

Dynamic brain activity states in ischemic pontine stroke

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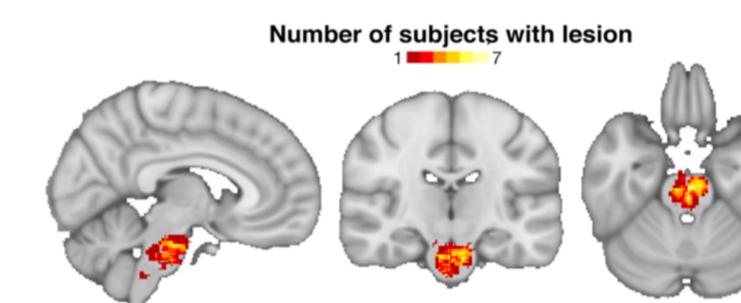
Background

Strokes disrupt the brain's functional and structural connections, triggering an elusive process of functional network reorganization to regain lost function. Recent work has shown that stroke subjects occupy distinct functional connectivity states (Bonkhoff et al., 2020). While dynamic functional connectivity analyses can capture communication between brain regions over time, recent approaches to study brain dynamics by considering whole-brain patterns of activations can capture meaningful brain activity at single-TR resolution (Cornblath et al., 2020).

Specifically, temporal sequences of brain activity at rest can be grouped into recurring 'brain states'. These states reflect canonical resting-state networks are modulated by age, task performance, and psychedelic drugs (Cornblath et al., 2020, Singleton et al., 2021).

Here, we apply this approach to study brain activity dynamics of ischemic pontine stroke subjects.

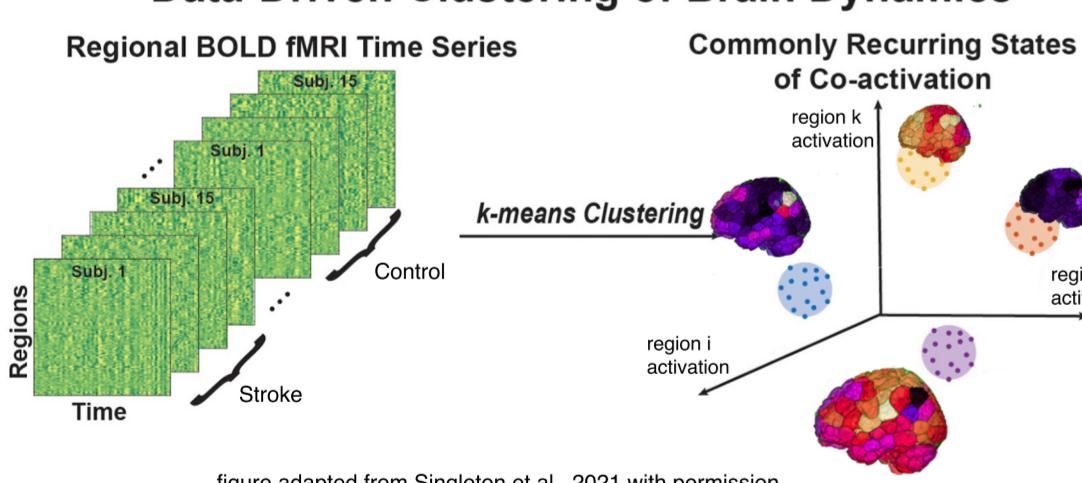
Eyes-open resting state fMRI was obtained at 5 longitudinal imaging sessions: 7, 14, 30, 90, and 180 days post-stroke, and at the same time intervals in age-matched healthy controls.



We hypothesize that stroke subjects will exhibit altered brain activity states relative to healthy controls.

Methods

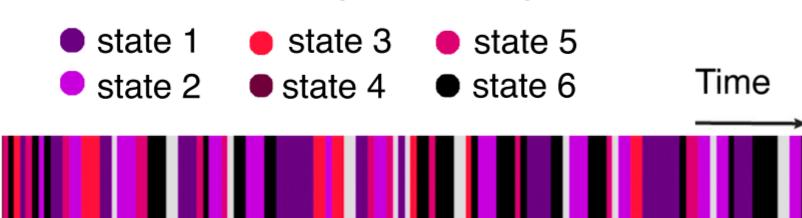
Data-Driven Clustering of Brain Dynamics



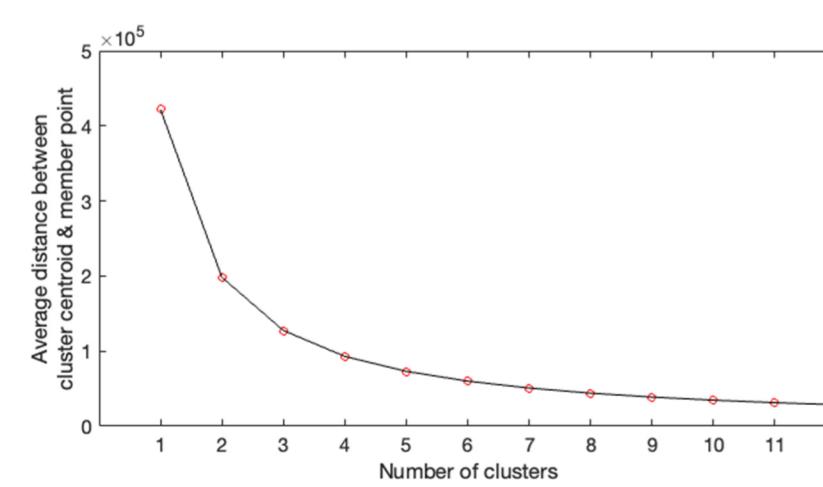
Dynamic brain activity states were generated with k-means clustering of the BOLD timeseries data (268 region Shen atlas, Shen et al., 2013). Timeseries data from stroke and control subjects at all time points were combined into a single large matrix, and k-means clustering was performed.

K-means clustering produces distinct 'brain states' that represent a vector of brain activity that commonly recurs over time. Example centroids of each cluster are plotted to visualize the spatial pattern of brain states.

Each TR is assigned a single brain state



Optimal # clusters identified with elbow criteria



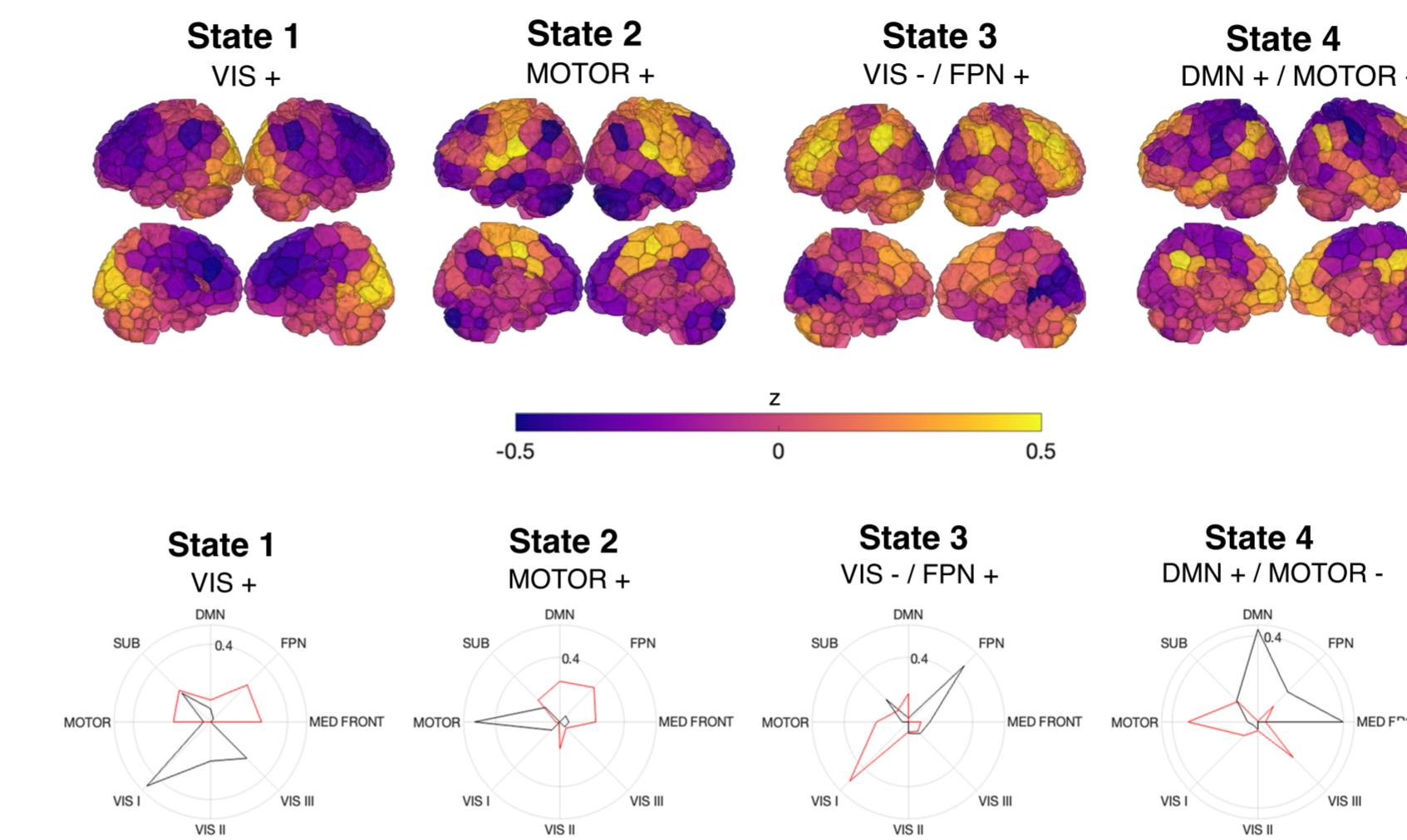
Fractional occupancy: probability of occurrence of each state (#TRs in a state/total #TRs)

Dwell time: average time spent in each state before switching states (avg. # consecutive TRs assigned to each state)

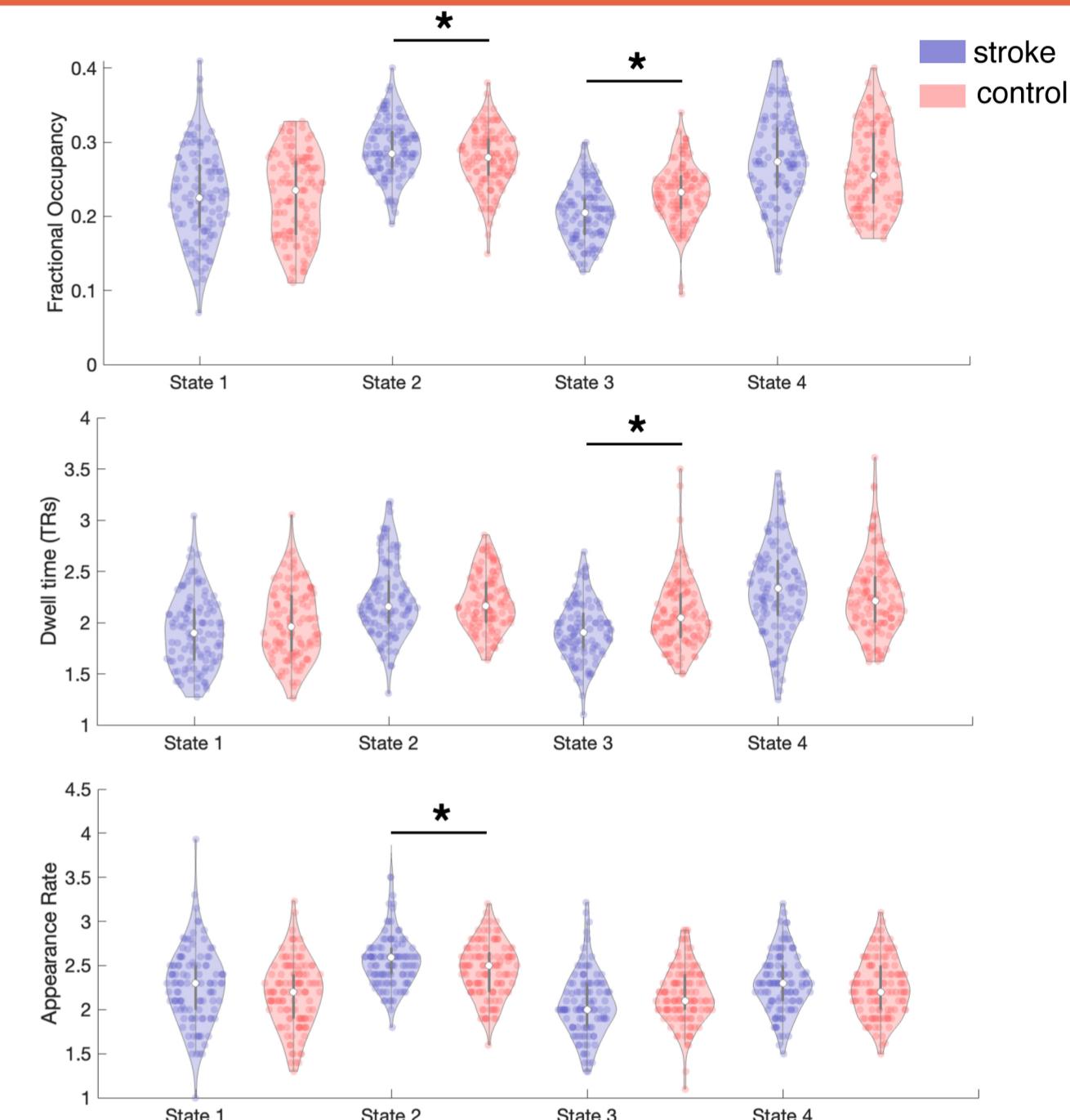
Appearance rate: number of times a state it transitioned into per minute

Transition probability: probability of switching to any given state *i* from state *j* (includes probability of transitioning to the same state)

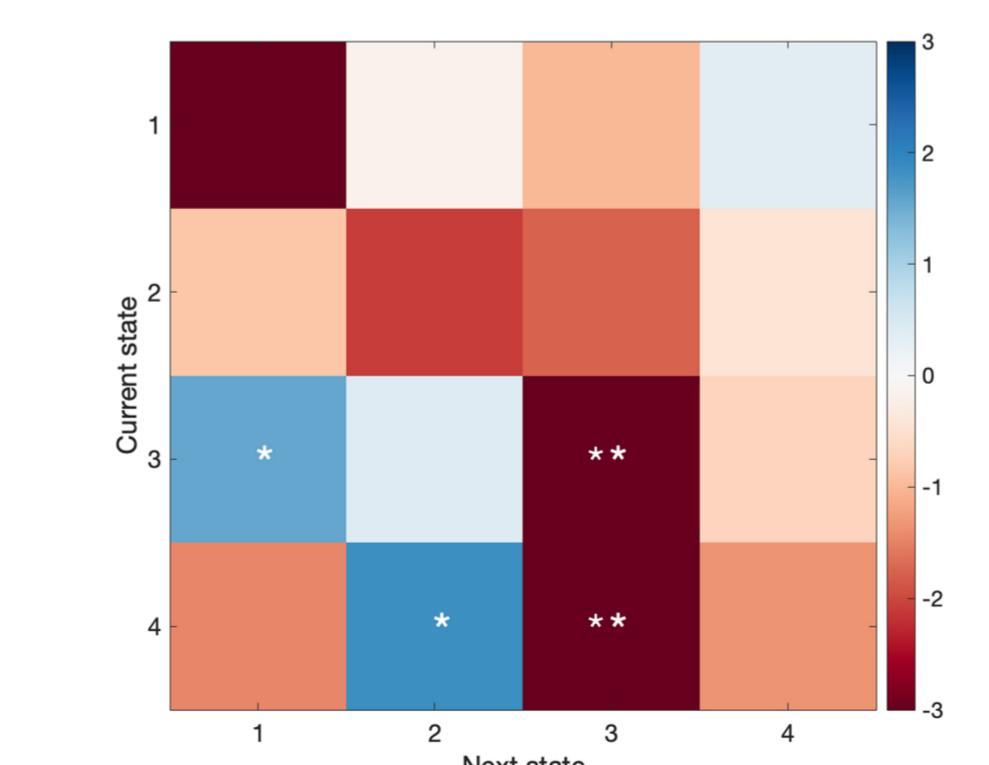
Results



Description of brain activity states. Top row: centroids of each state plotted on model brains. Labels for each state are derived from the cosine similarity between the spatial pattern of activations and the 8 networks identified by Finn et al., (2015). Bottom row: radial plots displaying cosine similarity between each cluster & each network; red indicates cosine similarity of negative activations, black indicates cosine similarity of positive activations. DMN = default mode network, FPN = frontoparietal network, MED FRONT = medial frontal network, VIS III = visual association network, VIS II = visual network 2, VIS I = visual network 1, MOTOR = motor network, SUB = subcortical/cerebellum network



Group differences across longitudinal sessions in fractional occupancy, dwell time, and appearance rate. Asterisks above violin plots indicate significant differences corrected for multiple comparisons. **Fractional occupancy:** stroke subjects spend less time in state 3 ($p(FDR) < 0.0001$) and spend more time in state 2 ($p(FDR)=0.0128$), compared to controls. **Dwell time:** stroke subjects remain in state 3 for less time than controls ($p(FDR)=0.0004$). **Appearance rate:** stroke subjects enter state 2 more often than controls ($p(FDR)=0.027$).



Differences in transition probabilities between stroke & control subjects. T-statistics (stroke-control) are displayed on the colormap; p-values < 0.05 (uncorrected) from 2-tailed permutation testing with 10,000 permutations on the transition probability matrices are represented by asterisks (double asterisk: significant after multiple comparisons correction). Top: all longitudinal sessions combined; right: each session analysed separately.

Conclusions

Stroke subjects spend more time in an activity state driven by motor network activation (state 2), possibly due to more transitions from state 4.

Stroke subjects spend less time in a state characterized by high frontoparietal and low visual network activity (state 3) potentially due to shorter dwell times in this state, and/or via reduced transitions from state 3 and 4.

We could not identify a relationship between brain activity dynamics and behaviour. Future work will examine whether a stroke's impact on the structural connectome influences state transitions by changing transition energies.