**Dissociable Default Mode Network Connectivity Patterns Underlie Distinct Symptoms in Psychosis Risk**

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**Abstract**

The Clinical High Risk (CHR) stage of psychosis is characterized by subthreshold symptoms of schizophrenia including negative symptoms, dysphoric mood, and functional deterioration. Hyperconnectivity of the default-mode network (DMN) has been observed in early schizophrenia, but the extent to which hyperconnectivity is present in CHR, and the extent to which such hyperconnectivity may underlie transdiagnostic symptoms, is not clear. As part of the Shanghai At-Risk for Psychosis (SHARP) program, resting-state fMRI data were collected from 251 young adults (158 CHR and 93 controls, M = 18.72, SD = 4.68, 129 male). We examined functional connectivity of the DMN by performing a whole-brain seed-to-voxel analysis with the MPFC as the seed. Symptom severity across a number of dimensions, including negative symptoms, positive symptoms, and affective symptoms were assessed. Compared to controls, CHRs exhibited significantly greater functional connectivity ($p < 0.001$ uncorrected) between the MPFC and 1) other DMN nodes including the posterior cingulate cortex (PCC), and 2) auditory cortices (superior and middle temporal gyri, STG/MTG). Furthermore, these two patterns of hyperconnectivity were differentially associated with distinct symptom clusters. Within CHR, MPFC-PCC connectivity was significantly correlated with anxiety ($r= 0.23$, $p=0.006$), while MPFC-STG/MTG connectivity was significantly correlated with negative symptom severity ($r=0.26$, $p=0.001$). Secondary analyses using item-level symptom scores confirmed a similar dissociation. These results demonstrate that two dissociable patterns of DMN hyperconnectivity found in the CHR stage may underlie distinct dimensions of symptomatology.

## Introduction

Individuals who are diagnosed with schizophrenia typically suffer from a combination of affective, cognitive, and psychomotor symptoms.[1] Schizophrenia onset is marked by the first episode of psychosis, which typically occurs in adolescence or young adulthood.[2] Prior to onset, many individuals experience a psychosis-risk, or Clinical High-Risk (CHR) syndrome, which is characterized by subthreshold symptoms of schizophrenia.[3] These syndromes may include negative symptoms (e.g., avolition, alogia, anhedonia)[4,5], dysphoric mood,[6] impaired self representation,[7] cognitive decline,[8] and functional deterioration in major life roles,[6] among others.

Recent advances in neuroimaging have enabled the study of functional connectivity, i.e., the statistical interdependence of blood-oxygen-level-dependent (BOLD) signals between brain regions. Functional connectivity has been characterized in a variety of clinical populations, including individuals with schizophrenia.[9] Large-scale disruptions in functional connectivity have been reported in chronic schizophrenia,[10–12] early-stage psychosis,[10,13–16], and CHR.[17,18]

More specifically, previous studies have reported hyperactivity and hyperconnectivity within the default mode network (DMN),[19–22] an intrinsic brain network which includes regions such as the medial prefrontal cortex (MPFC), posterior cingulate cortex (PCC), and angular gyri (AG). The DMN is active at rest and during internally focused and self-referential tasks.[23,24] Furthermore, stronger DMN functional connectivity is associated with worse psychotic symptoms in patients and in individuals with familial risk.[22] In CHR individuals, there is evidence of increased DMN connectivity,[25,26] although no association with symptom severity has been reported.

The auditory cortices, including the superior and middle temporal gyri (STG/MTG), also exhibit altered neurobiology in schizophrenia, including differences in brain volume and cortical thickness,[27–31] cerebral blood flow,[32,33] white matter microstructure,[34,35] activation,[36,37] and functional connectivity[27,38] compared to healthy controls. A recent meta-analysis found that STG

and MTG are among the main regions with structural alterations in gray matter volume and white matter integrity in schizophrenia patients with persistent negative symptoms.[39] Evidence also suggests that connectivity between the STG/MTG and DMN regions such as the MPFC is associated with negative symptoms in schizophrenia.[40] In addition to being associated with negative symptoms, DMN-STG/MTG connectivity may also be associated with another aspect of schizophrenia symptomatology, auditory verbal hallucinations (AVH). The "resting state hypothesis" of AVH was developed based on observations of elevated resting state activity in both the auditory cortex and anterior cortical midline DMN regions such as the MPFC. It posits that MPFC-STG hyperconnectivity underlies misattribution of internally generated phenomena as external.[41] However, evidence of MPFC-STG/MTG hyperconnectivity has not yet been reported in clinical high risk individuals or those with schizophrenia.

In the present study, we examined rsfMRI data in CHR and healthy control (HC) participants from the Shanghai At-Risk for Psychosis (SHARP) program. We hypothesized that compared to HCs, CHR participants would exhibit hyperconnectivity within the DMN as well as between the DMN and auditory regions. Within CHR participants, we tested associations between DMN functional connectivity and summary scores of psychotic and affective symptoms assessed via the Structured Interview for Psychosis-Risk Syndromes (SIPS), Hamilton Anxiety Rating Scale (HAM-A), and Hamilton Depression Rating Scale (HAM-D). We further explored associations between DMN functional connectivity and item-level symptom scores.

## Methods and Materials

### Participants

This study involved 158 CHR participants and 93 healthy controls (HCs) matched on age, sex, and education. Most were naïve to psychotropic medication at baseline clinical assessment (95%) and neuroimaging (80%). The CHR participants were help-seeking individuals who were recruited at the Shanghai Mental Health Center (SMHC) for possible

inclusion in the Shanghai At Risk for Psychosis Program (SHARP). Healthy control participants were recruited through advertisements. SHARP is a collaborative, international, NIMH-funded research effort[18,42–55,55–72] between the SMHC and Harvard Medical School at Beth Israel Deaconess Medication Center (BIDMC) and Brigham and Women's Hospital, the Massachusetts Institute of Technology, and Northeastern University. The program was approved by the Institutional Review Boards at both BIDMC and the SMHC. All subjects or their legal guardians provided written informed consent. Participants under 18 also provided assent. **Table 1** provides basic demographic and clinical information for the current sample, similar to previous publications that utilized SHARP resting state data.[18,44]

Clinical and cognitive assessment

Prodromal symptoms were assessed using a validated Chinese version of the Structured Interview for Psychosis-Risk Syndromes (SIPS)[61,73], including 19 items grouped into 4 subscales (SIPS-P: positive symptoms; SIPS-N: negative symptoms; SIPS-D: disorganization symptoms; SIPS-G: general symptoms). A Chinese version of the Scale of Psychosis Symptoms (SOPS) was derived from the SIPS to determine CHR staging. A score on the global assessment of functioning (GAF) scale was also generated based on the SIPS.[74] SIPS and GAF scores were collected at a baseline assessment and at a one year follow-up visit. The MINI International Neuropsychiatric Interview (MINI) was used to identify previous and current psychotic disorders. Current symptoms of anxiety and depression were assessed using the Hamilton Anxiety Rating Scale (HAM-A) and the Hamilton Depression Rating Scale (HAM-D), respectively. Overall cognitive ability (i.e., IQ) was estimated with the Wechsler Abbreviated Scale of Intelligence (WASI).[75]

Image acquisition

Magnetic resonance imaging (MRI) scans were acquired using a 3T Siemens MR B17 (Verio) system with a 32-channel head coil. A T1-weighted anatomical MRI scan was taken (MP-RAGE; TR = 2300 ms, TE = 2.96 ms, FA = 9°, FOV = 256 mm, voxel size 1 × 1 × 1 $mm^3$, 192 contiguous sagittal slices, duration 9′14″). A resting-state scan was also taken (149 functional volumes; TR = 2500 ms, TE = 30 ms, FA = 90°, FOV = 224 mm, voxel size 3.5 × 3.5 × 3.5 $mm^3$, 37 contiguous axial slices, duration 6′19″).

Image preprocessing

We preprocessed scans using the CONN toolbox.[76] In brief, preprocessing steps included segmentation of gray and white matter tissue, realignment, slice-timing correction, normalization to Montreal Neurological Institute (MNI) space, and smoothing with a 6mm FWHM Gaussian filter (see details in Collin et al 2020). Potential spurious correlations in rsfMRI time-series were assessed using the Artifact Detection Tool (ART; http://www.nitrc.org/projects/artifact_detect). Outliers, defined as volumes with head displacement in the x, y, or z greater than 1mm relative to the previous frame or a mean global intensity greater than 3 standard deviations from the mean intensity for the whole rsfMRI scan, were removed from the data via linear regression. Motion correction was performed using 3 rotational, 3 translational, and 1 composite motion parameters. The resulting time-series were corrected for artifactual covariates and signals within white matter (3 principal components) and cerebrospinal fluid (3 principal components). They were also band-pass filtered (0.008 Hz-0.09 Hz). We calculated averaged framewise displacement across all timepoints for each participant.[77]

Between-group functional connectivity analysis

We first created an *a priori* MPFC seed (**Figure 1A**): an 8mm sphere centered at MNI coordinates (-3, 44, -2).[78] Using the CONN toolbox, we computed Pearson's correlation

coefficients between the average time course within the seed and the time courses of all other voxels in the brain. We converted Pearson's *r values* to *z*-scores via Fisher's transform. We then performed a two-sample t-test (CHR vs. HC) to identify voxels whose functional connectivity to the MPFC was significantly different between groups. A voxel threshold of $p<.001$ (uncorrected) and a cluster threshold of $p<0.05$ (controlling for false discovery rate, or FDR[79]) were used. For further analysis, we extracted connectivity strength (Fisher transformed *z*-scores) between the MPFC seed and three clusters, i.e., the posterior cingulate cortex (PCC) as well as left and right STG/MTG (averaged to derive a single MPFC-STG/MTG connectivity measure). To determine if there was an effect of medication status on MPFC-PCC or MPFC-STG/MTG connectivity, we performed a t-test comparing medicated subjects to non-medicated subjects.

Next, we performed the above procedure again using other key nodes of the DMN as seeds. A PCC seed was defined *a priori* as an 8mm sphere centered at MNI coordinates (-3, -39, 39)[78] (**Figure S1B**). An angular gyri seed was defined *a priori* as an 8mm sphere centered at MNI coordinates (-47, -70, 37; 52, -71, 38)[78] and averaged across left and right hemispheres (**Figure S1C**). We examined the functional connectivity between these seeds and the rest of the brain in order to compare their connectivity profiles to that of the MPFC.

Identification of connectivity-symptom relationships

To test brain-behavior relationships (in R v4.2.2.[80,81]), we ran linear regressions with each relevant clinical assessment (SIPS-P subscale, SIPS-N subscale, GAF, HAM-A, and HAM-D) as the outcome variable and functional connectivity (i.e., MPFC-PCC and MPFC-STG/MTG connectivity) as the predictor variable and performed FDR correction[79] to account for multiple comparisons. (While SIPS-D and SIPS-G were not our primary measures of interest, we tested their associations with MPFC-PCC and MPFC-STG/MTG connectivity as well.)

The relationships between MPFC-PCC and MPFC-STG/MTG connectivity and symptom data from follow-up visits conducted one year post-baseline were also examined. SIPS-P and

SIPS-N at follow-up were used as the primary psychotic symptom scales while SIPS-G2, the dysphoric mood item of the general symptoms subscale, was used as a measure of affective symptom severity (measures of HAM-A and HAM-D were not obtained at follow-up). GAF at follow-up was also examined.

Secondary analyses of connectivity-symptom relationships

To further explore the associations between functional connectivity and symptoms, we ran two secondary analyses using all 19 SIPS items, GAF, HAM-A, and HAM-D, i.e., 22 symptom scales total. First, we ran 22 separate regressions with the symptom scales as outcome and performed FDR correction to account for multiple comparisons. For all regression analyses, we also ran sensitivity analyses controlling for age, sex and framewise displacement.

Second, we conducted a principal component analysis (PCA) in R to reduce dimensionality within the symptom scales in a data-driven manner. For each of the two PCs that accounted for the most variance in the symptom data, we summed the product of the symptom scores and the corresponding component loadings to derive a composite score for each participant. Correlations between the resulting composite scores and MPFC functional connectivity were identified via linear regression.

## Results

Increased functional connectivity in CHR vs. HC

Compared to HC, CHR exhibited significantly greater functional connectivity ($p < .001$, uncorrected) between the MPFC seed and several regions (**Figure 1B**), including bilateral auditory cortices (middle temporal gyrus and superior temporal gyrus; left hemisphere peak: -52, -24, -20; right hemisphere peak: 56, -6, -22) and the PCC (peak: -2, -58, 6) as the two largest clusters (**Figure 1C**). Eight smaller clusters also exhibited hyperconnectivity to the MPFC seed, including additional DMN regions such as bilateral angular gyri, superior frontal gyri and left

cerebellum Crus II (**Table S1**). Similar results were observed when we controlled for age, sex, and framewise displacement (**Figure S2)**. In medicated subjects compared to non-medicated subjects, there was no difference ($p > .05$) in MPFC-PCC connectivity or MPFC-STG/MTG connectivity (**Figure S3**). CHR also exhibited greater functional connectivity ($p < .001$, uncorrected) between the PCC and AG seeds and several regions (**Figure S1**). Notably, in CHR the PCC and AG were not hyperconnected to the STG/MTG region.

Associations between functional connectivity and clinical measures

Within CHR participants, we found dissociable relationships between MPFC hyperconnectivity and symptom severity (**Figure 2**). Specifically, controlling for FDR ($q_{FDR} < .05$), stronger MPFC-PCC connectivity was significantly associated with higher HAM-A scores ($r = 0.23$, $p = 0.006$), and not with the SIPS-N subscale ($r = 0.15$, $p = 0.056$; **Figure 2A**). Greater MPFC-STG/MTG connectivity was significantly ($q_{FDR} < .05$) associated with higher total SIPS-N score ($r = 0.26$, $p = 0.001$), but not with HAM-A ($r = 0.09$, $p = 0.286$; **Figure 2B**). Neither MPFC-PCC nor MPFC-STG/MTG connectivity was significantly associated with HAM-D, SIPS-P or GAF ($q_{FDR} < .05$).

Our tests also revealed a significant association between baseline MPFC-PCC connectivity and change in SIPS-G2 between baseline and follow-up ($r = -0.22$, $p = 0.010$; **Figure S4**). There were also trend-level associations between MPFC-PCC connectivity and 1) GAF change ($r = 0.15$, $p = 0.078$) and 2) SIPS-N change ($r = -0.16$, $p = 0.057$).

Secondary analyses on SIPS items revealed that, after FDR correction ($q_{FDR} < 0.05$), MPFC-PCC connectivity was significantly associated with two general symptom items (G2, Dysphoric Mood and G4, Impaired Tolerance to Normal Stress) and MPFC-STG/MTG connectivity was significantly associated with two negative symptom items (N5, Ideational Richness; N2, Avolition) (**Table S2**). See supplementary materials for a full correlation matrix for

all connectivity and clinical variables (including all SIPS subscales and individual items, GAF, HAM-A, and HAM-D; **Figure S5**).

A secondary PCA revealed two PCs that together explained 69.4% of variance (PC1: 46.4%; PC2: 23.0%) in scores on the 22 symptom scales (**Figure S6A**). PC1 and PC2 were characterized by strong loadings for negative symptoms and affective symptoms (including both anxiety and depression symptoms) respectively (**Figure S6B**). Stronger MPFC-PCC connectivity was significantly associated with higher PC2 scores ($r = 0.27$, $p < 0.001$) but not with PC1 scores ($r = -0.02$, $p = 0.821$; **Figure S7A**). Stronger MPFC-STG/MTG connectivity was significantly associated with PC1 scores ($r = -0.20$, $p = 0.016$) but not with PC2 scores ($r = 0.11$, $p = 0.106$; **Figure S7B**). PC1 and PC2 variable loadings can be found in **Table S3**.

Sensitivity analyses revealed that similar dissociations were found after controlling for age, sex, and motion (**Table S2**).

## Discussion

This study examined the functional connectivity changes that occur during the clinical high-risk stage of psychosis, thereby providing insight into the mechanisms underlying the development of the disorder. Our investigation of CHR functional connectivity patterns revealed that, compared to HCs, CHR individuals exhibited hyperconnectivity 1) within the DMN and 2) between the MPFC and STG/MTG. Within the CHR group, within-DMN hyperconnectivity was preferentially associated with affective symptoms (i.e., anxiety as measured by HAM-A). MPFC-STG/MTG hyperconnectivity, on the other hand, was preferentially associated with negative symptoms (i.e., negative symptoms as measured by SIPS) and decreased global functioning.

This dissociation was further confirmed by secondary analyses of the SIPS items (**Figure 3**). Affective symptoms (i.e., dysphoric mood) were found to be preferentially associated with MPFC-PCC connectivity, while negative symptoms (i.e., avolition, ideational

richness/alogia) were preferentially associated with MPFC-STG/MTG connectivity. Further, a principal component analysis identified dimensions of symptomatology within the sample. The first principal component seemed to capture variability within the negative symptom dimension of the SIPS and was associated with MPFC-STG/MTG connectivity. The second principal component seemed to capture variability within the affective dimension of CHR symptomatology and was associated with MPFC-PCC connectivity. Prior investigations into the dimensional structure of schizophrenia symptomatology have identified separate negative and affective symptom dimensions.[82–85] Our findings suggest that, in CHR, these two dimensions may be neurobiologically distinct, involving disparate pathophysiological mechanisms.

Hyperconnectivity within the DMN has been previously reported in patients and relatives of people with schizophrenia,[20–22,86] although the opposite, hypoconnectivity, has been observed as well.[87–89] Importantly, within-DMN hyperconnectivity is associated with greater symptom severity[22] and predicts worse outcome[90] in early stage psychosis. Past studies have also reported DMN hyperconnectivity in the CHR stage of psychosis.[25,26] The present study replicates these findings. Furthermore, our study reveals an association between baseline within-DMN hyperconnectivity and baseline affective symptoms, such as anxiety, dysphoric mood and impaired tolerance to normal stress. Within-DMN connectivity at baseline was also associated with improvement in dysphoric mood between baseline assessment and follow-up. The direction of this relationship is consistent with the observation that individuals with higher baseline pathology (i.e., more room for improvement) show more reductions in symptoms at a followup time point.[91,92,93]

Beyond schizophrenia, within-DMN hyperconnectivity was also observed in major depressive disorder,[94–98] chronic pain,[99] autism,[100] and post-traumatic stress disorder.[101] Furthermore, several studies have identified associations between DMN connectivity and affective symptom severity in these populations.[94–96,99] More specifically, rumination, a form of repetitive negative thinking defined by a focus on one's own negative mood, is associated with

DMN hyperconnectivity in both healthy[102] and depressed[95,98,103–105] populations. Rumination is a transdiagnostic feature of several psychiatric illnesses including major depressive disorder, generalized anxiety disorder, post-traumatic stress disorder, substance abuse disorders, eating disorders, and insomnia.[106,107] These findings suggest that within-DMN hyperconnectivity may be a transdiagnostic phenomenon underlying rumination across a range of psychiatric illnesses, including schizophrenia. This is consistent with evidence that some CHR individuals are later diagnosed with disorders other than schizophrenia, such as major depressive disorder and generalized anxiety disorder.[108,109]

Thus, in addition to contributing evidence of a transdiagnostic nature of DMN hyperconnectivity, the current study also provides motivation for interventions aimed at reducing MPFC-PCC hyperconnectivity and thereby ameliorating the associated symptoms across disorders. Previous studies have identified several non-invasive strategies for down-regulating the DMN, including exercise,[110] meditation,[111] cognitive behavioral therapy,[112] antidepressant medications,[113] transcranial magnetic stimulation,[114] and real-time fMRI neurofeedback.[115]

To our knowledge, the current study is the first to report DMN-STG/MTG hyperconnectivity and further link it to negative symptoms in CHR individuals. A previous study found a similar association between fronto-temporal connectivity and negative symptoms in schizophrenia patients, although no group difference was observed between patients and HCs.[40]. The mechanism linking DMN-STG/MTG hyperconnectivity to negative symptoms has not been fully elucidated. However, there is evidence that auditory processing deficits may underlie cognitive impairment,[116,117] which is associated with negative symptoms in schizophrenia.[118–120] This framework linking impaired processing of auditory information with negative symptoms[121] may be extended to the CHR stage given our current finding. At the same time, the MPFC, together with the dorsal subsystem of the DMN,[122] is implicated in mentalizing. The pathophysiology of the DMN is also linked to poor social cognition in schizophrenia.[123] It is noteworthy that ideational richness, the SIPS negative symptom item most associated with

MPFC-STG/MTG connectivity in our CHR group, measures inability to follow conversations and articulate thoughts.[73] Hyperconnectivity between the MPFC and STG/MTG may therefore contribute to negative symptoms via combined impairments in auditory processing and social cognition.[40]

Our novel hyperconnectivity findings in CHR may also provide support for the 'resting state hypothesis' of AVH, which posits that elevated resting state activity in the auditory cortex is a result of abnormal interactions between the auditory cortex and anterior DMN midline regions at rest.[41] This hypothesis is based on evidence of hyperactivity in the STG and MTG at rest, hyperactivity of the anterior DMN at rest, and decreased stimulus-induced auditory cortex activity in patients with schizophrenia.[22,32,37,124,125] Consistent with the resting state hypothesis, after real-time neurofeedback training aimed at reducing DMN activity, patients with schizophrenia exhibited reduced MPFC-STG connectivity associated with reduced AVH.[126] With our current study, we report the first evidence that an abnormal interaction between MPFC and STG is present in the prodromal stage of the disorder. Furthermore, we show that, within the DMN, hyperconnectivity with the STG/MTG is specific to the anterior cortical midline portion (MPFC) as hypothesized. However, it is noteworthy that we did not find any association between MPFC-STG/MTG connectivity and the SIPS item for hallucinations (P4: Perceptual abnormalities/hallucinations). This may be due to subthreshold AVH presence in CHR. The onset of negative symptoms, cognitive deficits and resultant functional impairment often precede the development of positive symptoms and the development of psychosis.[5,6,127,128] The broad nature of the SIPS P4 measure, which captures perceptual abnormalities and hallucinations across all sensory modalities, may also explain the lack of association.

The present study has identified distinct and dissociable patterns of DMN hyperconnectivity as potential biomarkers for affective and negative dimensions of prodromal symptom development. Future research should focus on tracking DMN hyperconnectivity and its associated symptoms over time, as a longitudinal design coupled with deep phenotyping of

within-individual changes can inform on conversion vs. remission trajectories, enable mechanistic mapping of observed brain-behavior links (e.g., MPFC-STG/MTG hyperconnectivity, negative symptoms and cognitive deficits), and suggest optimal time points for intervention.

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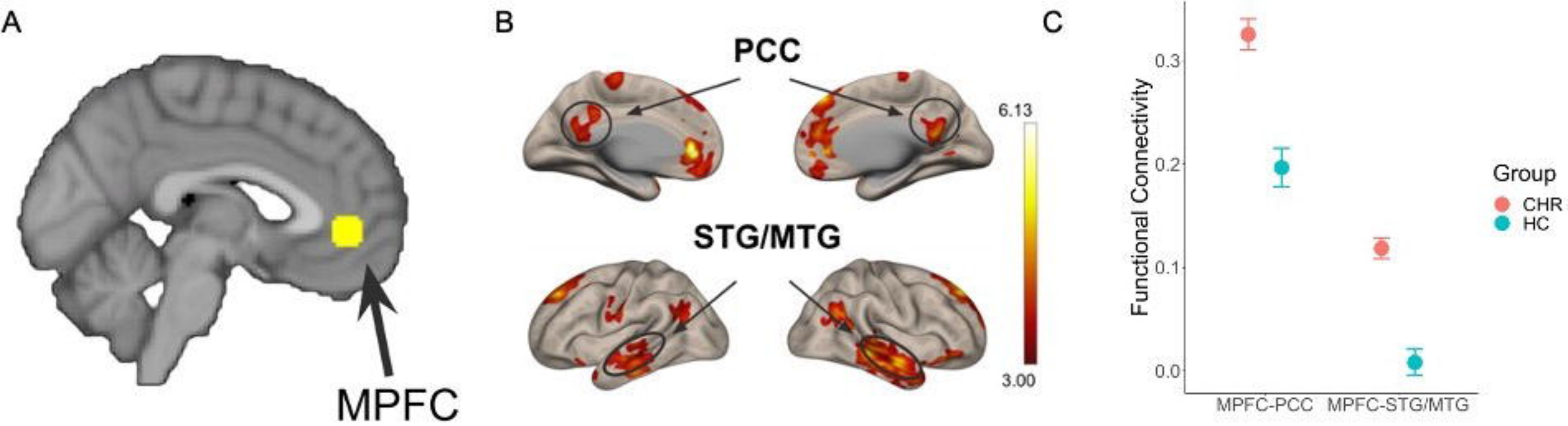
**Figure 1.** MPFC hyperconnectivity in CHR. **A)** We used an 8mm spherical seed in the MPFC.[78] **B)** A whole-brain search revealed hyperconnectivity between the MPFC seed and several regions, including auditory cortices and the posterior cingulate cortex ($p$ <.001, uncorrected). **C)** Group-level summary statistics for MPFC-STG/MTG and MPFC-PCC functional connectivity are displayed in magenta for CHR and in cyan for HC. Error bars indicate 1 standard error of the mean.

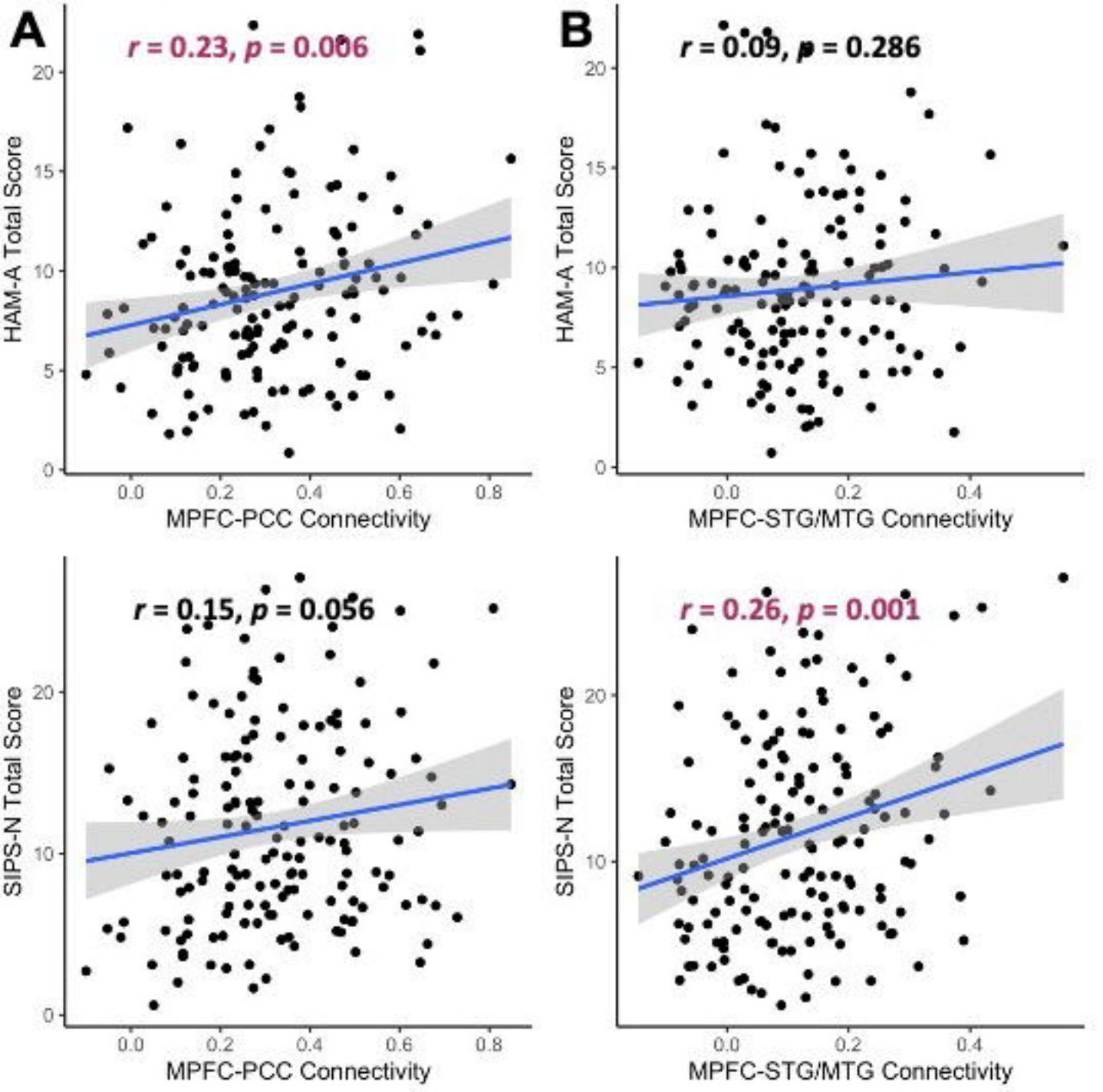
**Figure 2.** Dissociable relationships between MPFC connectivity and symptom severity in CHR. MPFC connectivity measures were defined based on CHR>HC comparison and independently of symptom measures. **A)** Individual differences in MPFC-PCC connectivity were significantly associated with variation in HAM-A scores and marginally so in SIPS-N scores. **B)** Individual differences in MPFC-STG/MTG connectivity were associated with variation in SIPS-N score, but not in HAM-A scores.

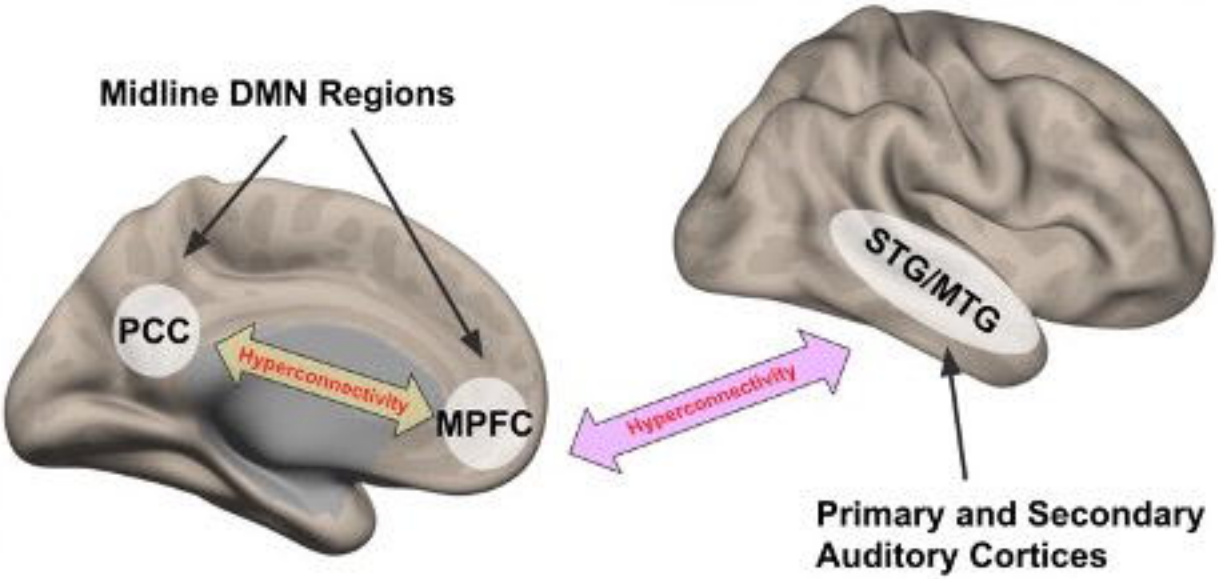
**Figure 3.** Hyperconnectivity in relation to SIPS items. MPFC-PCC hyperconnectivity in CHR was associated with HAM-A, Dysphoric Mood and Impaired Tolerance to Normal Stress. MPFC-STG/MTG hyperconnectivity in CHR was associated with SIPS-N total score, GAF, and the Ideational Richness and Avolition SIPS items.

**Table 1**. Demographic and clinical characteristics.

| | **Controls** (N=93) | **CHR** (N=158) | **Statistics** |
|---|---|---|---|
| Age, mean (sd) [range] | 18.7 (4.6) [12 - 35] | 18.8 (4.9) [13 - 34] | *t*=-0.43, p=0.671 |
| Sex, male/female | 49 / 44 | 80/78 | $X^2$=0.03, p=0.854 |
| Education in years, mean (sd) [range] | 10.8 (2.3) [6 - 17] | 10.5 (2.8) [4 - 19] | *t*=0.88, p=0.381 |
| IQ, mean (sd) [range] | 104.2 (11.1) [75 - 133] | 98.9 (12.8) [52 - 128] | *t*=3.24, p=0.001 |
| Framewise displacement, mean (sd) [range] | 0.1 (0.1) [0.0 - 0.4] | 0.1 (0.0) [0.0 - 0.3] | *t*=1.25, p=0.214 |
| Psychotropic medication | | | |
| At inclusion, N (%) | | 7 (4.4) | |
| At baseline MRI, N (%) | | 29 (18.4) | |
| Antipsychotics, N (%) | | 24 (15.2) | |
| Antidepressants, N (%) | | 7 (4.4) | |
| Other, N (%) | | 2 (1.2) | |
| Baseline SIPS scores | | | |
| Positive, mean (sd) [range] | 0.4 (0.8) [0-4] | 10.1 (3.6) [0 - 21] | *t*=-32.25, p<.001 |
| Negative, mean (sd) [range] | 0.3 (0.8) [0-4] | 11.7 (6.1) [1 - 27] | *t*=-23.05, p<.001 |
| Disorganized, mean (sd) [range] | 0.3 (0.5) [0-2] | 6.6 (3.2) [1 - 19] | *t*=-24.01, p<.001 |
| General, mean (sd) [range] | 0.6 (1.0) [0-4] | 9.1 (3.2) [1 - 17] | *t*=-30.79, p<.001 |
| Total, mean (sd) [range] | 1.6 (1.9) [0-9] | 37.4 (10.8) [13 - 79] | *t*=-40.46, p<.001 |
| Hamilton Anxiety Rating Scale Score | | 8.9 (4.3) [1 - 22] | |
| Hamilton Depression Rating Scale Score | | 14.3 (7.3) [3 - 46] | |


A
MPFC
B
PCC
STG/MTG
6.13
3.00
C
Functional Connectivity
0.3
0.2
0.1
0.0
MPFC-PCC
MPFC-STG/MTG
Group
CHR
HC


A
r = 0.23, p = 0.006
HAM-A Total Score
MPFC-PCC Connectivity
B
r = 0.09, p = 0.286
HAM-A Total Score
MPFC-STG/MTG Connectivity
r = 0.15, p = 0.056
SIPS-N Total Score
MPFC-PCC Connectivity
r = 0.26, p = 0.001
SIPS-N Total Score
MPFC-STG/MTG Connectivity




**MPFC-PCC hyperconnectivity**

- ❑ HAM-A

SIPS Items

- ❑ Dysphoric Mood
- ❑ Impaired Tolerance to Normal Stress

**MPFC-STG/MTG hyperconnectivity**

- ❑ SIPS-N total score

SIPS Items

- ❑ Ideational Richness
- ❑ Avolition