Exploring the functional dynamics of large-scale brain networks within and across individuals

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Background and Rationale

- Human cognition and behavior emerge from the synchrony of brain networks, and disruptions to this synchrony have been observed in human psychiatric illness[1].
- Resting state MRI has been studied using static analyses, but the brain is inherently dynamic. Understanding temporal shifts in network behavior may provide an additional dimension of specificity with which to identify biomarkers of disease.
- Recent evidence[2,3,4] suggests network coherence fluctuates across distinct states over time.
- Here we explored the dynamic organization of cortical networks in healthy young adults and patients with schizophrenia spectrum disorders or psychotic bipolar disorder.

Methodological Approach

Participants:

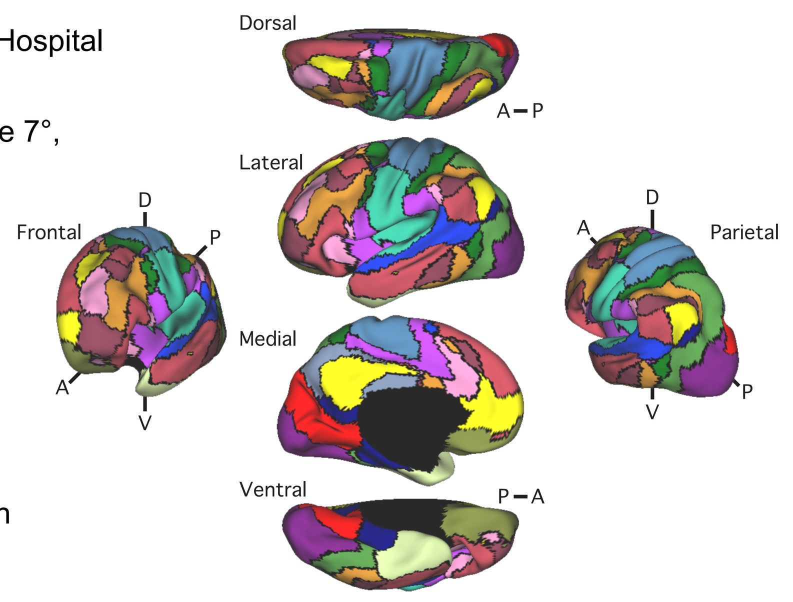
- n = 1,919 healthy participants between the ages of 18 and 35 (mean age 21.3; 56% F)[5]
- n = 79 participants who had at least two scans on separate days within 6 months of each other
- n = 157 participants with psychotic illness (mean age = 31.5, 38% F) and n = 358 matched controls (mean age = 37.1, 33% F)

Scanning Parameters:

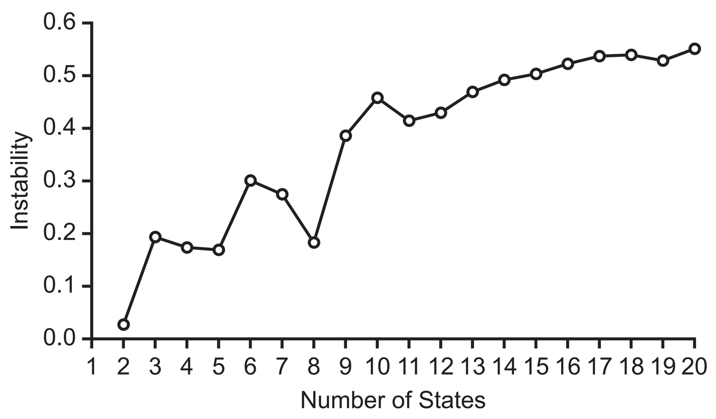
- Healthy participants were scanned at Harvard/Massachusetts General Hospital on a 3T Tim Trio. The clinical sample was scanned at McLean Hospital.
- MPRAGE: 144 1.2mm slices, TR=2.2s, TE=1.5/3.4/5.2/7.0 ms, flip angle 7°, 1.2x1.2x1.2-mm voxels, FOV 230.
- EPI sequences: 47 3mm slices, TR=3s, TE=30 ms, flip angle 85°, 3x3x3-mm voxels, FOV 216.

Analyses

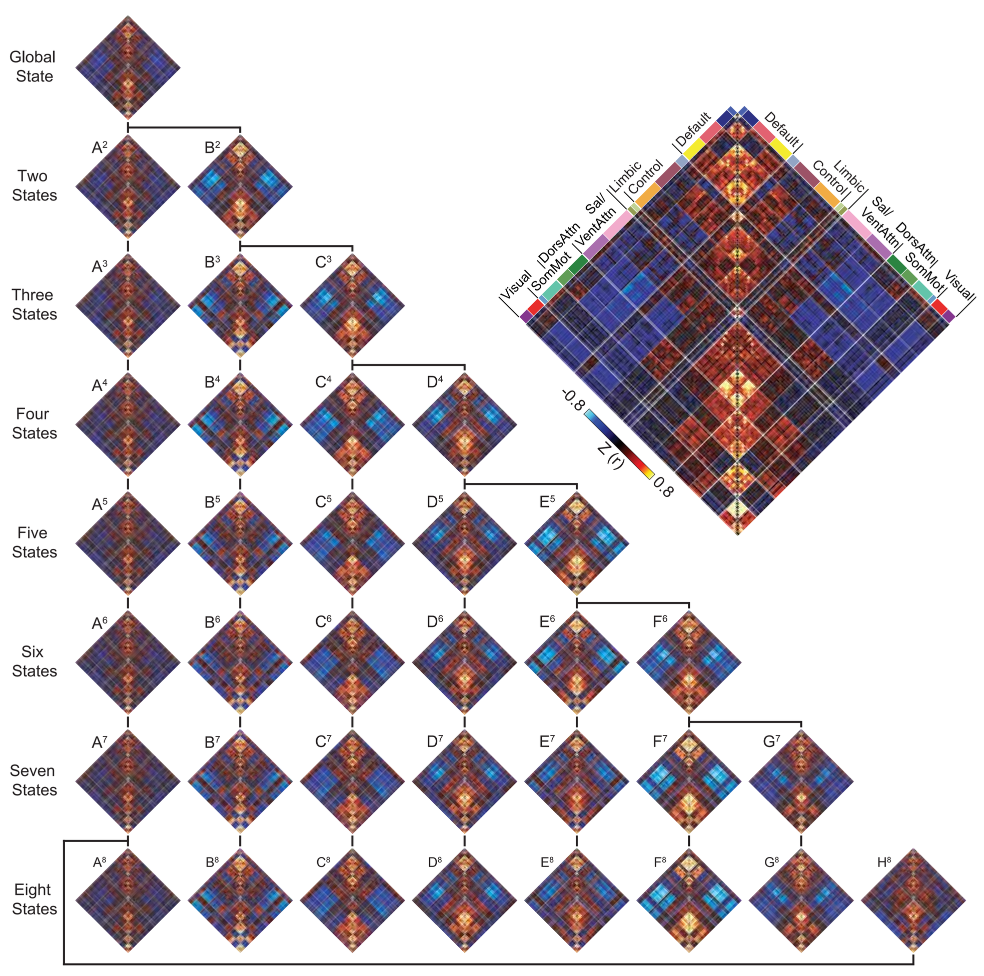
- Cortical networks (**right**) were parcellated according to prior work demonstrating reliable functional coupling across 57 ROIs in each hemisphere into 17 networks[6].
- Dynamic connectivity was computed through a sliding window approach using k-means clustering[2,3] and a 33 second window.



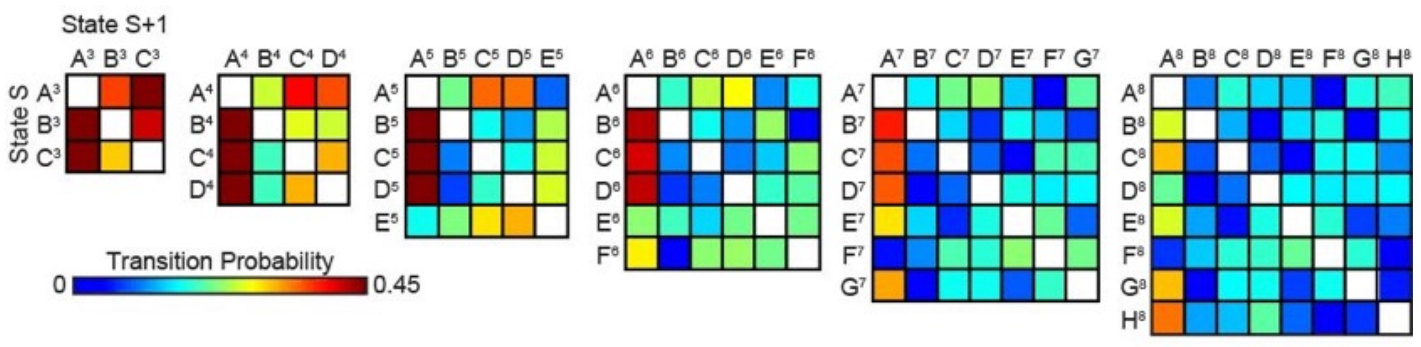
Network architecture shows reconfigurable hierarchy



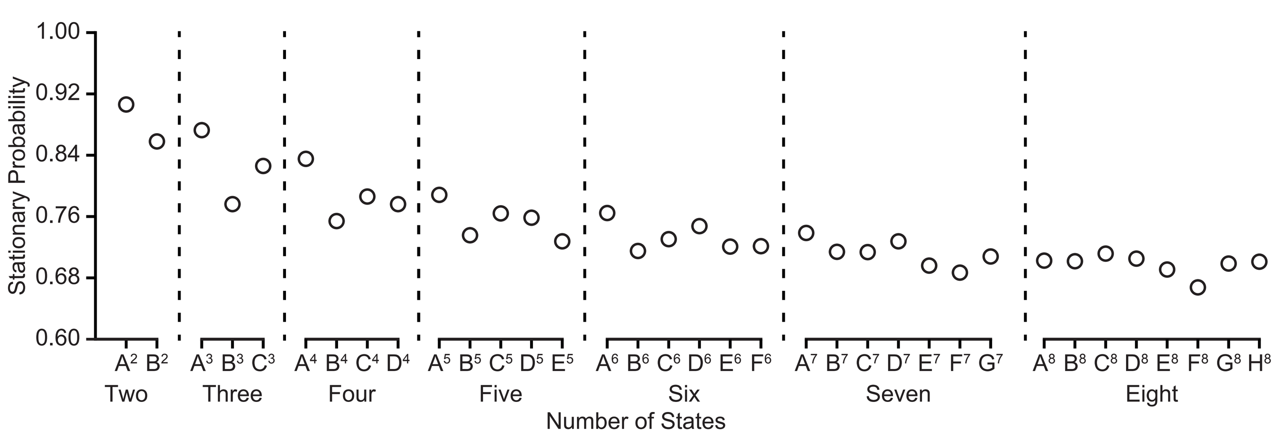
- 2 and 4,5, and 8 state solutions can be stably estimated.
- To quantify hierarchical relationships, we examined the scenario that two states of the (n+1) state solution were subdivisions of a component of the n state solution.
- Hungarian matching was used to determine which 2-state combination in n +1 was best matched to the n state solution.
- Correlation matrices Z(r) of the results for state solutions 1 through 8 are shown for each ROI.



State solutions reveal evidence for an attractor state

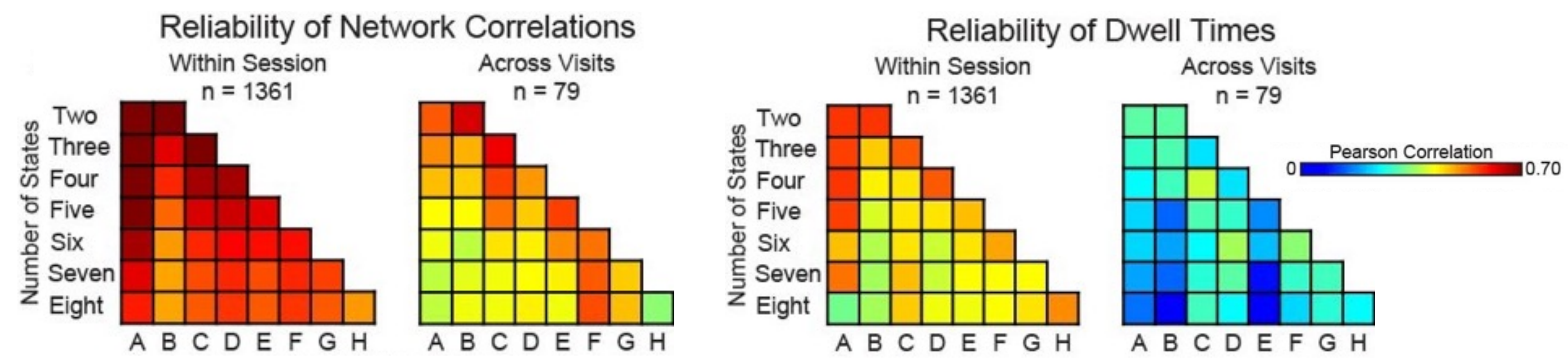


When transitioning between states participants display an increased probability of entering state A. The probability of transitioning to each state is shown for all non-redundant possible combinations across state solutions 3-8 (1,2 are obligated).

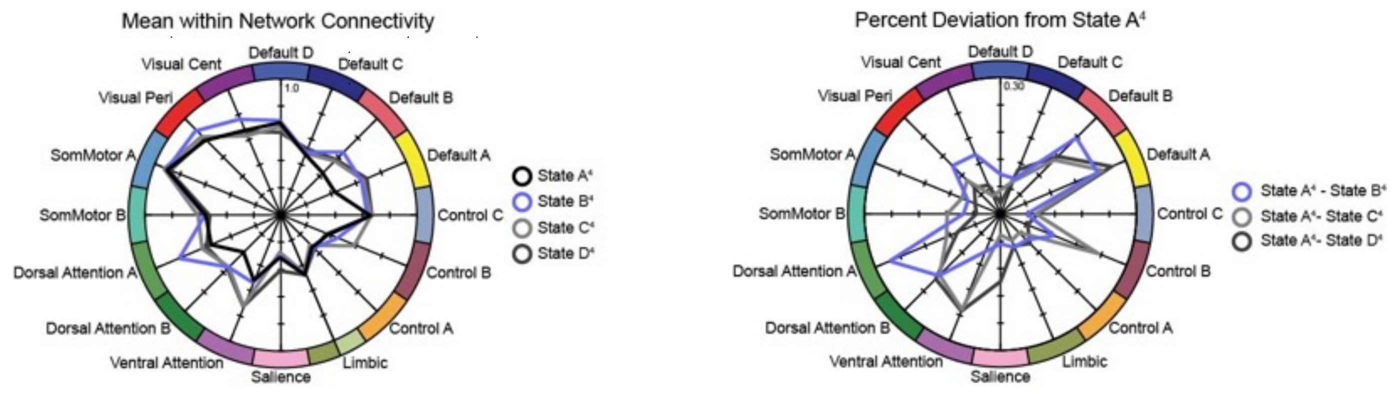


State A displays increased stationary probability for state solutions 2-7. Stationary probability for state solutions 2-8 show probability of remaining in a state from time point t to time point t +1.

Network architecture is distinct and specific to individuals

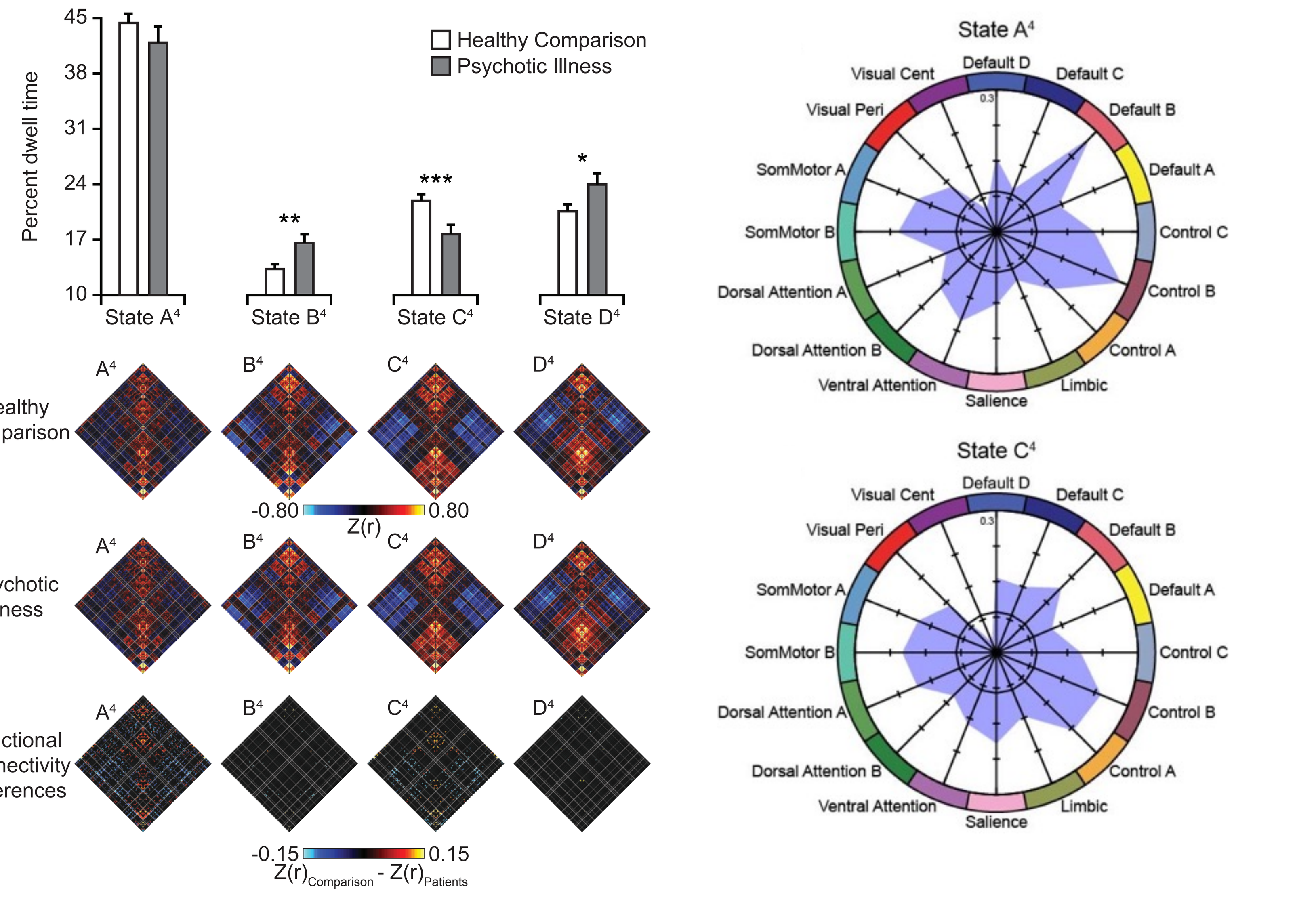


Pearson correlations between bold runs (left; n=1,361) and visits (right; n = 79) indicate a significant level of consistency within individual participant connectivity profiles.



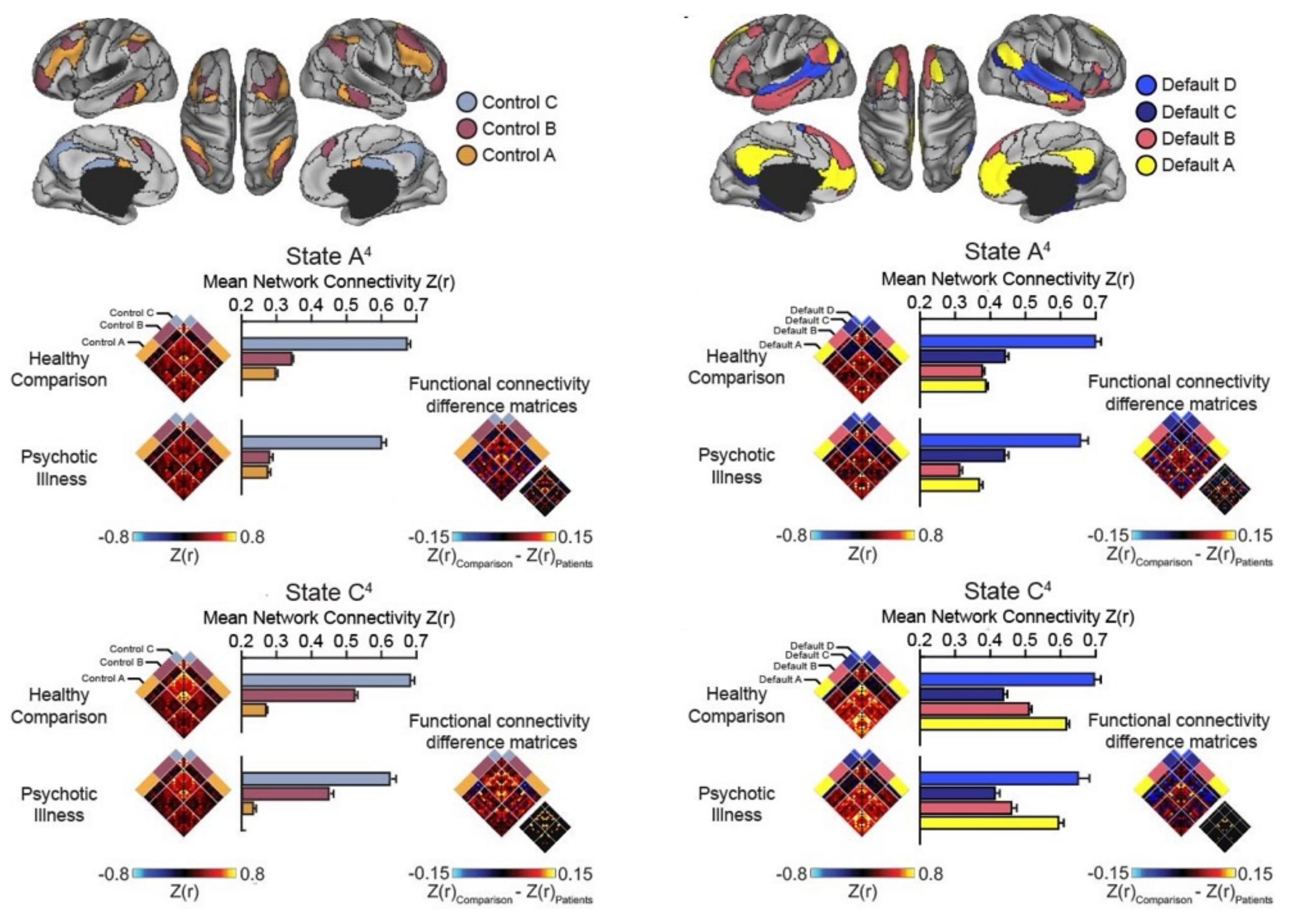
Polar plot shows the mean within-network connectivity for each state within the four state solution (left;) and percent deviation from State A^4 (right).

State expression is altered in psychosis



- Bar graphs display the dwell time for controls and patients within the four state solution.
- 2D grids display the complete coupling architecture within and between each group.
- Polar plots show percent difference in mean network connectivity between control and psychotic illness groups for States A^4 and C^4.

Network-specific disruptions are state-specific in psychosis



In psychosis, reduced frontoparietal and default network connectivity is evident in states A^4 and C^4. Bar graphs reflect mean network connectivity for each group within Control A-C and Default A-D. Results suggest that putative network disruption in psychosis may be state specific.

Conclusions

- The human brain oscillates across multiple architecturally distinct brain states.
- Across state solutions, dynamic brain states appear to organize into a reconfigurable hierarchy relative to an attractor state.
- Observed connectivity profiles are reliable within participants across scans and visits.
- Psychotic illness is associated with state-specific abnormalities in functional connectivity.
- These findings suggest that understanding temporal shifts in network coherence may elucidate the mechanisms that underlie psychosis.

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