontiers in Psychiatry*, *12*.

R Core Team. (2022). *R: A Language and Environment for Statistical Computing*. Vienna, Austria: R Foundation for Statistical Computing. Retrieved from https://www.R-project.org/

Rakesh, D., Allen, N. B., & Whittle, S. (2021). Longitudinal changes in within-salience network functional connectivity mediate the relationship between childhood abuse and neglect, and mental health during adolescence. *Psychological Medicine*, 1–13. Cambridge University Press.

Rakesh, D., Dehestani, N., & Whittle, S. (2024). Brain development. In W. Troop-Gordon & E. W. Neblett (Eds.), *Encyclopedia of Adolescence* (2nd ed., pp. 43–57). Oxford: Academic Press.

Rakesh, D., Kelly, C., Vijayakumar, N., Zalesky, A., Allen, N. B., & Whittle, S. (2021). Unraveling the Consequences of Childhood Maltreatment: Deviations From Typical Functional Neurodevelopment Mediate the Relationship Between Maltreatment History and Depressive Symptoms. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *6*(3), 329–342. Elsevier.

Rakesh, D., & Whittle, S. (2021). Socioeconomic status and the developing brain—A systematic review of neuroimaging findings in youth. *Neuroscience and Biobehavioral Reviews*, *130*, 379–407.

Rakesh, D., Zalesky, A., & Whittle, S. (2021). Similar but distinct – Effects of different socioeconomic indicators on resting state functional connectivity: Findings from the Adolescent Brain Cognitive Development (ABCD) Study®. *Developmental Cognitive Neuroscience*, *51*, 101005.

Rakesh, D., Zalesky, A., & Whittle, S. (2022). Assessment of Parent Income and Education, Neighborhood Disadvantage, and Child Brain Structure. *JAMA Network Open*, *5*(8), e2226208.

Reiss, F., Meyrose, A.-K., Otto, C., Lampert, T., Klasen, F., & Ravens-Sieberer, U. (2019). Socioeconomic status, stressful life situations and mental health problems in children and adolescents: Results of the German BELLA cohort-study. *PLOS ONE*, *14*(3), e0213700. Public Library of Science.

van Rooij, S. J. H., Santos, J. L., Hinojosa, C. A., Ely, T. D., Harnett, N. G., Murty, V. P., Lebois, L. A. M., et al. (2024). Defining the r factor for post-trauma resilience and its neural predictors. *Nature Mental Health*, 1–14. Nature Publishing Group.

Ross, M. C., Dvorak, D., Sartin-Tarm, A., Botsford, C., Cogswell, I., Hoffstetter, A., Putnam, O., et al. (2021). Gray matter volume correlates of adolescent posttraumatic stress disorder: A comparison of manual intervention and automated segmentation in FreeSurfer. *Psychiatry research. Neuroimaging*, *313*, 111297. Netherlands.

Saragosa-Harris, N. M., Chaku, N., MacSweeney, N., Guazzelli Williamson, V., Scheuplein, M., Feola, B., Cardenas-Iniguez, C., et al. (2022). A practical guide for researchers and reviewers using the ABCD Study and other large longitudinal datasets. *Developmental Cognitive Neuroscience*, *55*, 101115.

Sheynin, J., Duval, E. R., Lokshina, Y., Scott, J. C., Angstadt, M., Kessler, D., Zhang, L., et al. (2020). Altered resting-state functional connectivity in adolescents is associated with PTSD symptoms and trauma exposure. *NeuroImage. Clinical*, *26*, 102215. Netherlands.

Solmi, M., Radua, J., Olivola, M., Croce, E., Soardo, L., Salazar de Pablo, G., Il Shin, J., et al. (2022). Age at onset of mental disorders worldwide: Large-scale meta-analysis of 192 epidemiological studies. *Molecular Psychiatry*, *27*(1), 281–295.

Taylor, R. L., Cooper, S. R., Jackson, J. J., & Barch, D. M. (2020). Assessment of Neighborhood Poverty, Cognitive Function, and Prefrontal and Hippocampal Volumes in Children. *JAMA network open*, *3*(11), e2023774. United States.

Teicher, M. H., Samson, J. A., Anderson, C. M., & Ohashi, K. (2016). The effects of childhood maltreatment on brain structure, function and connectivity. *Nature Reviews Neuroscience*, *17*(10), 652–666.

Uddin, L. Q., Yeo, B. T. T., & Spreng, R. N. (2019). Towards a universal taxonomy of macro-scale functional human brain networks. *Brain topography*, *32*(6), 926–942.

Vossel, S., Geng, J. J., & Fink, G. R. (2014). Dorsal and Ventral Attention Systems. *The Neuroscientist*, *20*(2), 150–159.

Walsh, W. A., Dawson, J., & Mattingly, M. J. (2010). How are we measuring resilience following childhood maltreatment? Is the research adequate and consistent? What is the impact on research, practice, and policy? *Trauma, Violence, and Abuse*, *11*(1), 27–41.

Wang, S., Yang, C., Zhao, Y., Lai, H., Zhang, L., & Gong, Q. (2019). Sex-linked neurofunctional basis of psychological resilience in late adolescence: A resting-state functional magnetic resonance imaging study. *European Child & Adolescent Psychiatry*, *29*(8), 1075–1087. Springer.

Weller, B. E., Bowen, N. K., & Faubert, S. J. (2020). Latent Class Analysis: A Guide to Best Practice. *Journal of Black Psychology*, *46*(4), 287–311. SAGE Publications Inc.

Whittle, S., Pozzi, E., Rakesh, D., Kim, J. M., Yap, M. B. H., Schwartz, O. S., Youssef, G., et al. (2022). Harsh and Inconsistent Parental Discipline Is Associated With Altered Cortical Development in Children. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *7*(10), 989–997.

Whittle, S., Simmons, J. G., Hendriksma, S., Vijayakumar, N., Byrne, M. L., Dennison, M., & Allen, N. B. (2017). Childhood maltreatment, psychopathology, and the development of hippocampal subregions during adolescence. *Brain and behavior*, *7*(2), e00607. United States.

Whittle, S., Zhang, L., & Rakesh, D. (2024). Environmental and neurodevelopmental contributors to youth mental illness. *Neuropsychopharmacology*, 1–10. Nature Publishing Group.

WHO. (2020). Child maltreatment. Retrieved January 4, 2022, from https://www.who.int/news-room/fact-sheets/detail/child-maltreatment

Wysocki, A. C., Lawson, K. M., & Rhemtulla, M. (2022). Statistical Control Requires Causal Justification. *Advances in Methods and Practices in Psychological Science*, *5*(2), 25152459221095823. SAGE Publications Inc.

Yee, T. W. (2010). The VGAM Package for Categorical Data Analysis. *Journal of Statistical Software*, *32*, 1–34.

Zhang, L., Rakesh, D., Cropley, V., & Whittle, S. (2023). Neurobiological correlates of resilience during childhood and adolescence – A systematic review. *Clinical Psychology Review*, *105*, 102333.

Tables and Figures

Table 1.

Demographic Information

Characteristic	N (%); Mean (SD)
N (Female)	8,499 (48%)
Age at Baseline (years)	9.92 (0.62)
Age at T3 Follow-up	12.92 (0.64)
Average Parental Education (years)	15.32 (2.56)
Internalizing Groups (N); internalizing symptoms (Mean)	
Maladaptive	305 (3.6%); 68.1 (2.61)
Vulnerable	453 (5.3%); 68.2 (2.82)
Healthy	5,045 (59%); 52.4 (3.65)
Resilient	2,696 (32%); 52.6 (3.81)
Externalizing Groups (N); externalizing symptoms (Mean)	
Maladaptive	134 (1.6%); 67.6 (1.62)
Vulnerable	144 (1.7%); 67.3 (1.70)
Healthy	5,354 (63%); 51.4 (3.09)
Resilient	2,867 (34%); 51.6 (3.18)
Race (N)	
African American	1,081 (13%)
Asian	186 (2.2%)
Hispanic	1,639 (19%)
White	4,713 (55%)
Other	880 (10%)
Trauma Total	0.49 (0.90)
Binary Trauma Exposure (N)	

Non-Exposed	5,498 (65%)
Exposed	3,001 (35%)
Internalizing Symptoms (T Score)	53.9 (5.7)
Externalizing Symptoms (T Score)	52.0 (4.2)

Note. Symptom T score has a minimum of 50 which reflects a raw score of 0.

Table 2

Results for significant brain variable effects and sex by brain interaction effects

Brain variables	B	95% CI	Odds	Odds 95% CI	*p*	*p*FDR
Internalizing						
DAN – VAN	-0.094	[-0.150, -0.039]	0.910	[0.861, 0.962]	< .001	.0462
CON – Hippocampus	0.091	[0.035, 0.146]	1.095	[1.036, 1.158]	.001	.0462
VAN – Hippocampus	0.093	[0.038, 0.149]	1.098	[1.039, 1.160]	<.001	.0462
Externalizing						
DAN – VAN	-0.095	[-0.149, -0.041]	0.910	[0.862, 0.960]	<.001	.0498
VAN – Hippocampus	0.091	[0.037, 0.144]	1.095	[1.037, 1.155]	<.001	.0498
Sex interaction (internalizing)						
Fusiform area	-0.462	[-0.744, -0.180]	0.630	[0.475, 0.836]	.001	.0457
SMN (H) – VS	-0.486	[-0.758, -0.215]	0.615	[0.469, 0.807]	<.001	.0230
RTN – Hippocampus	0.491	[0.217, 0.765]	1.634	[1.242, 2.149]	<.001	.0230

Note. Odds > 1 indicate increased odds and < 1 indicates decreased odds of being in the healthy group relative to the resilient group, with increases in brain structure/connectivity. For example, the 0.91 odds for the DAN – VAN connectivity for internalizing group membership, is interpreted as indicating lower odds of being healthy relative to being resilient. However, for better interpretability, results in the main body have been reversed to have odds interpreted as being resilient versus healthy. The 0.91 odds for the DAN – VAN connectivity was interpreted as indicating higher odds of being resilient versus healthy, with every standard unit increase in connectivity. Abbreviations: dorsal attention network (DAN), ventral attention network (VAN), cingulo-opercular network (CON), sensorimotor hand network (SMN [H]), visual network (VN), retrosplenial temporal network (RTN), confidence interval (CI), and false-discovery rate corrected *p* values (*p*FDR).

Table 3.

Results for post-hoc group membership comparisons (maladaptive vs. resilient to internalizing symptoms) for the significant effects separately in males and females

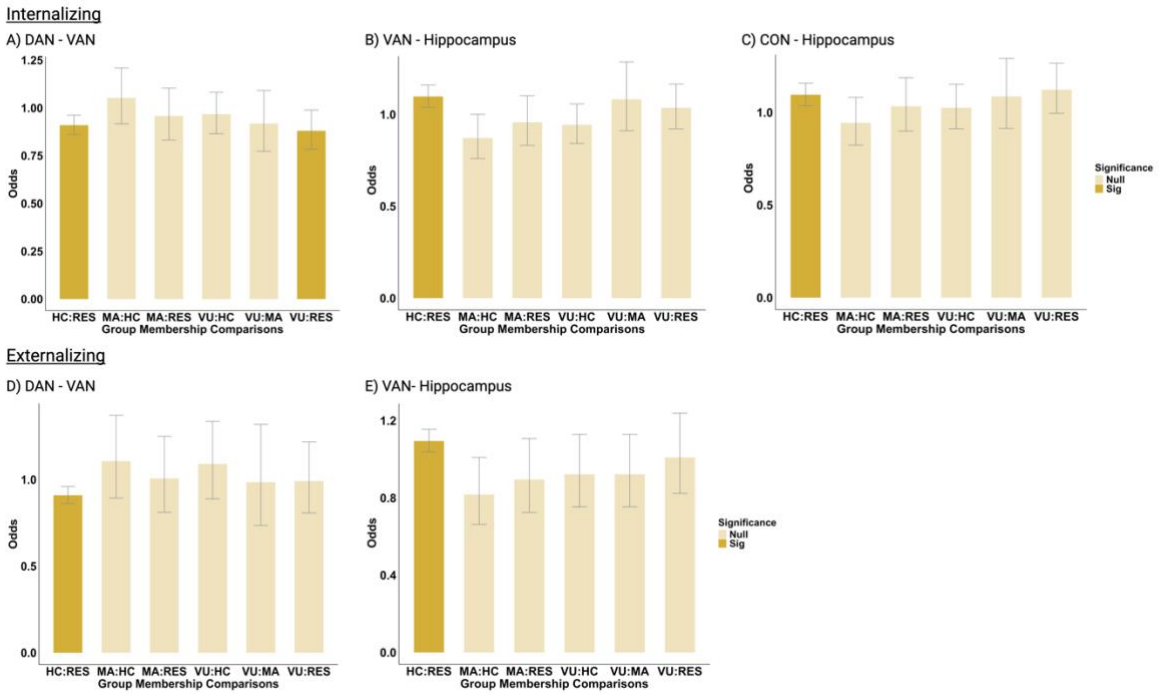
Brain variables	Males		Females	
	Odds (95% CI)	*p*	Odds (95% CI)	*p*
Fusiform area	1.25 (0.96-1.62)	.101	0.82 (0.60-1.11)	.192
SMN(H) - VN	1.33 (1.09-1.62)	.006*	0.80(0.66- 0.98)	.027*
RTN - Hippocampus	0.82 (0.68-1.00)	.051	1.34(1.10- 1.63)	.003*

Note. *Indicates significant results within subsamples of males and females (uncorrected $p <. 05$). Values > 1 indicate increased odds and < 1 indicate decreased odds of being maladaptive vs. resilient to internalizing symptoms group, with increases in brain structure/connectivity. Abbreviations: sensorimotor hand network (SMN [H]),

visual network (VN), retrosplenial temporal network (RTN), confidence interval (CI). Other group comparisons were also conducted separately in subsamples of males and females to be consistent with previous post-hoc analyses, see Table S5 for relevant results.

Figure 1

Bar plots for post-hoc results of significant brain effects



Note. Bars depict predicted odds of group membership for the relevant connectivity finding. Values > 1 indicate increased odds and < 1 indicate decreased odds of being in the group left of the colon relative to the group right of the colon, with increases in brain connectivity. For example, the leftmost bar in panel A depicts that increased DAN – VAN connectivity is associated with decreased odds of being healthy relative to being resilient to internalizing symptoms. Significance is determined by uncorrected $p < .05$. Error bars indicate 95% confidence intervals. Abbreviations explained: dorsal attention network (DAN), ventral attention network (VAN), cingulo-opercular network (CON),

healthy control (HC), maladaptive (MA), vulnerable (VU), resilient (RES), significant (sig).