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Cingulo-opercular network efficiency mediates the association between psychotic-like experiences and cognitive ability in the general population

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Abstract

Background—Psychosis is hypothesized to occur on a spectrum between psychotic disorders and healthy individuals. In the middle of the spectrum are individuals who endorse psychotic-like experiences (PLEs) that may not impact daily functioning or cause distress. Individuals with PLEs show alterations in both cognitive ability and functional connectivity of several brain networks, but the relationship between PLEs, cognition, and functional networks remains poorly understood.

Methods—We analyzed resting-state fMRI data, a range of neuropsychological tasks, and questions from the Achenbach Adult Self Report (ASR) in 468 individuals from the Human Connectome Project. We aimed to determine whether global efficiency of specific functional brain networks supporting higher-order cognition (the fronto-parietal network (FPN), cingulo-opercular network (CON), and default mode network (DMN)) was associated with PLEs and cognitive ability in a non-psychiatric sample.

Results—21.6% of individuals in our sample endorsed at least one PLE. PLEs were significantly negatively associated with higher-order cognitive ability, CON global efficiency, and DMN global efficiency, but not crystallized knowledge. Higher-order cognition was significantly positively associated with CON and DMN global efficiency. Interestingly, the association between PLEs and cognitive ability was partially mediated by CON global efficiency and, in a subset of individuals who tested negative for drugs (N=405), the participation coefficient of the right anterior insula (a hub within the CON).

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Conclusions—These findings suggest that CON integrity may represent a shared mechanism that confers risk for psychotic experiences and the cognitive deficits observed across the psychosis spectrum.

Keywords

psychotic-like experiences; resting-state networks; imaging; psychosis; cognition; graph theory

Introduction

Psychotic experiences, such as delusions and hallucinations, occur primarily in the context of serious mental health disorders. However research suggests that approximately 8–20% of clinically healthy individuals endorse occasional psychotic-like experiences (PLEs) that may or may not impact functioning (1, 2). As such, psychotic experiences occur on a continuum, with a subset of the general population experiencing PLEs in the absence of a diagnosable disorder, while another subset (e.g., individuals with schizophrenia) experience frequent and debilitating psychosis in conjunction with other psychiatric symptoms (3).

Under this continuum model, the psychosis phenotype expressed in the general population should show relationships with risk factors and neurobiological abnormalities associated with clinical psychosis, but with a lesser degree of severity (3). Research to date has provided some evidence in support of these predictions, revealing associations between PLEs and sub-clinical negative (4) and affective symptoms (5, 6). Interestingly, several studies have also shown associations between PLEs in the general population and cognitive ability (7, 8), an area of functioning that is robustly impaired in psychotic disorders (9). In fact, cognitive deficits are often present in individuals who later develop schizophrenia (10), and youths on the psychosis spectrum have been shown to have lower predicted age based on their cognitive functioning (11), suggesting that mechanisms supporting cognitive ability also affect mechanisms that give rise to the psychosis phenotype.

Recently, research exploring the neurobiological underpinnings of both PLEs and cognitive ability has focused on the role of brain networks in their development and maintenance (12–15). Brain networks derived from resting-state fMRI represent reliable and robust patterns of functional connectivity (16), and these networks appear to support different domains of information processing (17). Research has revealed that three networks supporting higher-order cognitive ability – the cingulo-opercular network (CON), fronto-parietal network (FPN), and default mode network (DMN) – have abnormal functional connectivity in psychotic disorders (18–20), which has been associated with both impairments in cognitive ability (21, 22) and psychotic symptoms (23, 24). Data from psychosis-spectrum youths has also revealed significantly altered functional connectivity of both the CON and DMN during rest, which was associated with cognitive ability (15), suggesting that functionally relevant connectivity abnormalities can be observed across the psychosis spectrum.

Given the complex literature on functional connectivity in psychotic disorders, which often reveals both increased and decreased connectivity between network nodes, graph analysis of a network's global efficiency allows for a parsimonious measure of a network's functional integration (25). Global efficiency also appears to be a predictive measure, as global

efficiency of the whole brain graph has been shown to be decreased in individuals with subclinical psychotic experiences (26), as well as in schizophrenia (27), and correlates with positive symptoms (28) and IQ (29). Although some studies have shown increased whole brain global efficiency in the context of psychosis (30, 31), previous work from our group looking at specific functional networks (CON and FPN) – taking into account the connectivity of only the nodes within that network -- have revealed associations between reduced global efficiency of these specific networks and decreased cognitive ability (32). Therefore, based on these studies, as well as consistently observed abnormalities in DMN connectivity in psychotic disorders (e.g. (33)), we predict that inefficient functioning of the FPN, CON, as well as the DMN, may contribute to the phenotypes of both psychosis and impaired cognition.

In the current study we tested the *a priori* hypothesis that reduced functional network efficiency of the CON, FPN, and DMN would be associated with both increased PLEs and reduced cognitive ability in a large cohort of relatively healthy young adults. This hypothesis was based on previous literature showing that greater PLEs (2, 7) and lower network efficiency (32) are associated with lower cognitive ability – associations we hoped to replicate and extend to the general population, in order to test the psychosis continuum model. Additionally, we hypothesized that efficiency of these networks would mediate the relationship between psychosis and cognitive ability, suggesting a shared mechanism between these two phenotypes.

Methods

Participants

Participants were recruited for the Human Connectome Project (HCP), a large-scale study focused on collecting high-quality neuroimaging data and extensive individual phenotyping in adult twins and their non-twin siblings (34). 468 individuals from the “S500” release (Table 1) were included in the current study after signing informed consent documents approved by the Washington University Internal Review Board. Potential participants were excluded if they or their sibling had a severe neurodevelopment disorder, a documented and treated neuropsychiatric disorder, neurological disorder, or other physical disorder that could influence brain function (34, 35).

Procedure

Participants completed testing over the course of two days at the Washington University School of Medicine. Each day included a drug screen, two 15-minute resting-state scans (as well as other scans not discussed in these analyses), and extensive behavioral assessments.

Cognitive Testing

Cognitive testing involved paradigms from the NIH Toolbox (www.nihtoolbox.org) and the University of Pennsylvania Computerized Neuropsychological Testing Battery (36, 37). Measures of cognition analyzed in the current study included the Picture Sequencing Task (episodic memory), Wisconsin Card Sort (executive function/cognitive flexibility), Flanker Task (executive function/inhibition), Penn Matrices Test (fluid intelligence), Penn Word

Memory Test (episodic memory), and List Sorting Task (working memory). Given that the CON, FPN, and DMN are believed to support all of these cognitive processes, and given that our interest in the current study was to measure “overall” cognitive functioning as supported by these networks, scores from these six tasks were included in a principal components analysis (PCA), and the first component was used as a measure of higher-order cognitive ability (35% of the total variance). Crystallized knowledge was measured as the average z-scores from two measures of language and reading comprehension: Picture Vocabulary and Oral Reading Recognition. NIH Toolbox scores were age and sex normed.

Psychotic-Like Experiences

Participants completed the Achenbach Adult Self Report (ASR) for ages 18–59 (38). Within the ASR, four questions were identified as measuring experiences similar to the positive symptoms of psychosis. These questions included: “I hear sounds or voices that other people think aren’t there”, “I see things that other people think aren’t there”, “I do things that other people think are strange”, and “I have thoughts that other people would think are strange”. Each question was scored on a scale of 0 (Not True), 1 (Somewhat or Sometimes True), or 2 (Very True or Often True). Scores for these four psychosis questions were summed to yield a PLEs score. Although the ASR is not commonly used for the measurement of PLEs, as these items are somewhat limited, we believe they provide a useful assessment of PLEs in the general population, given that the HCP did not include more complex measurements of clinical symptomatology.

Imaging Procedure

HCP imaging procedures have been detailed extensively in the literature (39, 40). All subjects were run on a customized Siemens Connectom 3T scanner with a 32-channel head coil and completed T1-weighted and T2-weighted structural scans (0.7mm isotropic), as well as four 15-minute resting-state BOLD scans, with their eyes open and fixated on a crosshair. Resting-state scans were acquired using a T2*-weighted multi-band (MB=8) EPI sequence with 72 axial slices per volume, 2x2x2mm voxels, FOV=208mm, TE=33.1ms, TR=720ms, and flip angle=52 degrees.

Preprocessing Pipelines

FMRI data from the HCP was run through minimal preprocessing pipelines (40) (see supplement for more details). Subsequently, CIFTI-format resting-state data (gray matter surface vertices plus subcortical gray matter voxels, collectively termed “grayordinates”) underwent additional functional connectivity preprocessing. Six rigid body motion parameters, their first derivatives, and their squares were used as regressors to correct for motion, and additional denoising was performed using FMRIB’s ICA-based X-noiseifier (FIX)(41),(42). Mean grayordinate timecourse was then regressed from the timeseries of each grayordinate, followed by temporal band-pass filtering (0.009–0.08Hz). All four resting-state runs were concatenated following preprocessing, yielding 60 minutes (4800 frames) of resting-state data. Movement estimates (average root mean square across frames in a run) were not associated with PLEs ($r = -.02$, $p = .67$), DMN efficiency ($r = .02$, $p = .68$), FPN efficiency ($r = -.02$, $p = .68$), or participation coefficients (all r ’s $< |-.09|$, all p ’s $> .05$), but were associated with cognition ($r = -.15$, $p = .001$) and CON efficiency ($r = -.19$, $p < .001$).

However, all analyses reported below held in pattern and effect sizes when covarying for motion estimates.

Graph Analysis

R to z transformed correlations were calculated between each cortical parcel in the Gordon parcellation scheme (43, 44), which includes 333 parcels assigned to 12 different functional brain networks. The Gordon parcellation was used because it has been shown to have greater parcel homogeneity and greater differentiation relative to a null model than seven other alternative parcellation schemes. We also used the same network assignments as the Gordon parcellation. Graph analysis was performed using functional connectivity data from parcels that comprised CON, FPN, and DMN (44). Global efficiency was the main metric of interest, as networks with higher global efficiency are thought to be more functionally integrated, with higher potential for information transfer between nodes within that network (25). Additionally, work from our group revealed that higher global efficiency of the CON and FPN is associated with better cognitive ability in both health and schizophrenia (32).

Graph analysis was performed on weighted, undirected graphs using the following steps: 1) thresholding of each individual subject's whole brain graph from 5%–10% edge density in 1% increments (all other connections reassigned as zeros), 2) isolation of parcels from the CON (n=40), FPN (n=24), and DMN (n=41) from thresholded whole brain graphs, 3) calculation of global efficiency for *a priori* networks using algorithms from the Brain Connectivity Toolbox (BCT) (25) at each edge density, 4) average global efficiency values from all six edge densities, yielding a single global efficiency value for each network. Follow-up analyses also included the participation coefficient of four *a priori* parcels (bilateral anterior insula, bilateral anterior cingulate cortex). Participation coefficient is a measure of a node's connectedness with other networks (more information on graph metrics provided in Supplement). Participation coefficient values for our *a priori* nodes were averaged across the 5%–10% thresholds and included in subsequent analyses.

Data Analysis

Associations between cognition, psychosis, and network metrics were calculated using bivariate correlations, with follow-up partial correlations including potential confounding factors (gender, depression, anxiety, and head motion) using SPSS v20. Given our strong *a priori* hypotheses, one-tailed significance tests were performed for all correlations, and only *a priori* networks (CON, FPN, and DMN) were assessed. Spearman's correlations were also performed to assess robustness of results in non-parametric tests (Supplement), and analysis of data *without* global mean confound regression was performed and is included in the Supplement. Bonferroni methods were used to correct for multiple comparisons of correlations with our network metrics (global efficiency: $.05/3=.017$; participation coefficient: $.05/4=.0125$) for both psychosis and cognition. Mediation analyses were performed using the PROCESS macro in SPSS (45), with bias-corrected 95% confidence intervals using 1000 bootstrap samples. The analogous correlation analyses were also performed after approximately adjusting for family structure in a Mixed Generalized Linear Model, with "family ID" as the highest level and "subject" as the second level (46), in order to assess whether significant findings were due to increased correlations between genetically

related subjects. Finally, analyses were performed excluding individuals who tested positive for drugs on the day of the testing ($N=63$), as well as when excluding a single subject with a psychosis score of six (all other scores were <6). Analyses controlling for these potential confounds, as well as variables such as age, sex, race, education, THC and tobacco use, are provided in the Supplement.

Results

PLEs and Cognitive Ability

21.6% of individuals reported at least one PLE. Of those 101 subjects, 7 subjects endorsed hearing sounds or voices other people think aren't there (7 = sometimes true), 5 endorsed seeing things other people think aren't there (4 = sometimes true; 1 = often true), 82 endorsed doing things that other people think are strange (68 = sometimes true; 14 = often true), and 67 endorsed having thoughts that other people would think are strange (56 = sometimes true; 11 = often true).

PLEs were significantly negatively associated with cognitive ability ($r = -.15$, $p < .001$), indicating that individuals with more self-reports of PLEs had worse higher-order cognition (Figure 1a). Interestingly, these individuals were significantly more likely to be male and African-American, had significantly lower personal education, significantly lower household income, and were one year younger on average than those who did not endorse any PLEs (Table 1), which is in line with the demographic differences reported between psychosis and non-psychosis spectrum youth from the Philadelphia Neurodevelopmental Cohort (47). Additionally, individuals who endorsed at least one PLE had significantly lower cognitive ability than individuals who endorsed no PLEs ($t(466)=3.15$, $p=.002$) (Figure 1b). Interestingly, PLEs were not significantly associated with crystallized knowledge ($r = -.07$, $p=.08$), there were no differences in crystallized knowledge between those who did and did not endorse PLEs ($t(466)=.82$, $p=.42$), and Meng's z-test for comparing the strength of correlations (48) revealed that PLEs were *significantly* more strongly associated with higher-order cognition than crystallized knowledge ($z=-2.01$, $p=.02$).

PLEs and Functional Network Efficiency

PLEs were significantly negatively associated with the global efficiency of the CON ($r = -.12$, $p=.004$) (Figure 1c) and the DMN ($r = -.11$, $p=.009$), indicating that individuals with more PLEs had lower global efficiency of the CON and DMN. Global efficiency of the FPN was not significantly related to PLEs ($r = -.01$, $p=.38$).

Cognition and Functional Network Efficiency

Higher-order cognitive ability was positively associated with global efficiency of the CON ($r = .14$, $p=.001$), indicating that individuals with better cognitive ability had higher CON global efficiency (Figure 2). Cognitive ability was not, however, associated with global efficiency of the FPN ($r = -.03$, $p=.26$) or the DMN ($r = -.03$, $p=.26$). Crystallized knowledge was not associated with global efficiency of any of the three networks (all r 's $< .05$, all p 's $> .12$).

Mediation Analysis

Mediation analysis revealed that CON global efficiency partially mediated the relationship between PLEs and cognitive ability (indirect effect (path *ab*) bias corrected 95% CI [−.0417, −.003]). This mediation was partial, as PLEs continued to significantly predict cognitive ability with CON global efficiency in the model ($t(2,465) = -3.08$, $p = .002$) (Figure 3). In addition, CON global efficiency remained a significant partial mediator when head motion was included as a covariate in the model (path *ab* indirect effect 95% CI [−.035, −.001]). Global efficiency of the DMN did not significantly mediate the relationship between PLEs and cognition (indirect effect 95% CI [−.002, .026]). These findings suggest that the observed association between increased PLEs and worse cognitive ability is in part accounted for by lower global efficiency of the CON.

Cognition, PLEs, and Participation

We performed follow-up analyses to assess whether connectedness of specific CON hub nodes was also related to PLEs and cognition. Right anterior insula (rAI) participation was significantly associated with cognitive ability ($r = .12$, $p = .006$), but not PLEs ($r = -.06$, $p = .09$). rAI participation did not significantly mediate the association between PLEs and cognitive ability in all subjects. However, when subjects who tested positive for drugs were removed, rAI participation was more strongly correlated with PLEs ($r = -.10$, $p = .04$) and was a significant partial mediator of PLEs and cognition (indirect effect 95% CI [−.0397, −.001]). This partial mediation was marginally significant when controlling for motion (indirect effect 95% CI [−.0381, 0.0001]). No other *a priori* hub nodes significantly correlated with cognition (all $r's < .08$, all $p's > .04$) or PLEs (all $r's < |-.07|$, all $p's > .06$) after correcting for multiple comparisons.

In order to assess whether rAI participation and CON global efficiency were independent predictors of cognition and PLEs, we included both variables as mediators in the same model, which included all subjects. We found that CON global efficiency continued to be a significant partial mediator of the relationship between PLEs and cognition (path *ab* indirect effect 95% CI [−0.037, −0.001]), but rAI participation was not a significant mediator in this model (95% CI [−0.024, 0.001]). These findings suggest that the CON's partial mediation of the relationship between PLEs and cognitive ability is not due to the connectedness of the rAI with other resting-state networks, and may instead be more dependent on the functional efficiency within the CON itself.

Discussion

The current study reveals a significant association between PLEs and higher-order cognition in the general population, showing that healthy individuals who self-report more PLEs have lower higher-order cognitive ability, but not lower crystallized knowledge. Further, we demonstrate that the relationship between PLEs and cognition is partially mediated by the global efficiency of the CON, suggesting that functional integration of the CON is associated with both cognitive ability and the experience of PLEs. Interestingly, this mediation was also present for the participation coefficient of the rAI, although the strength of the mediation was somewhat less robust. We observed a significant partial mediation when drug users were

removed, but this association was trending when motion was included as a covariate. Therefore, these findings suggest that connectedness of the rAI with other networks may also be an important underlying factor in the experience of PLEs and cognitive performance, but is likely a small piece of a much larger puzzle.

Although effect sizes for the relationships observed in the current study were small (r 's < .20), the magnitude is not unexpected, given that these relationships are being observed in individuals who are not diagnosed with a psychotic disorder, and have not sought more than 12 months of psychiatric treatment for any disorder, suggesting limited impairment due to lifetime psychiatric symptoms. The fact that these findings are both in line with the existing literature and can be detected in the general population provides further support for the relationship between psychosis, cognitive ability, and functional network efficiency across the psychosis spectrum. That said, these small effect sizes may also be the consequence, at least in part, of using a relatively crude measure of PLEs, only four questions from the Achenbach Adult Self-Report Scale (ASR). Using the ASR as our only measure of PLEs most likely reduced the variability of reported experiences in our sample, and therefore our ability to detect meaningful associations. Despite this limitation, these findings are the first to identify a common mechanism (i.e., the functional integrity of the CON) that is associated with both PLEs and cognitive ability in a non-psychiatric population. The small effect sizes observed in our sample do, however, suggest that other mechanisms may also influence both cognitive function and the experience of PLEs.

The CON is a functional brain network comprised of two major hub nodes: the dorsal anterior cingulate cortex and the anterior insula. This network is strongly coupled with the FPN and DMN, and nodes within the CON (primarily the anterior insula) have been shown to dynamically mediate activity between the FPN and DMN to gate salient information for further cognitive processing (49); a mediation that has been shown to be degraded in patients with schizophrenia (50). Meta-analysis of task-based fMRI data has revealed that nodes within the CON have increased activation during many different cognitive tasks, implicating this network in supporting a range of higher-order cognitive processes (51, 52). Further, strength of the rAI's modulation of FPN and DMN activity during rest correlates with cognitive performance in patients with schizophrenia (53), suggesting that disruption of the rAI contributes to cognitive impairments observed in schizophrenia. In addition, global efficiency of the CON and the participation coefficient of the rAI have been found to correlate with cognition in both schizophrenia patients and healthy controls (32), suggesting that more robust functional integration of this network supports better cognitive ability.

The CON is also thought to play a crucial role in the generation and maintenance of psychotic symptoms (54, 55). Kapur and colleagues have suggested that individuals with psychotic disorders inappropriately assign salience to environmental stimuli, as modulated by activity in the CON (56). They posit that individuals then work to explain why a stimulus is salient, leading to the development and maintenance of delusional thought and hallucinatory experiences (57, 58). Providing support for this theory, neuroimaging research has shown that activity of the rAI increases when individuals with schizophrenia experience auditory hallucinations (59), and that stronger functional connectivity of the anterior cingulate cortex correlates with psychotic symptom severity in individuals at risk for

developing schizophrenia (60). Furthermore, severity of delusions and hallucinations was negatively correlated with BOLD activation of the right insula and the anterior cingulate in a group of unmedicated first episode psychosis patients (61), suggesting that disruption of these nodes contributes to the experience of psychosis. Finally, individuals with schizotypal personality disorder, which is a disorder characterized by a relatively pervasive pattern of PLEs, have been shown to have significantly reduced gray matter volume of the insula and dorsolateral prefrontal cortex, and left insula volume had reduced functional connectivity with the putamen (62), further implicating the insula in PLEs across the psychosis spectrum.

Given the role of the CON in supporting higher-order cognitive ability, as well as its hypothesized involvement in the development and maintenance of psychotic symptoms, the current findings provide evidence that these relationships occur on a continuum that can be observed in healthy young adults. Previous studies have shown a link between PLEs in the general population and cognitive deficits, with one study revealing that worse verbal fluency skills relating to higher levels of PLEs (7), while data from the Philadelphia Neurodevelopmental Cohort revealed that psychosis-spectrum youths have a lower predicted age based on their cognitive ability (11). Additionally, healthy college students reporting PLEs have reduced functional connectivity of both the DMN and the CON with subcortical regions (e.g. thalamus, basal ganglia), and lower connectivity between the cerebellar network and the rAI was associated with higher positive symptom scores (12). Of note, neither this study in healthy individuals nor a previous study from our group with schizophrenia patients revealed robust differences in global efficiency between those with and without psychosis, limiting the strength of these findings in supporting the psychosis continuum model. The current study, however, is the first to demonstrate that efficiency of that CON *mediates* the association between PLEs and cognitive ability, identifying a potential mechanism underlying the psychosis continuum.

One important question that remains, however, is why the PLEs experienced by otherwise healthy individuals remain subclinical and do not appear to greatly impact functioning. Longitudinal research has shown that, of healthy individuals reporting PLEs at baseline, 8% reported persistent subclinical PLEs, 84% reported that their PLEs remitted, and 8% converted to a psychotic disorder (63). Although the cause for conversion to a psychotic disorder remains unknown, research has shown that transitory PLEs can become more persistent in the context of environmental risk factors, such as trauma (64), urbanicity (64, 65), and cannabis use (66), all of which have been previously identified as risk factors for the development of a psychotic disorders (67–69). Furthermore, there is a well-established genetic risk for psychotic symptoms (70), as evidenced by familial clustering of positive symptoms such as magical thinking and perceptual aberration (71, 72). Therefore, the psychosis-proneness continuum model suggests that a broadly distributed psychosis risk exists in the general population that, in some environments, leads individuals to experience only transitory PLEs, while in other environments leads to the expression of a more persistent psychosis phenotype that causes clinical distress (3). Given the forthcoming genotyping of these HCP subjects, future studies can analyze the contribution of genetic risk to the current mediation model and further explore this hypothesized psychosis continuum.

Conclusions

The current study reveals significant associations between psychotic-like experiences, cognitive ability, and the functional integrity of the cingulo-opercular network in individuals from the general population. Our findings reveal that the global efficiency of the CON, and possibly the participation coefficient of the right anterior insula, a hub within the CON, are partial mediators in the association between PLEs and cognitive ability, revealing that lower CON functional integration and lower rAI participation are associated with experiencing more PLEs and exhibiting worse higher-order cognitive ability. The identification of the CON as a potential mediator of PLEs and cognitive ability informs future research in both patients with psychotic disorders and healthy individuals, and helps to elucidate the neural underpinnings of complex psychotic disorders such as schizophrenia.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Psychotic-like experiences (PLEs) were significantly negatively associated with a) higher-order cognition. The relationship remained when removing the subject with a score of six ($r = -.16, p < .001$). b) Higher-order cognitive ability was significantly reduced in individuals who endorsed at least one PLE (summed score on four questions of interest from ASR were > 0) ($t(466) = 3.15, p = .002$), compared to those who endorsed no PLEs, however there was no difference between groups in crystallized knowledge ($t(466) = .82, p = .42$). PLEs were also significantly negatively associated with c) cingulo-opercular network (CON) global efficiency. The relationship remained significant when removing the subject with a score of six ($r = -.10, p = .02$). PLEs were measured using four questions from the Achenbach Adult Self Report Scale (“I hear sounds or voices that other people think aren’t there”, “I see things that other people think aren’t there”, “I do things that other people think are strange”, and “I have thoughts that other people would think are strange”). Higher-order cognition was measured as the first factor from a principal components factor analysis including the: Picture Sequencing Task (episodic memory), Wisconsin Card Sort (executive function/cognitive flexibility), Flanker Task (executive function/inhibition), Penn Matrices Test (fluid intelligence), Penn Word Memory Test (episodic memory), and List Sorting Task (working memory).

Figure 2. Global efficiency of the cingulo-opercular network (CON) significantly positively predicted higher-order cognitive ability. Global efficiency measures a network's functional integration and potential for information transfer, suggesting that more functionally efficient CON supports better cognitive ability.

Figure 3.

Cingulo-opercular network (CON) global efficiency partially mediated the association between psychotic-like experiences (PLEs) and cognition. The 95% bias corrected confidence interval for indirect effect (path *ab*), which measures the reduction of the effect between PLEs and cognition ability when CON global efficiency is included in the model, is $[-0.0417, -0.003]$, indicating a significant reduction, and therefore a significant mediation. The mediation is partial, since the association between PLEs and cognition remains significantly greater than zero (path *c'*) with CON global efficiency in the model.

Table 1

Subject demographics

Demographics	All Subjects (N=468)	Subjects who did NOT endorse any PLEs (N=367)	Subjects who endorsed at least one PLE (N=101)	Difference Between Those Who Did/Did Not Endorse PLEs
Age mean (SD), years	29.17 (3.51)	29.44 (3.49)	28.21 (3.42)	$t(466)=3.15, p=.002$
Gender (%female/%male)	58.3/41.7	61.6/38.4	46.5/53.5	$\chi^2 = 7.38, p=.007$
Race (%white/%African American/%other)	74.1/20.7/5.2	79.3/16.3/4.4	55.4/36.6/8.0	$\chi^2 = 34.26, p<.001$
Subject Education mean (SD), years	14.85 (1.85)	15.02 (1.79)	14.20 (1.94)	$t(465)=4.04, p<.001$
Annual Household Income (%<\$10K/ %10K-39,999/%40K-74,999/%75K-100K, %>100K/%missing data)	7.1/32/29.5/15.8/15.0/0.6	4.9/30.2/30.5/16.3/17.4/0.5	14.9/38.6/25.7/13.9/5.9/1.0	$\chi^2 = 25.30, p=.001$

Demographic variables for all subjects; demographics for only those subjects who did not endorse any PLEs (i.e. summed score on the four questions of interest from the Achenbach Adult Self Report Scale (ASR) = 0), and demographics for only those subjects who scored > 0 on the four questions of interest from the ASR, indicating endorsement of at least one PLE. Statistical analyses revealed differences in the demographic data between those who endorsed no PLEs on the ASR, and those who endorsed at least one PLE (summed score > 0). Individuals who endorsed at least one PLE were significantly younger, more likely to be male, more likely to be African-American, had lower subject education, and lower annual household income on average.