Resting State Functional Connectivity and Psychotic-Like Experiences in Childhood: Results from the Adolescent Brain Cognitive Development Study

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Abstract

Background: Psychotic-like experiences (PLEs) during childhood are associated with greater risk of developing a psychotic disorder (and other mental disorders), highlighting the importance of identifying neural correlates of childhood PLEs. Three major cortical networks- the cingulo-opercular network (CON), default mode network (DMN), and fronto-parietal network (FPN)- are consistently implicated in psychosis and PLEs in adults. However, it is unclear whether variation in functional connectivity is associated with PLEs in school-aged children.

Methods: Using hierarchical linear models, we examined the relationships between childhood PLEs and resting-state functional connectivity of the CON, DMN, and FPN, as well as the other networks using an *a priori* network parcellation, using data from 3,434 9–11-year-olds in the Adolescent Brain Cognitive Development (ABCD) study. We examined within-network, between-network, and subcortical connectivity.

Results: Decreased CON and DMN connectivity, as well as cingulo-parietal (CPAR) network connectivity, were associated with greater PLEs, even after accounting for family history of psychotic disorders, internalizing symptoms, and cognitive performance. Decreased DMN network connectivity was more strongly associated with increased delusional ideation, whereas decreased CON connectivity was more strongly associated with increased perceptual distortions. Increased CON-cerebellar and decreased CPAR-cerebellar connectivity were also associated with increased PLEs, and CPAR-cerebellar connectivity was more strongly associated with increased perceptual distortions.

Conclusion: Consistent with hypotheses about the dimensionality of psychosis, our results provide novel evidence that neural correlates of PLEs, such as reduced functional connectivity of

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higher-order cognitive networks, are present even in school-aged children. The results provide further validation for continuity of PLEs across the lifespan.

Keywords

Psychotic symptoms are not only experienced by individuals with a psychotic disorder, but also a small subset of the general population. Subclinical psychotic symptoms or "psychotic-like experiences" (PLEs) (1) are experienced by 13–15% of children and adolescents (2,3). Childhood PLEs are associated with greater risk of developing a psychotic disorder later in life (3,4), especially distressing (5) PLEs. Individuals with PLEs also share multiple risk factors with clinical psychosis, such as increased internalizing symptoms (6,7), cognitive impairments (8–10) and family history of psychosis (11). These findings provide evidence for psychosis as a phenotypic continuum existing across a spectrum of symptom severity, ranging from healthy individuals to chronic psychosis patients (12). To validate this phenotypic continuum both across the lifespan and across the spectrum of severity, it is critical to determine whether PLEs in childhood are associated with similar neural correlates as found in adults with PLEs or with more severe clinical manifestations of psychosis. The goal of the current study was to examine the relationships of childhood PLEs to variation in functional brain connectivity.

Resting-state functional magnetic resonance imaging (rsfMRI) has become an important tool in understanding the functional organization of brain networks as reflected in correlated activity among anatomically distinct brain regions (13,14). A number of studies have found abnormal functional connectivity present across the psychosis spectrum (15–19), potentially constituting an endophenotype of psychosis (20,21). Particularly, research has identified three major networks associated with higher-order cognition- the cingulo-opercular network (CON), default mode network (DMN), and fronto-parietal network (FPN)- that show abnormal functional connectivity in both psychotic disorders (22–30) and psychosis risk populations (31–33). Regions of the CON show increased activation during information integration, including salience attribution (34), stable task control (35,36), and performance monitoring (37). FPN regions show increased activation during attention-demanding tasks, particularly working memory and attention (38), and the FPN is thought to support adaptive task control and goal representation (35,36,39). In contrast, the DMN is a group of functionally correlated brain regions showing decreased activation during goal-oriented or attention-demanding tasks (40) and is involved in self-referential thinking and attention to internal states (41).

Dysfunction of these core networks has consistently been associated with psychotic symptoms in the general population (24). For example, Du and colleagues (16) found a significant step-wise worsening of abnormal connectivity in these networks from healthy controls to psychosis risk to early-onset schizophrenia patients, wherein regions of the CON showed decreasing connectivity and FPN regions showed increasing connectivity. However, the majority of studies find reduced connectivity with the CON and FPN in psychosis (42–

45). Similarly, studies have found reduced connectivity in the CON and FPN in psychosis risk (46,47), although other research reports no FPN connectivity impairments (48). The pattern for DMN connectivity is mixed, with some studies finding decreased connectivity for both psychosis and psychosis risk (24,46,49–52), and other studies finding increased connectivity (18,53,54). Despite some variability in results, connectivity findings in psychosis risk populations suggest that abnormal functional connectivity of key brain networks can develop in individuals experiencing subthreshold symptoms, and may worsen along the psychosis continuum. Additionally, psychosis-risk individuals also exhibit reduced functional connectivity between cortical regions of these networks and subcortical structures, particularly the thalamus (46,55), cerebellum (56), and striatum (57,58). Identifying abnormal functional connectivity patterns may aid in detecting early phases of psychosis (59), potentially enhancing treatment outcomes.

This is the first study to examine the relationship between childhood PLEs and resting-state functional connectivity (RSFC) of the CON, DMN, and FPN, using data from 9–11-year-olds in the Adolescent Brain Cognitive Development (ABCD) study. We tested the *a priori* hypothesis that impaired RSFC within and between these networks, as well as between these cortical networks and subcortical structures, would be associated with increased PLEs in school-aged children. Although the ABCD offers an unprecedented sample size (current sample n=3,434), enabling a well-powered and robust examination of functional connectivity in PLEs, we examined this *a priori* subset of networks to reduce the statistical problems associated with an exploratory approach (e.g., false positives) and because of the computational challenges of whole-brain analyses in large data sets with dense sampling. However, to examine specificity, we also examined 10 other networks from an *a priori* brain parcellation ("Gordon") (60–62). Follow-up analyses examined whether the type of PLE (e.g. delusional ideation or perceptual distortion) was differentially associated with altered functional connectivity. Importantly, when analyzing the relations between PLEs and functional connectivity, we examined multiple other factors that might be associated with functional connectivity (and previously shown to be associated with PLEs in the ABCD sample (63)), such as family history of psychotic disorders, internalizing symptoms, and neuropsychological test performance (with the latter two perhaps arising from connectivity impairments), to better characterize the nature of the association between childhood PLEs and functional connectivity.

Methods

Participants

A sample of 4,524 individuals was obtained from the ABCD study, a large-scale study tracking approximately 11,500 9–11-years-olds recruited from 20 research sites across the United States (see Supplement for study-wide exclusionary criteria) (64). These data were accessed from the National Institutes of Mental Health Data Archive (see Acknowledgments). Participants were removed from analyses in the current study either for not have at least one resting state scan that passed quality assurance criteria (n=332) or in the case of missing data (n=758, due to n=523 missing at least one relevant imaging variable,

n=387 missing income to needs; see Supplemental Table 1). The final sample size was 3,434 individuals (see Table 1).

Measures

Prodromal Questionnaire-Brief Child Version (PQ-BC)—Participants completed the PQ-BC, a 21-item self-report questionnaire (see Supplemental Table 2) (63). The PQ-BC demonstrates validity in the ABCD sample (63). Children first answered each question either yes or no. For each "yes", children were asked "Did it bother you?". For each "yes", children were subsequently asked: "Please choose the number below the appropriate picture that shows us how much that bothered you when it happened.", with the numbers corresponding to the pictures ranging from 1 to 5. Missing data were coded as "no"s (see Supplement for details) (65).

Distress scores were calculated as the total number of endorsed questions weighted by level of distress [i.e., 0=no, 1=yes (but no distress), 2–6=yes (1+score on distress scale)], consistent with previous research (63,65,66). For follow-up analyses, PQ-BC distress scores were also divided into two separate scores, one for questions pertaining to delusional ideation and another for perceptual distortions (see Supplemental Table 2).

Internalizing Symptoms—The youth versions of the validated Kiddie-Structured Assessment for Affective Disorders and Schizophrenia (KSADS) for DSM-5 (67,68) were used in current analyses as measures of internalizing psychopathology (64). We examined an internalizing symptoms composite (i.e., summation of depression and Generalized Anxiety Disorder symptoms), as has been previously used in the ABCD sample (63).

Family History of Psychosis—The history of psychotic disorder in first-degree relatives was assessed using the parent-rated Family History Assessment Module Screener (69), scored as either present or absent.

Neuropsychological Test Battery—Participants completed all tests within the National Institutes of Health Toolbox Cognitive Battery (NIHTB-CB; see Supplement and Weintraub et al. (70) for descriptions of individual NIHTB-CB tests) (70,71). The current study utilized uncorrected NIHTB-CB scores, but all analyses include age and sex as covariates. Since we were interested in examining the association between "overall" cognitive functioning with PQ-BC scores and connectivity, scores from each of the NIHTB-CB tasks were included in a principal components analysis (PCA), and the first component was used as a measure of higher-order cognitive ability (38.41% of the total variance).

Imaging Procedure

ABCD imaging procedures have been detailed in the literature (72). All children were run on a 3T scanner (either Siemens, General Electric, or Phillips) with a 32-channel head coil and completed T1-weighted and T2-weighted structural scans (0.7mm isotropic). Participants also completed four 5-minute resting-state BOLD scans, with their eyes open and fixated on a crosshair. Resting state images were acquired in the axial plane using an

EPI sequence. Other resting-state image parameters varied by 3T scanner and have been previously detailed (https://abcdstudy.org/images/Protocol_Imaging_Sequences.pdf)(72).

A data analysis pipeline, using the Multi-Model Pressing Stress software package, was created to analyze RSFC data (see Supplement and (73,74) for details). Pair-wise correlations were examined for ROIs within functionally-defined parcellations (i.e., Gordon networks) (60) and subcortical ROIs (i.e., cerebellum, thalamus, caudate, and putamen) (75). The Fisher Z-transform of the correlation values were examined within and between each network, and between networks and subcortical ROIs. Subcortical ROIs focused on the cerebellum, thalamus, caudate, and putamen, since there was an a priori reason to believe these subcortical ROIs would be associated with psychosis spectrum symptoms (45,55,57,76,77).

Statistical Analyses

Hierarchical linear models (HLMs) were conducted in R lme4 package (78), with family unit and the 20 research sites modeled as random intercepts [to account for nonindependence of observations (e.g., n=419 siblings)], and age, sex, income to needs, average motion, scanner type, and ethnicity included as covariates. All analyses were False Discovery Rate corrected (FDR-corrected) for multiple comparisons. HLMs analyzed the associations between PQ-BC scores and: 1) within-network connectivity for each of the 13 Gordon networks (60) [Auditory, Cingulo-Opercular (CON), Cingulo-Parietal (CPAR), Default Mode (DMN), Dorsal Attention, Fronto-Parietal (FPN), None (also referred to as "Unassigned" network), Retrosplenial-Temporal, Salience, Sensorimotor-Hand, Sensorimotor-Mouth, Ventral Attention, Visual; 13 FDR-corrected comparisons; follow-up analyses also examined whether PQ-BC scores also predicted family history of psychosis, internalizing symptoms, and neuropsychological test performance; furthermore, subsequent analyses were conducted for any network with significant within-network connectivity associations with PQ-BC scores), 2) between-network connectivity, focusing on connectivity between CON, DMN, and FPN networks with each of the other 12 Gordon networks (12 FDR-corrected comparisons per network), 3) subcortical connectivity to the CON, DMN, and FPN networks, focusing on connectivity to the cerebellum, thalamus, caudate, and putamen [both bilaterally (8 FDR-corrected comparisons per network) and an average of the two hemispheres (4 FDR-corrected comparisons per network)]. For all results passing FDR correction, follow-up analyses also examined whether the delusional ideation or perceptual distortion PQ-BC questions were associated with altered connectivity. Differences between significant correlations with all other network correlations were examined using Meng's z-test procedures (79). Variables were examined for violations of normality assumptions, and based on previous recommendations (80), any variable with substantial (>1.96) positive skewness was logarithmically transformed [formula= LG10(X + 1); PQ-BC Distress score skewness=3.01; DMN within-network connectivity skewness=2.41]. Results are expressed as standardized estimates (βs) with 95% bootstrapped (5000 iterations) confidence intervals (CIs) and effect sizes are expressed as R^2 (both full model and partial model with just the variable of interest). For Figure 1, PQ-BC scores were binned using R OneR package (81). Inclusion of total intercranial volume, number of usable scans, or exclusion of observations with residuals >2.5 SD, did not significantly alter any results.

Results

Within-Network Connectivity

As predicted, reduced within-network connectivity in both the CON and DMN were correlated with increased PQ-BC scores (β −.05, FDR-corrected ps<.05; full model R^2s=. 03, partial R^2s .004; see Table 1 for information about overall PQ-BC scores; Figure 1 and Table 2; Supplemental Figure 1 for scatterplots). Of the covariates, greater motion, less income to needs, being younger, and being African American were all associated with greater PQ-BC scores (Supplemental Table 3). However, we did not see the predicted relation with reduced FPN connectivity. Unexpectedly, reduced connectivity within the CPAR network was also associated with increased PQ-BC scores (β=−.07, FDR-corrected p<.001; full model R^2=.04, partial R^2=.009; Figure 1 and Table 2). Associations between CON, DMN, and CPAR connectivity and PQ-BC scores were significantly stronger than the associations between PQ-BC scores and FPN, "None", Sensorimotor-Hand, Sensorimotor-Mouth, Ventral Attention, and Visual network connectivity (Zs>1.91, ps<.05). Additionally, the associations between both CON and CPAR connectivity and PQ-BC scores were also significantly stronger than the associations between Auditory, Dorsal Attention, and Salience connectivity and PQ-BC scores (Zs>1.73, ps<.05). Lastly, the association between CPAR connectivity and PQ-BC scores was significantly stronger than the association between Retrosplenial-Temporal connectivity and PQ-BC scores (Z=2.11, p=.02).

When examining PLE symptom type, reduced CON within-network connectivity was significantly associated with both increased delusional ideation (β=−.04, p<.05) and perceptual distortions (β=−.07, p<.001). However, in a model with both delusional ideation and perceptual distortions, *perceptual distortions* (β=−.007, p<.001), but not delusional ideation (β=.001, p=.97), significantly predicted reduced CON connectivity. Reduced DMN within-network connectivity was also significantly associated with both increased delusional ideation (β=−.05, p<.01) and perceptual distortions (β=−.04, p<.05), although in a model with both perceptual distortions and delusional ideation, *delusional ideation* (β=−.04, p<. 05), but not perceptual distortions (β=−.01, p=.65), significantly predicted reduced DMN connectivity. Reduced CPAR within-network connectivity was also significantly associated with both increased delusional ideation (β=−.06, p<.001) and perceptual distortions (β=−.06, p<.001), though neither delusional ideation (β=−.01, p=.10) nor perceptual distortions (β=−. 01, p=.14) significantly predicted reduced CPAR connectivity when both were in the model. Overall, there is evidence that perceptual distortions were significantly more associated with reduced CON within-network connectivity than was delusional ideation, while the opposite was found for DMN within-network connectivity.

In addition, reduced CON (βs>−.05, p<.01), DMN (βs>−.05, p<.01), and CPAR (βs>−.05, p<.001) within-network connectivity continued to predict increased PQ-BC scores in models that included family history of psychotic disorder, internalizing symptoms, and neuropsychological test performance [note that family history of psychotic disorder (βs>.05, ps<.005), internalizing symptoms (βs=.27, ps<.001), and neuropsychological test performance deficits (βs>−.11, ps<.001) all significantly predicted increased PQ-BC scores].

Between-Network Connectivity

Next, we examined whether PQ-BC scores were associated with alterations in between-network connectivity. Given our a priori hypotheses regarding networks of interest (i.e., CON, DMN, and FPN), coupled with exploratory within-network findings (i.e., significant CPAR within-network deficits), the subsequent analyses focused on the connectivity between these four and the other twelve Gordon networks. No hypothesized between-network associations with PQ-BC scores survived FDR-correction (Supplemental Tables 4–7; see Supplemental Tables 8–16 for results for other networks).

Subcortical Connectivity

We then examined whether connectivity between Gordon networks and subcortical regions were associated with PQ-BC scores, again focusing on the CON, DMN, FPN, and CPAR networks (see Supplemental Tables 17–20). In terms of CON to subcortical region connectivity, *increased* CON to average cerebellum connectivity was associated with increased PQ-BC scores (β=.04, p<.01, FDR-corrected p=.03; full model R^2=.03, partial R^2=.003). The relationship of CON-cerebellar connectivity with PQ-BC scores was significantly stronger than the relationships of PQ-BC scores and cerebellar connectivity to both the FPN and CPAR networks (Zs>−2.17, ps<.05; for DMN, Z=−1.45, p=.07), and stronger than the relationships between PQ-BC scres and CON connectivity to the other subcortical structures (i.e., caudate, putamen, and thalamus; Zs>−1.86, ps<.05). Decreased CON to average cerebellum connectivity also predicted both increased delusional ideation (β=.04, p<.01) and increased perceptual distortions (β=.05, p<.01), though neither delusional ideation (β=.02, p=.42) nor perceptual distortions (β=.03, p=.14) significantly predicted increased connectivity when both were in the model.

Decreased CPAR to average cerebellum connectivity was significantly associated with increased PQ-BC scores (β=−.07, p<.001, FDR-corrected p<.001; full model R^2=.04, partial R^2=.007). The relationship between CPAR-cerebellar connectivity with PQ-BC scores was significantly stronger than the relationships between PQ-BC scores and cerebellar connectivity in the other three networks (i.e., CON, DMN, and FPN; Zs>2.51, ps<.01), and stronger than the relationships between PQ-BC scores and CPAR connectivity to the other subcortical structures (Zs>2.69, ps<.005). Decreased CPAR to average cerebellum connectivity also predicted both increased delusional ideation (β=−.05, p<.001) and increased perceptual distortions (β=−.07, p<.001), although in a model with both, *perceptual distortions* (β=−.06, p<.01), but not delusional ideation (β=−.01, p=.66), significantly predicted increased connectivity. No connectivity to subcortical regions with either the DMN or FPN were significant (ps .08).

Discussion

The current study is the first to examine functional connectivity and psychotic-like experiences in school-age children. The results indicate that early manifestations of non-clinical psychosis risk already show evidence of an association with alterations in functional connectivity that are analogous to those seen individuals with psychotic disorders. The current study found novel evidence that reduced connectivity in the CON, DMN, and CPAR

networks was associated with increased childhood PLEs. Importantly, the associations were not better accounted for by demographic factors, cognitive impairments, or general psychopathology. For subcortical connectivity, both increased CON- and reduced CPAR-cerebellar connectivity were associated with increased PLEs. Finding associations between connectivity alterations and increased distressing PLEs provides further validation of the psychosis phenotypic continuum of functional connectivity impairments across the spectrum of psychosis.

The current study demonstrated that alterations in within-network connectivity in several networks associated with higher-order cognitive functioning are associated with increased distressing PLEs. These findings are largely consistent with work finding reduced connectivity for the CON and DMN networks associated with PLEs in adults (48), youth (47,52), and clinical high-risk (CHR) groups (82,83). The CON network has been linked to switching between large-scale brain networks (i.e., mediating between the DMN and FPN networks), stable task control (36), and conflict detection (37). Therefore, impaired connectivity may lead to disrupted integration of information (84). One speculative hypothesis is that early mild impairments of information integration and performance monitoring in childhood may cascade into further impairments in cognition, and lead to exacerbation of PLEs, in early adulthood.

The current study also found evidence that reduced connectivity within the DMN, a network associated attention to internal states and self-referential thinking (41), was associated with increased PLEs. As previously noted, the evidence regarding the direction (i.e., increased or decreased) of impaired DMN connectivity in psychosis risk is inconsistent, with several studies finding hyperconnectivity (18,54,85) and others, similar to the current study, finding hypoconnectivity within the DMN associated with the endorsement of PLEs (48,86). It is unclear what drives the variability in the directionality of DMN connectivity impairments associated with psychosis. Key factors may include characteristics of the sample assessed (e.g., stage of illness, severity of symptoms, etc.) or the degree to which sufficient methods for motion control were implemented. Since the DMN is thought to regulate attention to internal states, altered connectivity may result in impairments in self-referential thoughts and internally generated thinking, cognitive activities which may be important in the early development of PLEs.

Lastly, reduced connectivity in the CPAR network was associated with increased PLEs. The CPAR network consists of portions of the posterior cingulate cortex (PCC) and the precuneus (60). Regions of the CPAR have also been found to be activated during cognitive tasks, including visual-spatial information processing and mental imagery (87). Coupled with the CON findings, the association between increased PLEs and reduced CPAR connectivity might suggest a role for disruptions in higher-order cognition in the early development of PLEs. However, the FPN, consistently implicated in higher-order cognition, such as adaptive task control (35,36,39), was not significantly associated with PLEs, consistent with other research on PLEs in adults (48). Importantly, the fact that only a specific subset of networks showed relationships to PLEs, with these relationships being significantly stronger than the relationships with other networks, suggests a level of specificity in terms of functional brain networks associated with childhood PLEs. These

results also raise the possibility that early deficits in networks such as the CON, DMN, and CPAR may be early harbingers of deficits in other networks that may emerge with either greater severity or duration of illness. Perhaps as connectivity impairments in these networks worsen, it gives rise to impairments in other networks, such as the FPN, which in turn leads to worsening of symptoms and cognitive functioning (88). Alternatively, FPN connectivity impairments may only emerge after prefrontal lobe maturation (e.g., in later adolescence and/or adulthood).

In addition to finding evidence for CON, DMN, and CPAR hypoconnectivity associated with increased PLEs, the current study also found evidence that altered connectivity within these networks was associated with specific types of PLEs (i.e., either perceptual distortions or delusional ideation). Hypoconnectivity of the CON was more strongly associated with perceptual distortions, consistent with evidence that the CON, and specifically the insula, is activated during hallucinations (89). The CON is critical for the attribution of salience to environmental stimuli (34,90), and therefore impaired connectivity may be associated with the misattribution of importance to stimuli, leading to the development and maintenance of perceptual distortions. Likewise, several previous studies have linked DMN dysfunction to positive symptoms (53,91), including both delusions and hallucinations. We found evidence that DMN was associated with both delusional ideation and perceptual distortions, although it was more strongly associated with delusional ideation. As previously mentioned, the DMN is involved in self-referential thinking, such as perspective taking (92). Early mild within-network DMN hypoconnectivity may contribute to disruptions in self-referential and internally-generated cognitive impairments, which may be important in the generation of delusional ideation.

In terms of between-network connectivity, none of the hypothesized associations in the current study survived FDR-correction. These findings are in contrast to several other studies of PLEs, which have found impaired connectivity between CON, CPAR, and DMN networks with a number of other regions, including both sensory regions as well as other higher order cognitive networks (e.g., DAN, VAN, FPN) (46,47,86). Again, one intriguing possibility is that there is a developmental cascade of disruptions in functional connectivity, with within-network disruptions appearing earlier than between-network disruptions. Longitudinal studies following children with early PLEs will be needed to test such a hypothesis.

For connectivity to subcortical regions, increased CON-cerebellar and decreased CPAR-cerebellar connectivity were associated with increased PLEs (and CPAR-cerebellar connectivity was more strongly associated with perceptual distortions than delusional ideation). These CON-cerebellar findings are consistent with first-episode psychosis research (93). In contrast to the findings of the current study, previous research has found increased connectivity between CPAR regions (e.g., PCC and precuneous) and the cerebellum in both individuals with schizophrenia and their siblings (76) as well as individuals at high risk for psychosis (19). Again, the discrepancies with previous research in terms of direction of connectivity alterations may be due to several factors, including the stage of illness, or methodological concerns, including quality control methods and motion control. Importantly, we also did not see evidence for a relationship between PLEs and

reduced connectivity between FPN and subcortical regions, as has been seen in prior work (55,88,94).

Several limitations should be noted. The ABCD data are cross-sectional. Without longitudinal data, the nature of associations between RSFC and PLEs cannot be fully understood, including whether RSFC variation predicts the course of PLEs. Further, as expected, PLEs in this sample of school-age children are most frequently of mild severity (e.g., not diagnosable). It will be important for future research to confirm the associations between RSFC and PLEs using a greater range of severity of PLEs (i.e., from mild PLEs to full psychotic symptoms), to further characterize the phenotypic continuum of psychosis and its relationship to functional brain differences. Future research should also examine functional connectivity in sibling and/or twin pairs discordant for PLEs, to better understand heritability of the associations between connectivity impairments and PLEs. In addition, future research should examine subregions within subcortical structures (eg, cerebellum (95), striatal regions (96), and thalamus (55)) to examine specificity of associations with PLEs, and examine the results using another parcellation definition (eg, Yeo atlas (26)) to examine the generalizability of results. Lastly, ideally, all participants would have been run using identical scanning protocols (eg, FIRMM software).

Conclusions

The results of the current study demonstrate that distressing PLEs in childhood are associated with altered connectivity in several networks previously implicated in the development of psychotic symptoms. The results indicate associations between alterations in functional connectivity in higher-order cognitive networks and PLEs may be evident as early as 9-years-old, with within-network connectivity alterations potentially representing an endophenotype of psychotic disorders. While associations between within-network connectivity and PLEs were in the small range (βs −.07), this is expected for non-clinical symptoms assessed prior to the onset of significant functional impairment. The current study helps characterize the relations between connectivity alterations and PLEs in school-age children, indicating that abnormal functional connectivity may be detectable in non-clinical psychotic-like experiences. These results are consistent with a neurodevelopmental model in which connectivity deficits emerge and worsen over the course of development, perhaps due in part to genetic factors that may influence neural factors (e.g, the gene C4 may contribute to synaptic alterations in adolescence) (97,98). Thus, the networks implicated in childhood PLEs (e.g., CON, CPAR, DMN, and connectivity with the cerebellum) may be particularly vulnerable to synaptic alterations in adolescence.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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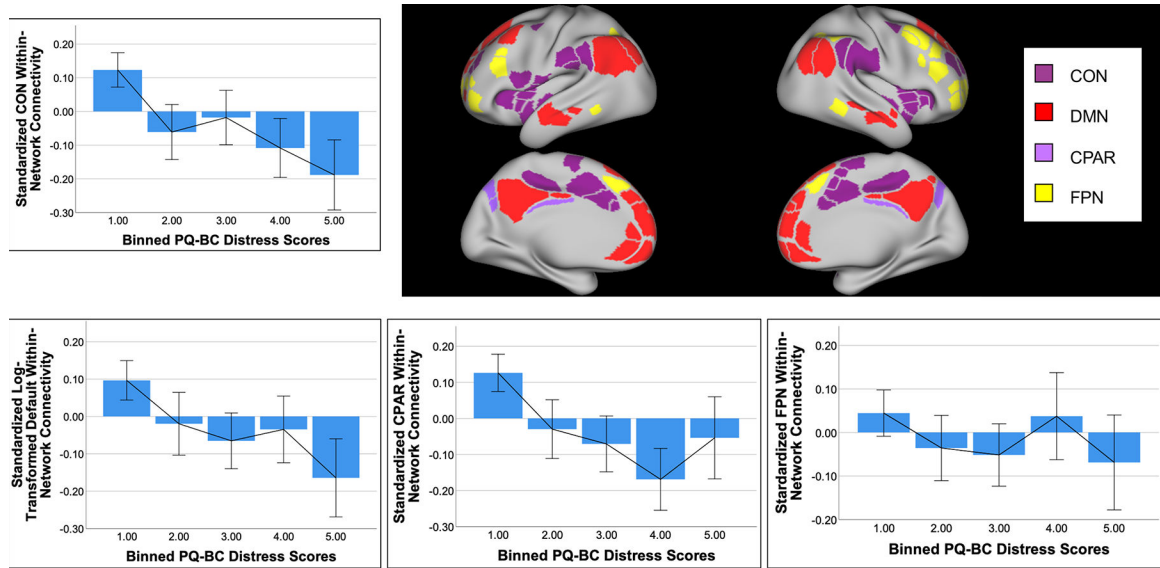
Figure 1.

The relation between mean (+ SE) binned log-transformed PQ-BC scores and standardized within-network connectivity for four Gordon networks [cingulo-opercular network (CON), log-transformed default mode network (DMN), fronto-parietal network (FPN), and cingulo-parietal network (CPAR); line depicts spline interpolation].

Table 1.

Demographic Characteristics for Sample (n=3434)

Variable	Mean (SD; range) or N (%)
Income to Needs[a]	4.78 (2.89; 0.12–16.58)
Age	10.04 (0.61; 9–11)
Average Motion[b]	0.25 (0.23; 0.03–1.91)
Sex, N(%) female	1646 (47.9%)
Ethnicity	
Caucasian	2119 (61.7)
African American	295 (8.6)
Hispanic	626 (18.2)
Other	394 (11.5)
Scanner Type	
Siemens	2120 (61.7)
Philips	462 (13.5)
GE	852 (24.8)
PQ-BC Distress Scores	
Distress	5.96 (10.11; 0–96)
Log-Transformed Distress	0.52 (0.52; 0–1.97)

Abbreviation: PQ-BC = Prodromal Questionnaire-Brief Child version.

[a] Income to needs is defined as the ratio of family income to the appropriate poverty threshold.

[b] Average motion is defined as average framewise displacement in mm.

[c] Income to needs is defined as the ratio of the family income to the appropriate poverty threshold.

Table 2.

Model Estimates for Within Network Connectivity Relationships to Psychotic-Like Symptoms[a]

	β	lower CI	upper CI	t	p	FDR-corrected p
Auditory	−0.02	−0.05	0.01	−1.24	.22	.47
Cingulo-Opercular	**−0.06**	**−0.09**	**−0.02**	**−3.31**	**.001**	**.007**
Cingulo-Parietal	**−0.07**	**−0.11**	**−0.04**	**−4.34**	**<.001**	**<.001**
Default	**−0.05**	**−0.08**	**−0.02**	**−2.84**	**.005**	**.022**
Dorsal Attention	−0.02	−0.06	0.01	−1.38	.17	.44
Fronto-Parietal	−0.01	−0.05	0.02	−0.73	.47	.76
None	0.00	−0.04	0.03	−0.22	.82	.89
Retrosplenial-Temporal	−0.03	−0.06	0.01	−1.60	.11	.36
Sensorimotor-Hand	0.00	−0.03	0.03	0.14	.89	.89
Sensorimotor-Mouth	0.00	−0.04	0.03	−0.29	.78	.89
Salience	−0.01	−0.04	0.02	−0.78	.44	.76
Ventral Attention	0.00	−0.04	0.03	−0.17	.87	.89
Visual	−0.01	−0.04	0.03	−0.39	.70	.89

Abbreviations: β=standardized regression coefficient; CI=95% confidence interval; t=t-test test statistic; p=p-value; FDR=False Discovery Rate.

[a]Significant model estimates are in bold.