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# Dynamic Functional Connectivity States Reflecting Psychotic-Like Experiences

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## Abstract

**BACKGROUND—**Psychotic-like experiences (PLEs) are associated with lower social and occupational functioning, and lower executive function. Emerging evidence also suggests that PLEs reflect neural dysfunction resembling that of psychotic disorders.

**METHODS—**The present study examined dynamic connectivity related to a measure of PLEs derived from the Achenbach Adult Self-Report, in an otherwise-healthy sample of adults from the Human Connectome Project. 76 PLE-endorsing and 153 control participants were included in the final sample. To characterize network dysfunction, dynamic connectivity states were examined across large-scale resting-state networks using Dynamic Conditional Correlation (DCC) and k-means clustering.

**RESULTS—**Three dynamic states were identified. The PLE-endorsing group spent more time than controls in State 1, a state reflecting hyper-connectivity within Visual regions and hypo-connectivity within the Default Mode Network, and less time in State 2, a state characterized by robust within-network connectivity for all networks and strong Default Mode Network anti-correlations. Within the PLE-endorsing group, worse Executive Function was associated with more time spent in and more transitions into State 1 and less time spent in and fewer transitions into State 3.

**CONCLUSIONS—**PLEs are associated with altered large-scale brain dynamics, which tip the system away from spending more time in states reflecting more "typical" connectivity patterns toward more time in states reflecting Visual hyper-connectivity and Default Mode hypo-connectivity.

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**Keywords**

Psychotic Experiences; Psychosis; Dynamic Connectivity; Executive Function; Network; Default Mode Network

## Background

There is a growing consensus that psychosis occurs along a continuum that spans from subsyndromal symptoms observed in healthy individuals to clinically-significant symptoms observed in psychotic disorders. Subsyndromal symptoms, often referred to as Psychotic-Like Experiences (PLEs) include hallucinations and delusions, which are quantitatively but not qualitatively different from clinically significant psychotic symptoms (1). While only about 0.72% of individuals will be diagnosed with schizophrenia in their lifetime (2), the number that will experience PLEs is substantially higher, with prevalence estimates of 7.2% in adults (1, 3) and up to 40–60% (usually transitory experiences) in children and adolescents (4, 5). Individuals with PLEs may have no history of clinical diagnosis and may never develop a disorder; however, they tend to exhibit impairments in social and occupational functioning similar to, albeit less severe than, those observed in schizophrenia (6), supporting the notion that PLEs represent a more subtle form of psychosis. While in some cases, PLEs are indicative of risk for a psychotic disorder; in the majority of cases, symptoms either remit entirely or persist sub-clinically (3).

Consistent with the notion that they represent the low end of the psychosis continuum (1, 7), PLEs are associated with neural alterations that often resemble attenuated versions of those observed in schizophrenia (8). These include functional and structural changes across the brain, particularly within cognitive and reward systems (9–12). A number of studies have found alterations to the cingulo-opercular and default mode systems (11, 13–15), including reduced within-network connectivity and reduced between-network anti-correlation. In youths with PLEs, connections across these two systems emerged as the most-profoundly impacted across the brain (11). In addition, network efficiency is reduced within both of these systems in individuals endorsing PLEs and has been shown to scale with symptom severity (13).

Patients with psychotic disorders also exhibit alterations in frontoparietal connections. Both functional and structural connections are reduced between frontal and parietal nodes of this network in first-episode psychosis and schizophrenia (8, 16, 17). These regions have an established role in working memory and executive function and pathological activation patterns have been associated with impaired working memory in these disorders (18–20) as well as in healthy populations (19, 21). Moreover, alterations of the executive network have been found in individuals at genetic (19, 22, 23) and clinical (10, 24, 25) risk for schizophrenia, indicating that such deficits are present to varying degrees along the psychosis spectrum. In individuals endorsing PLEs, the findings have been mixed (14) with some suggesting that stronger frontoparietal connections may be a protective factor for individuals with sub-clinical PLEs that prevents or delays conversion (1, 14, 16).

While much of the resting-state literature has focused on static connectivity, or the correlation between regions across the scan duration, there has been recent interest in dynamic functional connectivity. Dynamic connectivity assesses changes in connectivity throughout the scan duration. Reoccurring connectivity patterns are commonly characterized as "states" that the brain moves in and out of over time. While alterations in connectivity have been identified in individuals with PLEs, to-date no published studies have examined alterations in dynamic connectivity associated with PLEs. Compared to static measures, dynamic connectivity improves classification accuracy (26, 27); and some studies that find few or no group differences in static connections, find more extensive disrupted connectivity when examining dynamic states (28, 29). Numerous studies find altered dynamic states in schizophrenia patients (26, 27, 29–31), suggesting that altered function may be due to disrupted dynamics for particular brain states. We therefore expect that examining large-scale dynamic connectivity states will reveal novel patterns of network alteration associated with PLEs.

The current study examined re-occurring dynamic states in the Human Connectome Project (HCP). The HCP is ideal for examining dynamic connectivity due to its high temporal resolution, long scan lengths, and multiple scan sessions. PLEs were derived from this dataset using four questionnaire items on the Achenbach Adult Self-Report (ASR) for ages 18–59 (32). These items have previously been used to examine PLEs and were robustly associated with graph metrics of functional connectivity in selected brain networks (13). For the current study, a large-scale network approach was taken to determine whether altered connectivity associated with PLEs reflect altered dynamic states.

## Methods and Materials

### Participants

Data for 820 healthy adult participants were available from the HCP 900 Subjects Data Release (http://humanconnectome.org/documentation/S900). To identify PLEs, ratings were summed across four items reflecting psychosis-like symptoms on the ASR:

1. I hear sounds or voices that other people think aren't there
2. I see things that other people think aren't there
3. I do things that other people think are strange
4. I have thoughts that other people would think are strange.

Participants could rate a 0, 1, or 2 for each item, reflecting: 0 not true, 1 somewhat or sometimes true, or 2 very true or often true. Across the full HCP sample, participants' summed ratings ranged between 0 and 6 across the four items, with the majority of participants scoring a total of 0. We defined the "high sub-clinical PLE" group (HP) as those participants that rated a 2 or more and the "low sub-clinical PLE" group (LP) as those participants that rated a 0 across the four ASR items. Fifty participants with a rating of 1 were excluded from the analysis in order to maximize group differences and to reduce noise that may have been related to participants' fuzzy interpretation of the Achenbach items.

The full HCP dataset included sets of siblings. To ensure that group differences were not affected by relatedness, only unrelated participants were included in the analyses. If two or more participants were related, the person that met criteria for the HP group was chosen and the other siblings were excluded. If at least two participants met for the HP group or at least two met for the LP group then one was randomly chosen and the other siblings were excluded. This resulted in 76 unrelated HP and 205 unrelated LP participants. The two groups were then matched for age, sex, handedness, race, ethnicity, and two measures of scan motion (mean absolute motion and mean relative motion, i.e. root mean square frame-wise displacement) by excluding LP participants. After matching, the final groups consisted of 76 HP and 153 LP participants, between 22 and 37 years old (Table 1).

## HCP Imaging Acquisition and Data Processing

As part of the HCP protocol, each participant completed four 14 minute, 33 second resting-state fMRI (rs-fMRI) runs on two separate days. The resting-state runs were eyes-open and participants were instructed to keep their eyes on the fixation cross. Scans were acquired on a Siemens connectome-Skyra 3T scanner with 32-channel head coil (multiband sequence, acceleration factor of 8, TR = 0.72 sec, 2 mm isotropic spatial resolution) (33).

Dynamic connectivity measures were computed on the time-courses from the "*Parcellation-Timeseries-Netmats (PTN) extensively processed resting-state fMRI dataset*" that were included in the HCP900 Data Release. This publically-released dataset had undergone the following preprocessing by the HCP (34, 35): artifact removal using ICA+FIX (36, 37), temporal demeaning and variance normalization (38), and data reduction using MELODIC for Incremental Group-PCA (39) and then spatial Group-ICA at several dimensionalities (34, 38). For the current study, the time-courses from the 300-dimensional ICA, that were extracted using the dual-regression approach, were used to examine dynamic connectivity.

## Network Identification

The volumetric MNI152 3D-space version of the 300-dimensional Group-ICA component spatial maps were automatically labeled based on spatial overlap with the Yeo 7-network parcellation (40). This consisted of first thresholding each of the 300 component ICA spatial maps so that only 5% of voxels with the highest intensity values were included. Each thresholded component map was then labeled as one of the seven networks: Visual (VN), Somatomotor (SMN), Dorsal Attention (DAN), Ventral Attention (VAN), Limbic (LN), Frontoparietal (FPN), or Default Mode (DMN), if: (1.) at least 500 suprathreshold voxels overlapped with one network; and (2.) over 55% of suprathreshold voxels fell within one network.

If the component failed these classification criteria for all seven networks, then it was labeled as "noise". This resulted in 65 "signal" components (29 VN, 8 SMN, 3 DAN, 2 VAN, 8 FPN, and 15 DMN). Dynamic connectivity measures were computed for the time-courses corresponding to these 65 "signal" components. The remaining 235 "noise" components were excluded from further processing and analysis.

## Dynamic Connectivity

Dynamic connectivity was computed using the Dynamic Conditional Correlation (DCC) approach (https://github.com/canlab/Lindquist_Dynamic_Correlation), a multivariate volatility method (41). Unlike sliding-window approaches that estimate connectivity over a fixed window length, this is a model-based method that estimates the contribution of surrounding time-points to the covariance matrix. Pairwise-dynamic connectivity values were obtained for every time-point of each participant's four resting state runs. This resulted in a matrix of connectivity values that was 1200 (time-points) × 2080 (connections) for each participant and each run.

K-means clustering was performed to identify the commonly occurring 'brain states' across the set of 2080 connections. This was done for each of the four runs by concatenating the matrix of connectivity values across all participants, resulting in a matrix that was 274,000 by 2080 (i.e. 229 subjects × 1200 time-points by 2080 connections). This matrix served as the input to the k-means clustering algorithm. Clustering was performed using the squared Euclidean distance to minimize distance to the centroid and was replicated five times for each run using different initial centroid values. The clustering was performed using a varying number of states (k = 2, …, 9) and the optimal cluster solution was identified by computing the Within-Cluster Sums of each time-point's Euclidean Distance to Centroid (sumd) for each cluster solution. This is done by plotting the sumd for each cluster solution choosing the optimal solution as the point at which reductions in sumd taper off. In addition, the reliability of the State Centroids across the four runs was assessed using the Intra-Class Correlation (ICC) coefficient to validate the optimal cluster solution.

The following dynamic connectivity summary measures were computed and used to investigate group differences: *1. Dwell Time* - the percent of time-points in each state. *2. Transitions* - the sum of time-points in which the state changed from time t-1 to time t. *3. Distance to Centroid* - the average of the squared Euclidean distance between connectivity at each time-point and the cluster centroid. Previous examination has shown low reliability of dynamic connectivity state summary measures across runs, which may be due to the low occurrence of some states for some participants (42). For this reason, each measure was first computed within each run and then averaged across the four runs to get a single value per participant.

Primary models tested for group by state interactions and included root mean square Frame-wise Displacement (FD) as a covariate to account for the effects of scan-to-scan motion on the dynamic connectivity measures. For Dwell Time and Transitions, multinomial logistic regression models included the proportion of time-points in each of the k-states compared to the total of any state as a response variable and assumed a multinomial distribution with a logit link function. Psychosis group (LP or HP) and FD were included as explanatory variables. For Distance to Centroid, a repeated-measures ANOVA model tested for a group by state interaction. Group membership was the between-subjects factor, while state was the within-subjects factor. Before ANOVA testing, the Distance to Centroid measures were natural log-transformed to ensure that they were normally distributed for each state.

Primary analyses were multiple-comparisons corrected by dividing p = 0.05 by 3 to get a critical p-value of p = 0.017 (i.e. by performing Bonferroni correction). For those dynamic connectivity measures in which significant group by state interactions were found at this corrected threshold, post-hoc tests examining group differences, while accounting for FD, were performed. In the case of Dwell Time and Transitions, binomial logistic regression was used for post-hoc tests of group effects in each state; while in the case of Distance to Centroid, this was done using general linear models testing for group effects in each state.

Phenotype associations were examined for the Thought Problems summary score of the ASR. In addition, a measure of Executive Function was created by averaging the unadjusted scores from the NIH toolbox (www.nihtoolbox.org) Executive Function tests: Card Sort, Flanker, and Working Memory/List Sort. Multinomial logistic regression (for Dwell Time and Transitions) and ANOVA (for Distance to Centroid) models were similar to the primary models testing for group effects, except that, in addition to testing the group effect, the models also included terms for phenotype and for the group by phenotype interaction. These models tested for whether the two groups differed in their phenotype by state interactions and included FD as a covariate. Multiple-comparisons were again accounted for by Bonferroni correction. In this case, six analyses were performed (i.e. testing the effects of 3 dynamic connectivity measures * 2 phenotypes), which resulted in a corrected p-value of 0.0083. If the group by phenotype interaction was determined to be significant, follow-up analyses were performed that tested for group, phenotype and group by phenotype interactions within each state. Analyses examining the phenotype association, which also included FD as a covariate, were also performed within the HP group alone to ensure that associations existed within that group. Finally, if there were no group by phenotype associations (at a subthreshold p-value of $p<0.05$), then associations across the two groups were performed by examining models that tested for group and phenotype effects (while excluding the group by phenotype interaction terms).

## Results

Using the elbow criterion to select the minimum-distance solution, k=3 was identified as optimal (Figure S1). Dynamic state summary measures were computed for the three-state solution. The centroid connectivity matrices for each of the three states were matched across the four runs by minimizing the sum of the Euclidean Distance. This resulted in high reliability of the State Centroids across the four runs (ICC = 0.994, 0.996, and 0.997 for States 1, 2, and 3, respectively). Due to the high similarity of the State Centroids between runs (Figure S2), each of the State Centroids were averaged across the four runs (Figure 1).

All three states generally showed the strongest connectivity for within-network connections in the seven labeled networks and weak or negative connectivity between the default mode and other networks. The most common state was State 3 with an average Dwell Time, or percent of time spent in state, of 49%, followed by State 2, with an average Dwell Time of 28%, and then State 1, with an average Dwell Time of 23%. Figure 2 displays the distributions for each state's Dwell Time, Transitions, and Distance to Centroid for both groups.

Table S1 displays the connectivity values for each state averaged over each network. State 3, the most frequent state, was characterized by weak within-network VN and SMN connectivity, and weak between-network connectivity for these two networks. This state also showed strong within-network DMN connectivity and strong anti-correlations between the DMN and other task-positive networks, particularly with the DAN and VAN. State 2, showed strong within-network connectivity for all networks and strong connectivity within and between the DAN and VAN components. In addition, like State 3, connectivity in State 2 tended to be more anti-correlated between the DMN and the DAN, VAN, and VN. State 1, the least frequent state, was characterized by stronger connectivity within Visual regions, but weaker connectivity within the DMN. In this state, DMN anti-correlations with the DAN and VAN were also weaker and connectivity within and between the DAN and VAN were weaker.

Table 2 displays the results for the psychosis by state effects for Dwell Time, Transitions, and Distance to Centroid. There was a significant group by state interaction in Dwell Time for States 1 and 2 (p= 0.74, p = 0.0062) and a marginal group by state interaction in Dwell Time for States 1 and 3 (B = 0.46, p = 0.049). However, after applying the multiple-comparisons threshold ($\alpha = 0.017$), only the Dwell Time effect for States 1 and 2 was significant. Follow-up tests of the group effect in States 1 and 2 revealed that the probability of spending time in State 1 was higher for the HP group (B = 0.56, p = 0.014), while the probability of spending time in State 2 was lower for the HP group (B = −0.44, p = 0.023). Examination of group by state interactions for Transitions revealed a marginal interaction for States 1 and 2 (B = 0.25, p = 0.047). However, this effect was not significant after multiple-comparisons correction. The group by state interaction for Distance to Centroid was also marginal (F(1.48,333.61) = 3.60, p = 0.042), but was not significant after multiple comparisons correction.

Results from the tests for phenotypic associations are displayed in Tables 3 and 4. Table 3 shows that Thought Problems were not associated with Dwell Time. Although there was a large group difference in Thought Problems ($p = 4.35 \times 10^{-26}$), this was not associated with Dwell Time when group effects were included in the model. Executive Function was differentially associated with dynamic connectivity measures for States 1 and 3 (Table 4). For Dwell Time, there was a subthreshold group by phenotype interaction (B = −0.093, p = 0.010). In the HP group, there was a differential association between Dwell Time and Executive Function in States 1 and 3 (B = −0.092, p = 0.005). More Dwell Time in State 1 was associated with worse Executive Function (B = −0.082, p = 0.016), while more Dwell Time in State 3 was associated with better Executive Function (B = 0.065, p = 0.028) (Figure 3A). For Transitions, there was a significant group by phenotype interaction (B = −0.068, p = 0.001) for States 1 and 3. Transitions were also significantly associated with Executive Function for the HP group only. For the HP group, more Transitions into State 1 were associated with worse Executive Function (B = −0.048, p = 0.009) and more Transitions into State 3 were associated with better Executive Function (B = 0.036, p = 0.009) (Figure 3B).

## Discussion

The current study examined functional dynamics underlying psychotic experiences in otherwise healthy individuals. Our sample was drawn from the HCP dataset, which is ideal for examining dynamic connectivity due to its high temporal resolution, large number of datapoints (i.e. four ~14.5 minute sessions), and high-dimensional spatial decomposition, which are well-suited for detecting recurring large-scale brain states. Dynamic Conditional Correlation (DCC) was used to compute dynamic connectivity at each timepoint. Unlike sliding-window approaches, this method does not require the a priori selection of a sliding-window length. Further, DCC provides more reliable connectivity estimates, which are less susceptible to noise (41). We found robust alterations in large-scale functional dynamics associated with PLEs. The results corroborate previous findings of profound functional alterations associated with psychosis, even for relatively mild symptoms in otherwise healthy individuals (13, 14). Control participants, those who did not endorse any PLEs, spent significantly more time in State 2. In addition, there were marginal effects suggesting that control participants made slightly more Transitions into State 2, and had lower Distance to the Centroid for State 2. This state generally reflected strong within-network connectivity for all networks, strong connectivity within and between DAN and VAN regions, and strong anti-correlation between the DMN and the DAN, VAN, and most Visual components; which is a relatively typical connectivity pattern as evidenced by static connectivity (43). Therefore, this state may reflect coordination between visual and higher-order networks for goal-directed behavior. Both our observed group differences and phenotypic associations suggest that State 2 reflects a healthier network configuration associated with lower symptomatology; while State 1 reflects pathology associated with PLEs. Within the HP group, spending more time in State 1 was also associated with worse Executive Function, suggesting that spending less time in State 1 is associated with healthier cognition.

The results are consistent with previous dynamic connectivity findings in the schizophrenia literature, in which there was altered connectivity in particular states (28, 44, 45). For example, one study focused on dynamic connectivity within the DMN and found that healthy controls spent more time in a state which reflected stronger connectivity between anterior and posterior sub-networks of the DMN; while patients with schizophrenia spent more time in a dis-connected DMN state (44). This is in line with the current finding that relative to those with PLEs, control participants spent more time in a state associated with robust DMN connectivity (State 2) and less time in a state with reduced DMN connectivity (State 1). This is particularly interesting, as it demonstrates how dynamic investigations can expand our understanding of the previously-observed static connectivity findings of disrupted executive-DMN network interactions in schizophrenia (46–49). It may be that not only overall static connectivity differences between the DMN and other networks is important, but also that the amount of time spent in states reflecting connectivity or dysconnectivity within the DMN may be important for psychosis.

Most studies examining PLEs have specifically focused on cognitive networks, such as the cingulo-opercular network, FPN, and DMN. However, the current study finds that dysfunction within those networks is only part of the story. Individuals experiencing PLEs spend less time in a state characterized by more typical connectivity within and between

both cognitive and sensory networks (State 2); however, perhaps more interestingly, they also spent more time in a state characterized by not just DMN hypo-connectivity but also visual hyper-connectivity (State 1). While a few studies have reported atypical connectivity in sensory regions associated with psychosis (14, 50), visual hyper-connectivity may be integral to PLEs and should be explored further. For example, visual hyper-activity observed in this state could potentially be the basis for certain psychotic symptoms, such as visual hallucinations. Future investigations could focus on the relationship between these states and severity of specific symptom domains.

## Future Considerations

PLEs were currently assessed in a large publically-available dataset using self-report items that were not specifically designed to examine psychosis. For this reason, assessment accuracy may be lower than that of other studies using assessments designed to examine subclinical psychosis. In addition, symptom variability was limited. Future studies, which recruit individuals with psychotic-like symptoms, could provide more accurate assessment and greater variability in psychosis symptoms.

The current study used k-means clustering across all timepoints and participants to identify re-occurring dynamic connectivity states. While this method is commonly used, other clustering algorithms may improve detection of aberrant connectivity patterns by combining group-level as well as subject-level information (28), or using non-linear boundaries to more accurately identify sub-states (51). Future studies may find that other algorithms are even more sensitive to atypical dynamic connectivity associated with PLEs.

Finally, the current study examined neural differences between psychosis-spectrum and control individuals. Future studies should examine how these differences relate to dynamic connectivity in individuals with a psychotic disorder. Some previous findings suggest that neural alterations underlying subclinical psychosis are similar to that of psychotic disorders; while others suggest that some neural alterations show compensatory patterns, which may confer resilience to conversion (7).

## Conclusions

Here we have demonstrated that psychotic-like experiences are associated with alterations in large-scale network dynamics. Specifically, individuals experiencing PLEs differed in their time spent in two dynamic connectivity states. They spent less time in a state exhibiting a more “typical” connectivity pattern across networks (State 2); and they spent more time in a state reflecting hyper-connectivity within Visual regions and hypo-connectivity in the DMN (State 1). Consistent with findings of executive alterations across the psychosis spectrum, spending more time in State 1 and less time in State 3 was associated with worse Executive Function in individuals experiencing PLEs. Overall, results suggest that the pattern observed in State 1 reflects pathology related to psychosis. This finding highlights the need to investigate not only static connectivity, but dynamic fluctuations in functional connectivity, and indicates that such dynamic fluctuations are sensitive to even subtle symptomatic change, potentially representing a novel endophenotype for psychosis.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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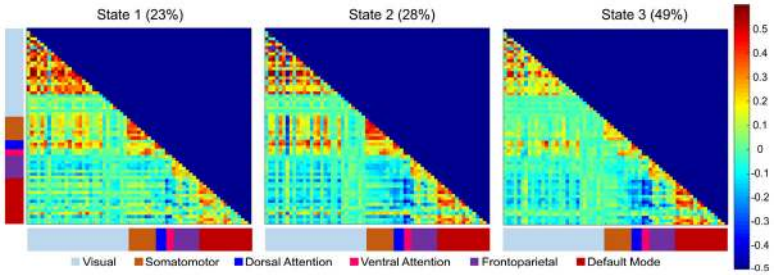


**Figure 1.**

Dynamic Connectivity States for k = 3. Each State Represents the Mean Cluster Centroid Across the Four Resting-State Runs. The Colorbar on the Right Represents the Strength of Each Connection and Ranges Between a Correlation of −0.5 to +0.6. Each Row and Column is One of the 65 Independent Components Classified as a "Signal Component" and the Color Labels on the X- and Y-Axes Indicate Their Network Affiliation. The Mean Dwell Time for All Participants is Displayed Next to Each State Title

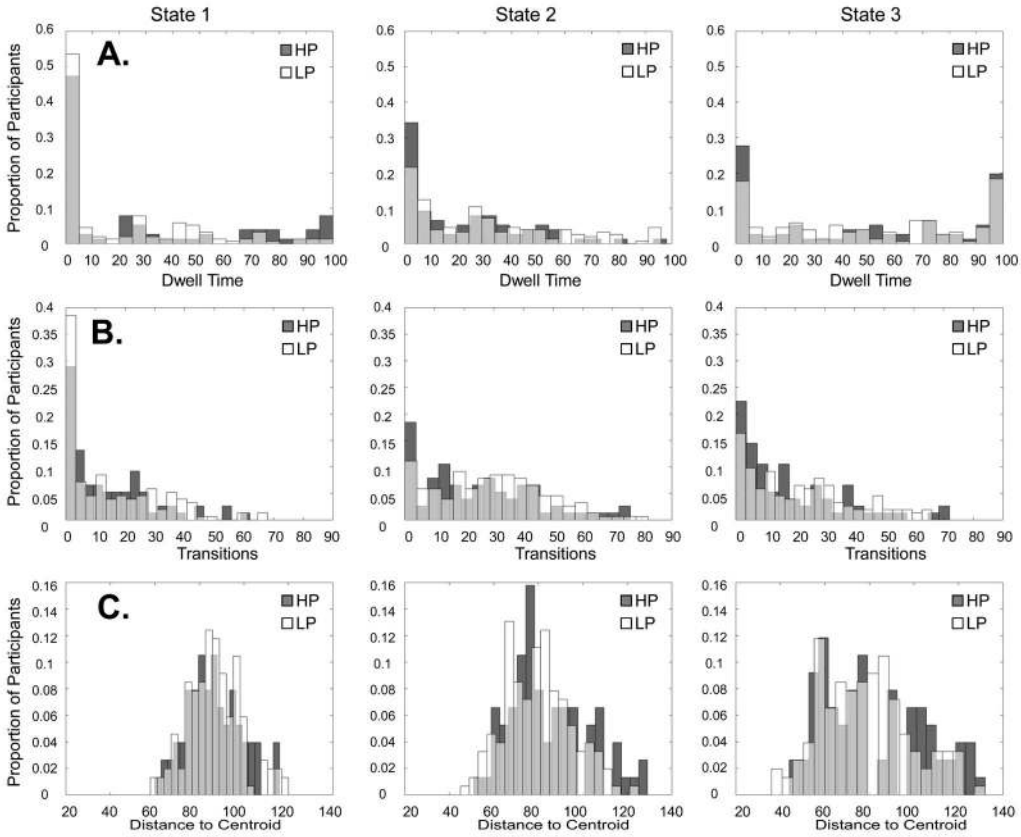


**Figure 2.**

Distributions for (A.) Dwell Time - Percent of Time in State, (B.) Total Transitions – Number of Timepoints Transitioning Into State, and (C.) Distance to Centroid – Average Distance to the Cluster Centroid, for the Low Psychosis (LP) and High Psychosis (HP) Groups

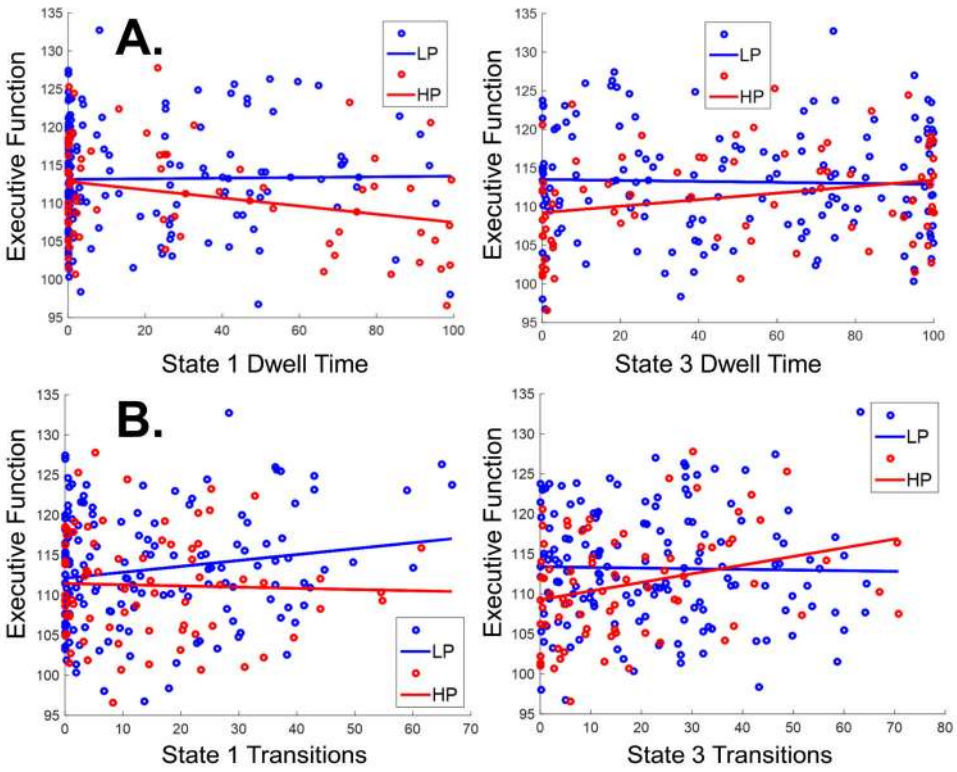


**Figure 3.**

Phenotypic Associations with Dynamic Connectivity Measures for (A.) Executive Function with Dwell Time in States 1 and 3, and (B.) Executive Function with Transitions into States 1 and 3. The Low Psychosis (LP) group is displayed in blue and the High Psychosis (HP) group is displayed in red.

**Table 1**

Participant Characteristics for the Low Psychosis (LP) and High Psychosis (HP) Groups

| | LP | HP | p-value |
|---|---|---|---|
| **N** | 153.00 | 76.00 | - |
| **Age** | 27.90 | 27.67 | 0.66 |
| **Sex (% male)** | 50.00% | 46.41% | 0.61 |
| **Handedness** | 66.41 | 64.74 | 0.77 |
| **Race (% caucasian)** | 63.16% | 71.24% | 0.23 |
| **Ethnicity (% hispanic)** | 11.84% | 13.73% | 0.69 |
| **Absolute Motion** | 0.76 | 0.72 | 0.32 |
| **Relative Motion** | 0.080 | 0.078 | 0.42 |
| **Income** | 5.14 | 4.36 | 0.010 |
| **Executive Function** | 113.22 | 111.24 | 0.039 |
| **Thought Problems** | 51.75 | 62.34 | 0.000 |

**Table 2**

Primary Results Examining Group by State Effects for Dwell Time, Transitions, and Distance to Centroid. The Findings Reported in Dark Blue are Significant at the Multiple-Comparisons Corrected Threshold of $p < 0.017$, While Findings in Light Blue are No Longer Significant After Correction. Significant Follow-up Tests for the Individual States are Highlighted in Orange. The Mean and Standard Deviation (SD) for the Low Psychosis (LP) and High Psychosis (HP) Groups are Displayed Below the Statistical Results for Each Measure

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | | **p-value** | |
| | **State 1 vs State 2** | **State 1 vs State 3** | **State 2 vs State 3** | **State1 vs State 2** | **State 1 vs State 3** | **State 2 vs State 3** |
| **intercept** | −0.730 | −1.330 | −0.601 | 0.125 | 0.002 | 0.136 |
| **psychosis** | 0.742 | 0.460 | −0.282 | 0.006 | 0.049 | 0.235 |
| **motion** | 3.829 | 5.271 | 1.442 | 0.486 | 0.282 | 0.762 |
| | | **beta** | | | **p-value** | |
| | **State 1** | **State 2** | **State 3** | **State 1** | **State 2** | **State 3** |
| **intercept** | −1.769 | −0.801 | | 0.000 | 0.014 | |
| **psychosis** | 0.559 | −0.437 | | 0.014 | 0.023 | |
| **motion** | 4.754 | −0.307 | | 0.316 | 0.936 | |
| | | **mean** | | | **SD** | |
| | **State 1** | **State 2** | **State 3** | **State 1** | **State 2** | **State 3** |
| **LP** | 20.06 | 30.46 | 49.48 | 26.44 | 27.43 | 36.12 |
| **HP** | 30.20 | 22.07 | 47.73 | 35.89 | 22.53 | 38.92 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | **Transitions** | | | |
| | | **beta** | | | **p-value** | |
| | **State 1 vs State 2** | **State 1 vs State 3** | **State 2 vs State 3** | **State1 vs State 2** | **State 1 vs State 3** | **State 2 vs State 3** |
| **intercept** | −0.920 | −0.646 | 0.274 | 0.000 | 0.005 | 0.151 |
| **psychosis** | 0.248 | 0.214 | −0.034 | 0.047 | 0.100 | 0.753 |
| **motion** | 1.319 | 0.961 | −0.358 | 0.610 | 0.721 | 0.873 |
| | | **mean** | | | **SD** | |

**Transitions**

| | beta | | | p-value | | |
|---|---|---|---|---|---|---|
| | State 1 vs State 2 | State 1 vs State 3 | State 2 vs State 3 | State1 vs State 2 | State 1 vs State 3 | State 2 vs State 3 |
| | State 1 | State 2 | State 3 | State 1 | State 2 | State 3 |
| **LP** | 14.96 | 29.05 | 21.90 | 16.04 | 18.19 | 17.62 |
| **HP** | 14.20 | 25.13 | 18.11 | 14.69 | 19.69 | 17.94 |

**Distance to Centroid**

| | F | df effect | df error | p-value |
|---|---|---|---|---|
| **psychosis** | 0.846 | 1.000 | 226.000 | 0.359 |
| **motion** | 5.826 | 1.000 | 226.000 | 0.017 |
| **state** | 5.359 | 1.476 | 333.607 | 0.011 |
| **state × psychosis** | 3.600 | 1.476 | 333.607 | 0.042 |

| | mean | | | SD | | |
|---|---|---|---|---|---|---|
| | State 1 | State 2 | State 3 | State 1 | State 2 | State 3 |
| **LP** | 87.02 | 79.94 | 78.46 | 12.10 | 14.94 | 20.06 |
| **HP** | 86.34 | 84.42 | 82.09 | 12.22 | 17.78 | 23.46 |

**Table 3**

Phenotypic Results Examining Group by State Effects for Thought Problems (TP). The Findings Reported in Dark Blue are Significant at the Multiple-Comparisons Corrected Threshold of p <0.0083, While Findings in Light Blue are No Longer Significant After Correction. Significant Follow-up Tests for the Individual States are Highlighted in Orange.

| | | | | | p-value | |
|---|---|---|---|---|---|---|
| **both groups** | **State 1 vs State 2** | **State 1 vs State 3** | **State 2 vs State 3** | **State1 vs State 2** | **State 1 vs State 3** | **State 2 vs State 3** |
| **intercept** | 3.568 | 0.591 | 2.976 | 0.174 | 0.780 | 0.177 |
| **psychosis** | −2.767 | 1.344 | −4.110 | 0.431 | 0.640 | 0.183 |
| **TP** | −0.014 | −0.017 | 0.003 | 0.709 | 0.588 | 0.934 |
| **psychosis × TP** | −0.043 | 0.031 | −0.074 | 0.501 | 0.540 | 0.180 |
| **motion** | −3.226 | −5.636 | 2.409 | 0.561 | 0.254 | 0.618 |
| | **beta** | | | | **p-value** | |
| **both groups** | **State 1 vs State 2** | **State 1 vs State 3** | **State 2 vs State 3** | **State1 vs State 2** | **State 1 vs State 3** | **State 2 vs State 3** |
| **intercept** | 2.350 | 1.519 | 0.832 | 0.139 | 0.254 | 0.552 |
| **psychosis** | −0.399 | −0.417 | 0.018 | 0.325 | 0.233 | 0.960 |
| **TP** | −0.032 | −0.004 | −0.028 | 0.277 | 0.878 | 0.281 |
| **motion** | −3.632 | −5.266 | 1.634 | 0.510 | 0.283 | 0.733 |
| | **beta** | | | | **p-value** | |
| **HP only** | **State 1 vs State 2** | **State 1 vs State 3** | **State 2 vs State 3** | **State 1 vs State 2** | **State 1 vs State 3** | **State 2 vs State 3** |
| **intercept** | −1.201 | −1.303 | −0.103 | 0.653 | 0.555 | 0.967 |
| **Thought Problems** | 0.015 | 0.014 | −0.002 | 0.695 | 0.671 | 0.966 |
| **motion** | 7.233 | −0.208 | −7.441 | 0.485 | 0.980 | 0.438 |

| | **Transitions** | | | | | |
|---|---|---|---|---|---|---|
| | **beta** | | | | **p-value** | |
| **both groups** | **State 1 vs State 2** | **State 1 vs State 3** | **State 2 vs State 3** | **State1 vs State 2** | **State 1 vs State 3** | **State 2 vs State 3** |
| **intercept** | 0.740 | −0.335 | 1.075 | 0.522 | 0.776 | 0.246 |

| | Transitions | | | | | |
|---|---|---|---|---|---|---|
| | beta | | | p-value | | |
| both groups | State 1 vs State 2 | State 1 vs State 3 | State 2 vs State 3 | State1 vs State 2 | State 1 vs State 3 | State 2 vs State 3 |
| psychosis | 0.071 | 0.467 | −0.396 | 0.964 | 0.773 | 0.766 |
| TP | −0.002 | 0.005 | −0.007 | 0.896 | 0.778 | 0.637 |
| psychosis × TP | 0.006 | 0.014 | −0.008 | 0.841 | 0.625 | 0.720 |
| motion | −1.331 | −1.078 | −0.253 | 0.611 | 0.693 | 0.911 |
| | beta | | | p-value | | |
| both groups | State 1 vs State 2 | State 1 vs State 3 | State 2 vs State 3 | State1 vs State 2 | State 1 vs State 3 | State 2 vs State 3 |
| intercept | 0.590 | −0.413 | 1.003 | 0.585 | 0.714 | 0.278 |
| psychosis | −0.242 | −0.195 | −0.048 | 0.055 | 0.138 | 0.667 |
| TP | 0.003 | 0.009 | −0.006 | 0.755 | 0.336 | 0.420 |
| motion | −1.128 | −0.338 | −0.791 | 0.672 | 0.903 | 0.732 |
| | beta | | | p-value | | |
| HP only | State 1 vs State 2 | State 1 vs State 3 | State 2 vs State 3 | State 1 vs State 2 | State 1 vs State 3 | State 2 vs State 3 |
| intercept | −0.586 | 0.307 | 0.893 | 0.627 | 0.806 | 0.409 |
| Thought Problems | 0.001 | −0.007 | −0.008 | 0.944 | 0.709 | 0.610 |
| motion | −0.778 | −3.022 | −2.244 | 0.864 | 0.518 | 0.575 |

| | Distance to Centroid | | | |
|---|---|---|---|---|
| both groups | F | df effect | df error | p-value |
| psychosis | 1.456 | 1.000 | 223.000 | 0.229 |
| TP | 0.039 | 1.000 | 223.000 | 0.844 |
| psychosis × TP | 5.567 | 1.000 | 223.000 | 0.009 |
| motion | 6.702 | 1.000 | 223.000 | 0.010 |
| state | 0.930 | 1.470 | 327.917 | 0.370 |
| state × psychosis | 0.190 | 1.470 | 327.917 | 0.758 |
| state × TP | 0.495 | 1.470 | 327.917 | 0.553 |
| state × psychosis × TP | 0.712 | 1.470 | 327.917 | 0.246 |

| Distance to Centroid | | | | | |
|---|---|---|---|---|---|
| **both groups** | **F** | **df effect** | **df error** | **p-value** | |
| **HP only** | **F** | **df effect** | **df error** | **p-value** | |
| **Thought Problems** | 1.609 | 1.000 | 73.000 | 0.209 | |
| **motion** | 0.668 | 1.000 | 73.000 | 0.416 | |
| **state** | 0.185 | 1.417 | 103.411 | 0.864 | |
| **state × Thought Problems** | 0.147 | 1.417 | 103.411 | 0.789 | |

**Table 4**

Phenotypic Results Examining Group by State Effects for Executive Function (EF). The Findings Reported in Dark Blue are Significant at the Multiple-Comparisons Corrected Threshold of p <0.0083, While Findings in Light Blue are No Longer Significant After Correction. Significant Follow-up Tests for the Individual States are Highlighted in Orange.

| | | | | | p-value | |
|---|---|---|---|---|---|---|
| **both groups** | **State 1 vs State 2** | **State 1 vs State 3** | **State 2 vs State 3** | **State1 vs State 2** | **State 1 vs State 3** | **State 2 vs State 3** |
| **intercept** | 0.767 | 2.267 | −1.501 | 0.779 | 0.367 | 0.498 |
| **psychosis** | −7.421 | −10.825 | 3.404 | 0.108 | 0.008 | 0.397 |
| **EF** | 0.059 | 0.084 | −0.025 | 0.092 | 0.005 | 0.422 |
| **psychosis × EF** | −0.061 | −0.093 | 0.033 | 0.144 | 0.010 | 0.359 |
| **motion** | −2.289 | −3.739 | 1.449 | 0.686 | 0.462 | 0.768 |
| | | **beta** | | | **p-value** | |
| **HP only** | **State 1 vs State 2** | **State 1 vs State 3** | **State 2 vs State 3** | **State 1 vs State 2** | **State 1 vs State 3** | **State 2 vs State 3** |
| **intercept** | 6.742 | 10.228 | 3.486 | 0.127 | 0.008 | 0.373 |
| **Executve Function** | −0.060 | −0.092 | −0.032 | 0.110 | 0.005 | 0.338 |
| **motion** | 2.970 | −6.143 | −9.113 | 0.773 | 0.459 | 0.340 |
| | | **beta** | | | **p-value** | |
| **HP only** | **State 1** | **State 2** | **State 3** | **State 1** | **State 2** | **State 3** |
| **intercept** | 8.480 | | −7.884 | 0.032 | | 0.024 |
| **Executve Function** | −0.082 | | 0.065 | 0.016 | | 0.028 |
| **motion** | −3.295 | | 7.129 | 0.700 | | 0.370 |

| | **Transitions** | | | | | |
|---|---|---|---|---|---|---|
| | | **beta** | | | **p-value** | |
| **both groups** | **State 1 vs State 2** | **State 1 vs State 3** | **State 2 vs State 3** | **State1 vs State 2** | **State 1 vs State 3** | **State 2 vs State 3** |
| **intercept** | 2.352 | 2.108 | 0.244 | 0.064 | 0.112 | 0.819 |
| **psychosis** | −5.428 | −7.837 | 2.409 | 0.009 | 0.000 | 0.183 |

| | Transitions | | | | | |
|---|---|---|---|---|---|---|
| | beta | | | p-value | | |
| both groups | State 1 vs State 2 | State 1 vs State 3 | State 2 vs State 3 | State1 vs State 2 | State 1 vs State 3 | State 2 vs State 3 |
| EF | 0.034 | 0.055 | −0.021 | 0.030 | 0.001 | 0.116 |
| psychosis × EF | −0.047 | −0.068 | 0.022 | 0.013 | 0.001 | 0.174 |
| motion | −1.114 | −0.392 | −0.722 | 0.673 | 0.887 | 0.753 |
| | beta | | | p-value | | |
| both groups | State 1 | State 2 | State 3 | State 1 | State 2 | State 3 |
| intercept | −2.361 | | 1.172 | 0.334 | | 0.577 |
| psychosis | 9.679 | | −7.479 | 0.014 | | 0.038 |
| EF | −0.076 | | 0.058 | 0.010 | | 0.035 |
| psychosis × EF | 0.082 | | −0.066 | 0.020 | | 0.039 |
| motion | 3.199 | | −2.586 | 0.513 | | 0.566 |
| | beta | | | p-value | | |
| HP only | State 1 vs State 2 | State 1 vs State 3 | State 2 vs State 3 | State 1 vs State 2 | State 1 vs State 3 | State 2 vs State 3 |
| intercept | 3.795 | 6.845 | 3.050 | 0.047 | 0.001 | 0.067 |
| Executve Function | −0.037 | −0.061 | −0.023 | 0.022 | 0.001 | 0.100 |
| motion | −3.014 | −6.325 | −3.310 | 0.497 | 0.171 | 0.401 |
| | beta | | | p-value | | |
| HP only | State 1 | State 2 | State 3 | State 1 | State 2 | State 3 |
| intercept | 4.464 | | −5.011 | 0.036 | | 0.002 |
| Executve Function | −0.048 | | 0.036 | 0.009 | | 0.009 |
| motion | −4.491 | | 4.339 | 0.357 | | 0.252 |

| | Distance to Centroid | | | |
|---|---|---|---|---|
| both groups | F | df effect | df error | p-value |
| psychosis | 2.344 | 1.000 | 226.000 | 0.127 |

| Distance to Centroid | | | | |
|---|---|---|---|---|
| **both groups** | **F** | **df effect** | **df error** | **p-value** |
| **EF** | 1.525 | 1.000 | 226.000 | 0.218 |
| **psychosis × EF** | 2.172 | 1.000 | 226.000 | 0.142 |
| **motion** | 4.889 | 1.000 | 226.000 | 0.028 |
| **state** | 0.756 | 1.483 | 332.223 | 0.434 |
| **state × psychosis** | 6.381 | 1.485 | 332.223 | 0.012 |
| **state × EF** | 5.077 | 1.485 | 332.223 | 0.013 |
| **state × psychosis × EF** | 4.704 | 1.485 | 332.223 | 0.018 |
| **HP only** | **F** | **df effect** | **df error** | **p-value** |
| **EF** | 0.135 | 1.000 | 226.000 | 0.713 |
| **motion** | 5.381 | 1.000 | 226.000 | 0.021 |
| **state** | 0.421 | 1.485 | 335.707 | 0.596 |
| **state × EF** | 0.875 | 1.485 | 335.707 | 0.390 |