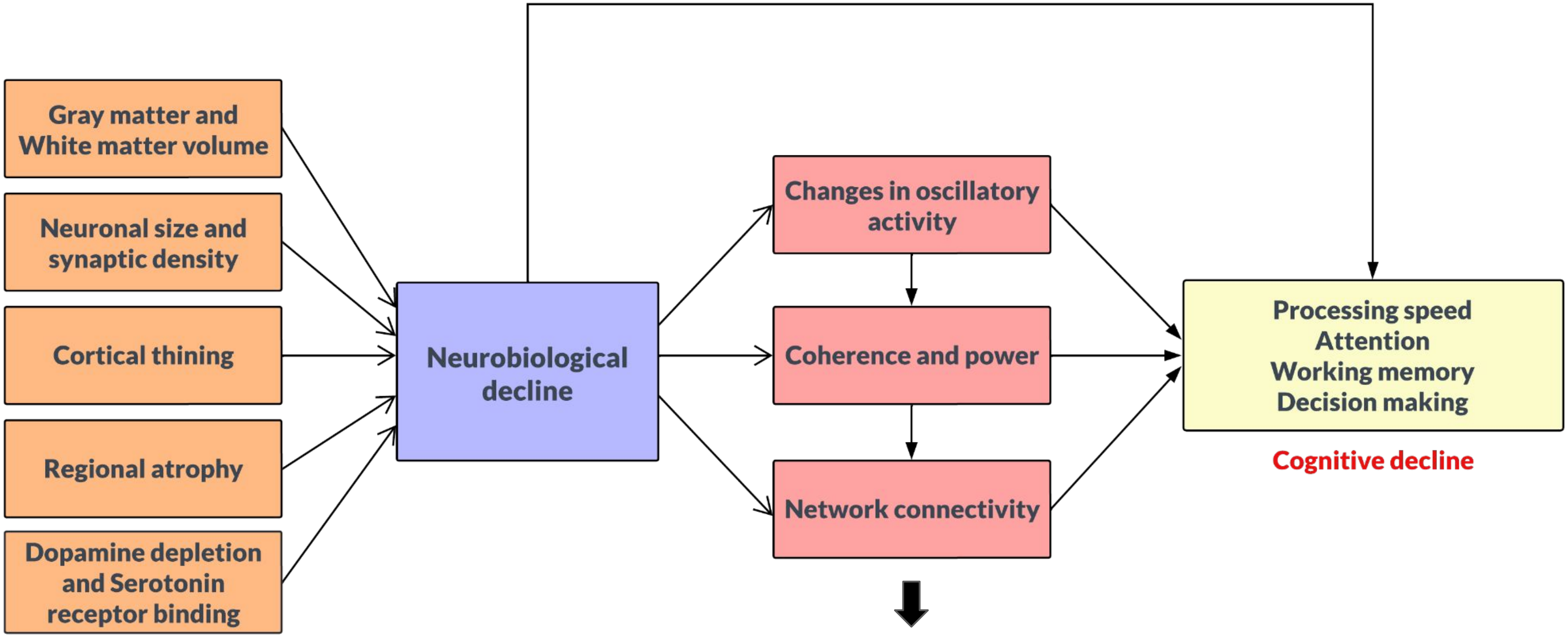
Characterizing temporally resolved connectivity patterns in transient brain states with lifespan aging

Mrittika Dey
MSc Neuroscience Dissertation
Supervisor: Dr. Dipanjan Roy

National Brain Research Centre
NH-8, Manesar, Gurgaon
Haryana-122052

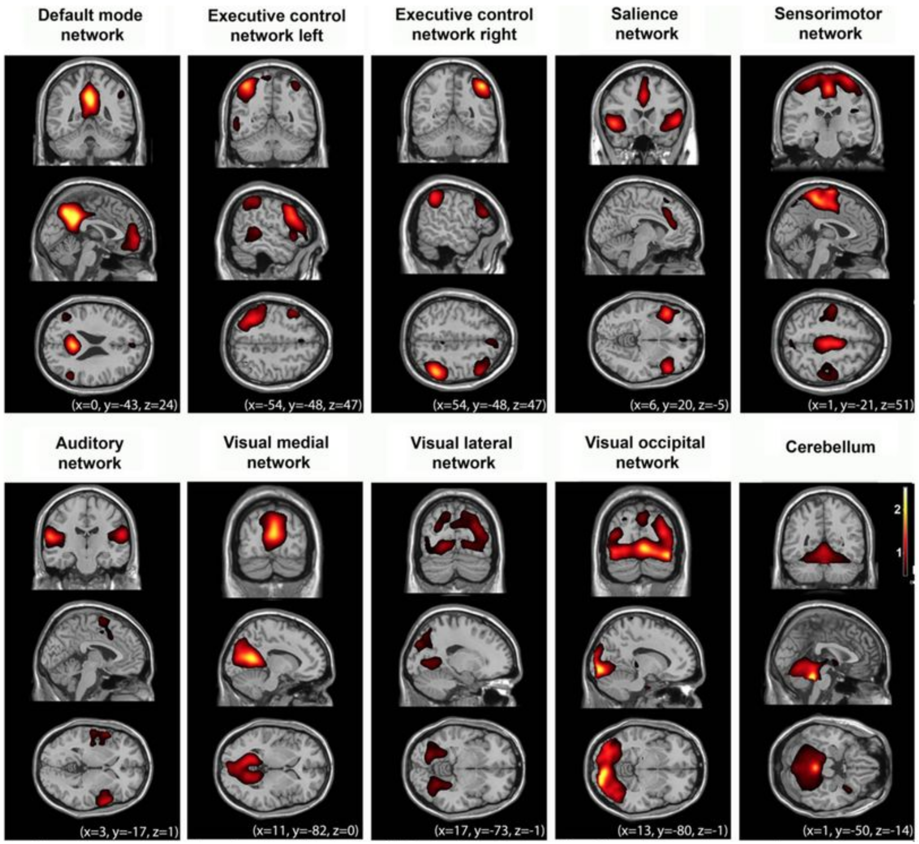
Introduction

Healthy aging is associated with :



Resting state transient brain networks

Resting state brain networks



- Functionally connected brain regions
- Correlation of activity over time
- Usually characterised using fMRI data

Transient connectivity between brain regions

⬇

Functionally connected networks

Background

- Age-related decline in activity of resting-state networks reflect the decline in task-related activity and poor cognitive performance.
- Previous studies have found age-associated disruptions in the resting-state functional architecture of the brain, especially in the default mode network (DMN), using fMRI techniques.
- The temporal variability of the network dynamics has been seen to be associated with behavioral traits (Vidaurre et al., 2017). However, a complete picture of the temporal variability in the fluctuation of neural dynamics and how it is related to aging is still missing.

Nashiro et al., 2017, Baker et al., 2014

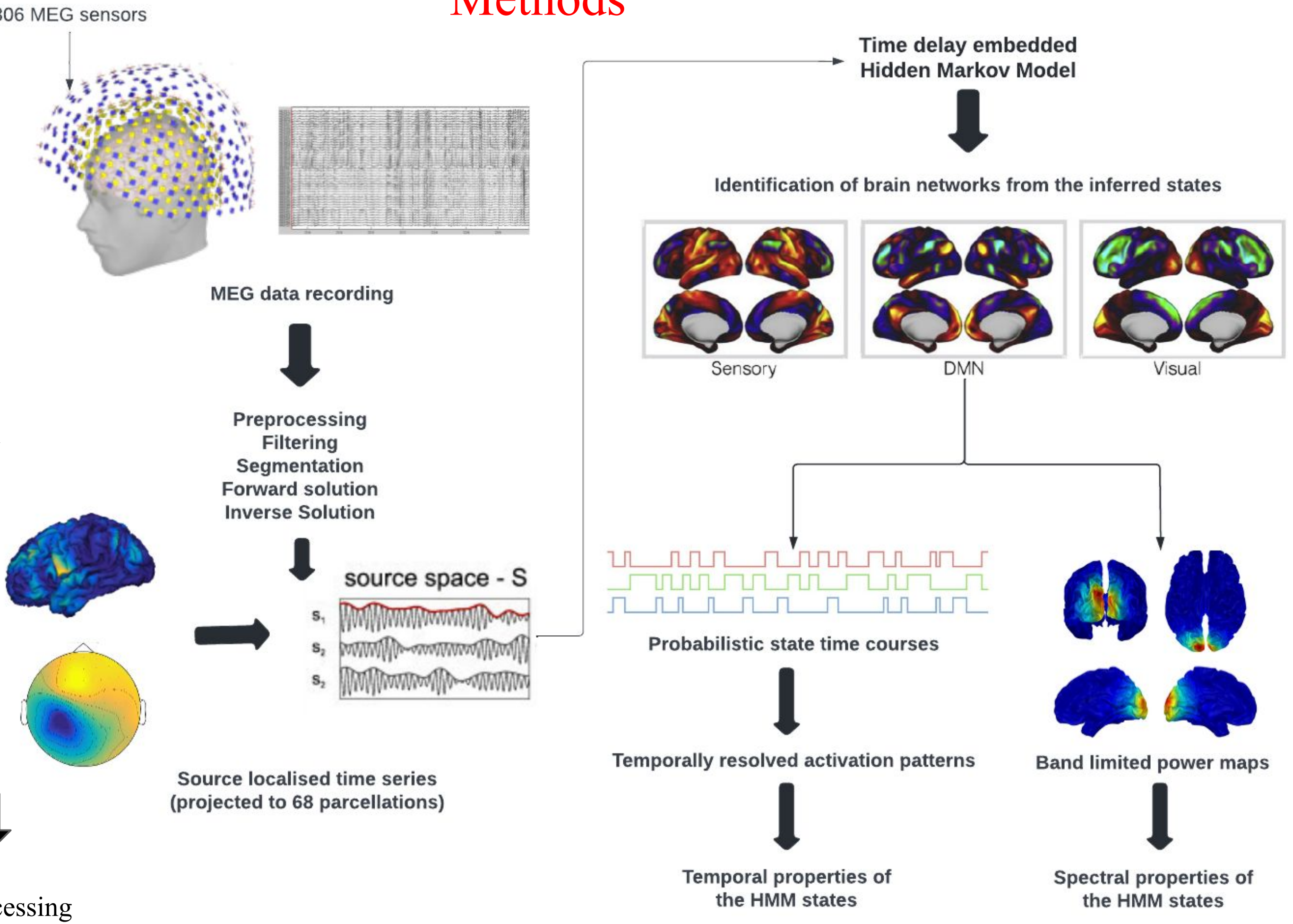
- Our study aimed to delineate age-associated changes in spatial, temporal, and spectral characteristics of the spontaneous brain activity at a high resolution.
- We predicted that the changes in rapid reorganisation of the functional networks can provide a meaningful insight into the age-related disruption in cognition.

Methods

From the Cam-CAN dataset
(650 subjects)

200 subjects randomly selected
for source reconstruction

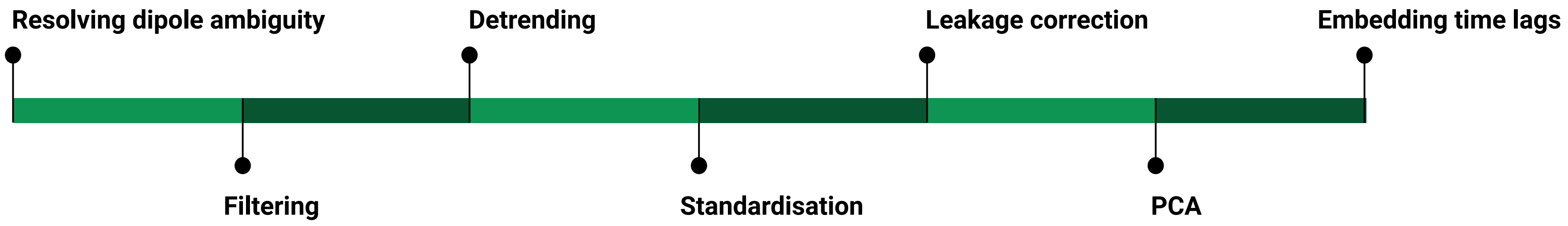
Source time series for each
subject is calculated



Preprocessing

Preprocessing

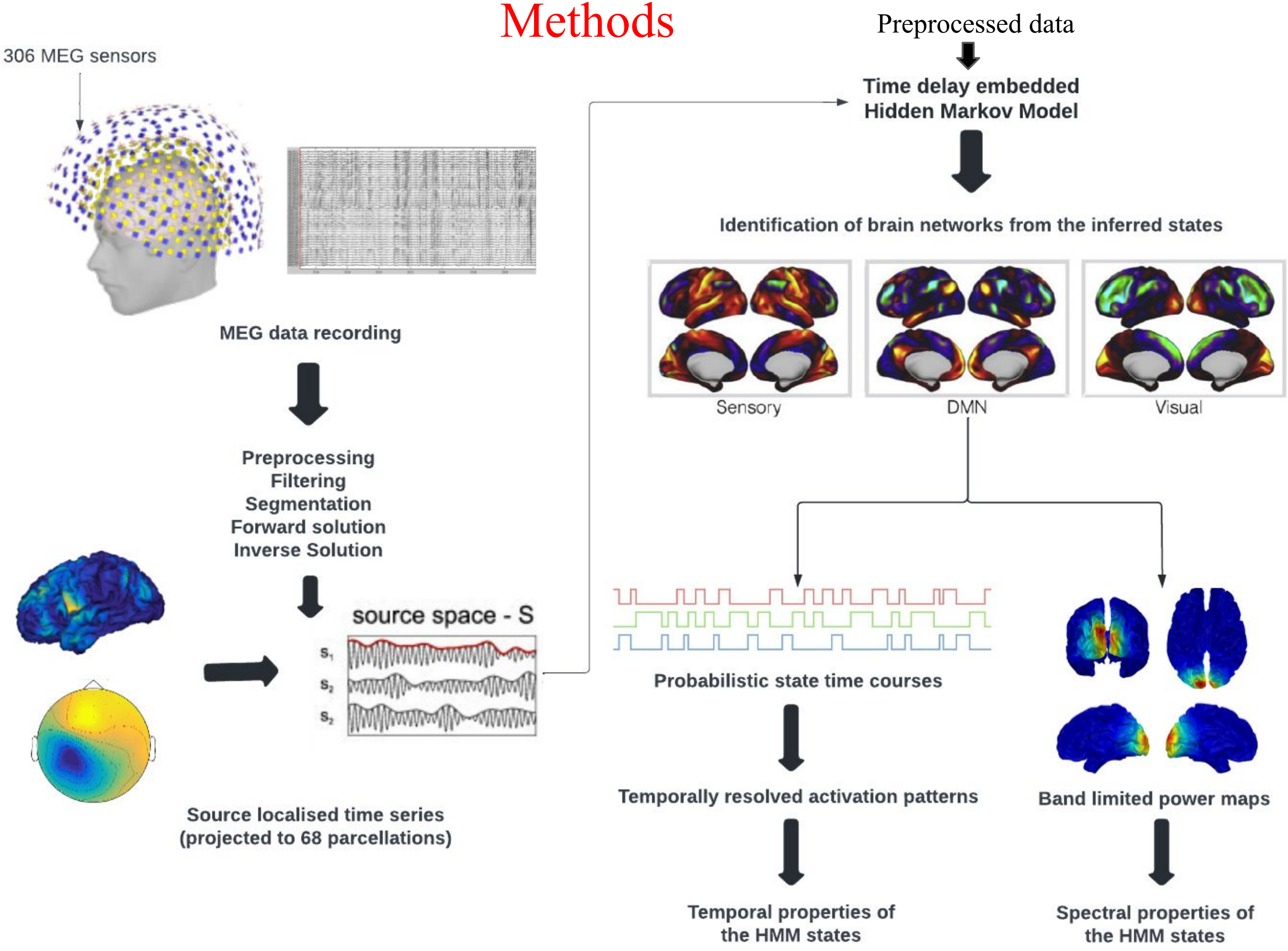
- First one minute of data was extracted from each subject
- Data from all subjects were concatenated



The preprocessed source time series data was also divided into four age groups:

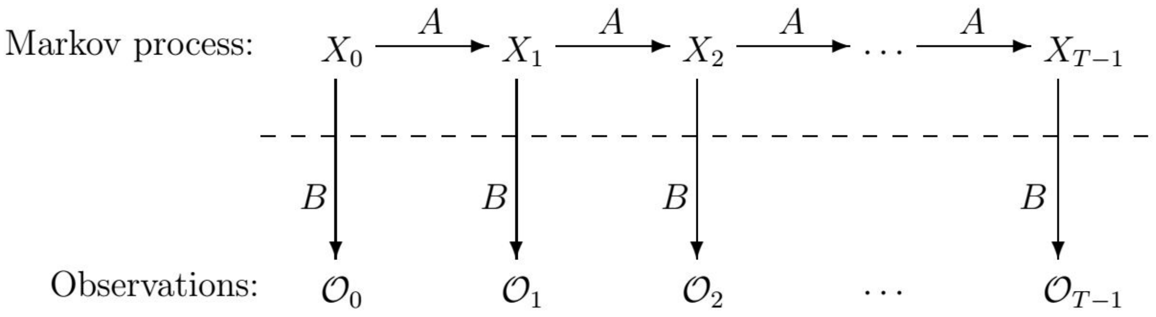
- Young (18 - 34 years)
- Early middle-aged (35 - 49 years)
- Late middle-aged (50 - 64 years)
- Old (65 - 88 years)

Methods



Preprocessed data
Time delay embedded
Hidden Markov Model
306 MEG sensors
MEG data recording
Preprocessing
Filtering
Segmentation
Forward solution
Inverse Solution
source space - S
Source localised time series
(projected to 68 parcellations)
Identification of brain networks from the inferred states
Sensory
DMN
Visual
Probabilistic state time courses
Temporally resolved activation patterns
Temporal properties of
the HMM states
Band limited power maps
Spectral properties of
the HMM states

Hidden Markov Models

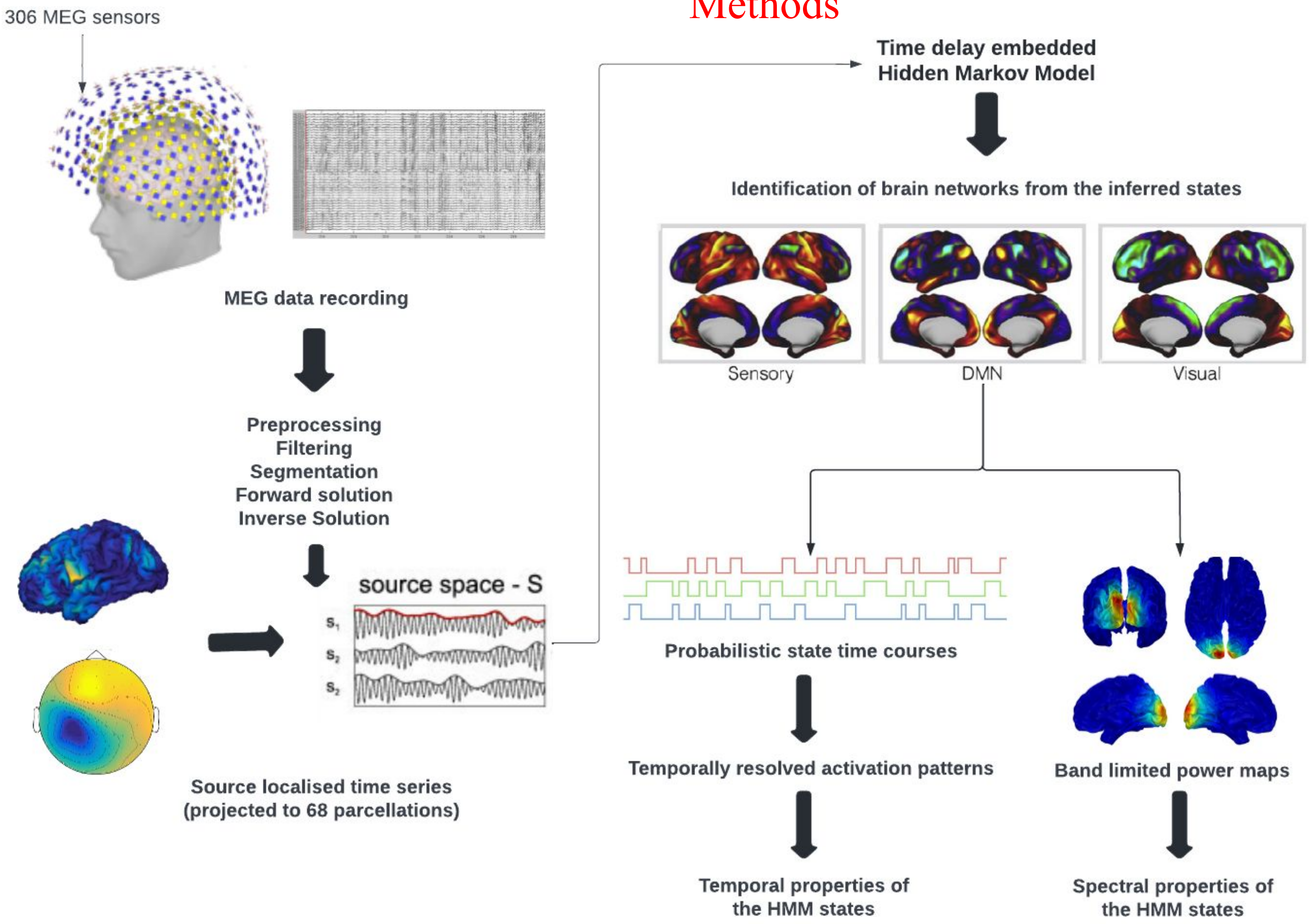


X : States (hidden)
O : Observations
A : Transition probability
B : Emission probability

- A Markov chain is a random process in which the probability of a state depends only on the previous state.
- Additional information about past states are not required to predict the future behaviour.
- The sequence of observations helps us predict the sequence of states.

Observation: MEG timeseries
Hidden states: Transient brain networks

Methods



Eight transient states were inferred from the concatenated data from all subjects

The state time courses were re-inferred to obtain group level probability distributions

Data driven decomposition of spectra in specific frequency bands

Statistical tests

- Dagos P test and Chi-squared test
- Two way ANOVA : 4 X 8 factorial design

States (8 levels)

Age group (4 levels)	1	2	3	4	5	6	7	8
Young	Young - State 1	Young - State 2	Young - State 3	Young - State 4	Young - State 5	Young - State 6	Young - State 7	Young - State 8
Early Middle	Early middle - State 1	Early middle - State 2	Early middle - State 3	Early middle - State 4	Early middle - State 5	Early middle - State 6	Early middle - State 7	Early middle - State 8
Late Middle	Late middle - State 1	Late middle - State 2	Late middle - State 3	Late middle - State 4	Late middle - State 5	Late middle - State 6	Late middle - State 7	Late middle - State 8
Old	Old - State 1	Old - State 2	Old - State 3	Old - State 4	Old - State 5	Old - State 6	Old - State 7	Old - State 8

- Bonferroni correction for multiple comparisons
- Post Hoc Tukey’s test

Results

Hypothesis

1. The inferred states will show some spatial overlap with established resting state networks and describe unique patterns of whole brain spontaneous activity.
2. The functional connectivity pattern will show age-related differences in the states overlapping known networks which can be related to behavior.
3. The temporal characteristics of the inferred states and their alteration with age may give us an insight into the behavioral changes (inhibitory control, cognitive flexibility, processing speed, etc.) seen in older individuals.
4. Leveraging the fact that our model is spectrally and temporally resolved, we hoped to see frequency band specific changes in the intra-network global coherence with age. The change in synchronisation between regions can underlie the reduction in efficient communication and specificity of information processing as we grow older.
5. We wanted to examine how the communication between brain regions changes with age within a network. We hypothesized that there will be a decrease in anterior-posterior connections and within posterior connectivity in the state resembling the default mode network.

Spatial activation pattern projected back into the brain space

Volumetric maps showing spatial activation in each state for all age groups. Brain regions getting activated (functional connectivity higher than the grand average) are marked in red.

Default Mode Network

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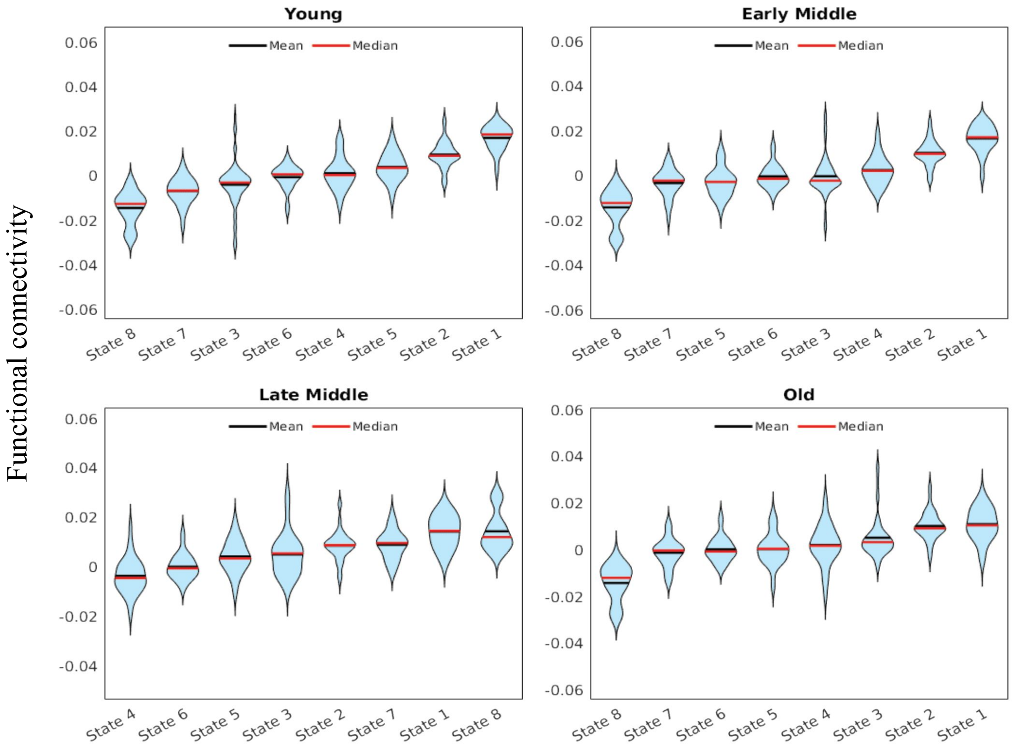
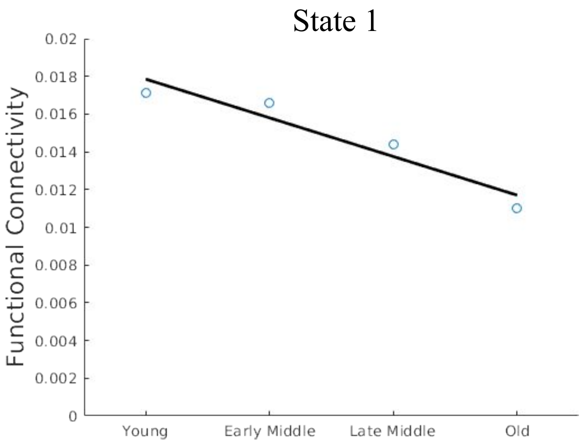
Functional connectivity in the states overlapping DMN decreases with age



Mean activation in each state arranged in the ascending order for all age groups

- Significant main effect of both state and age at $p < 0.001$
- State 1 has an overall higher mean activation (M = 0.0097, SD = 0.0004)



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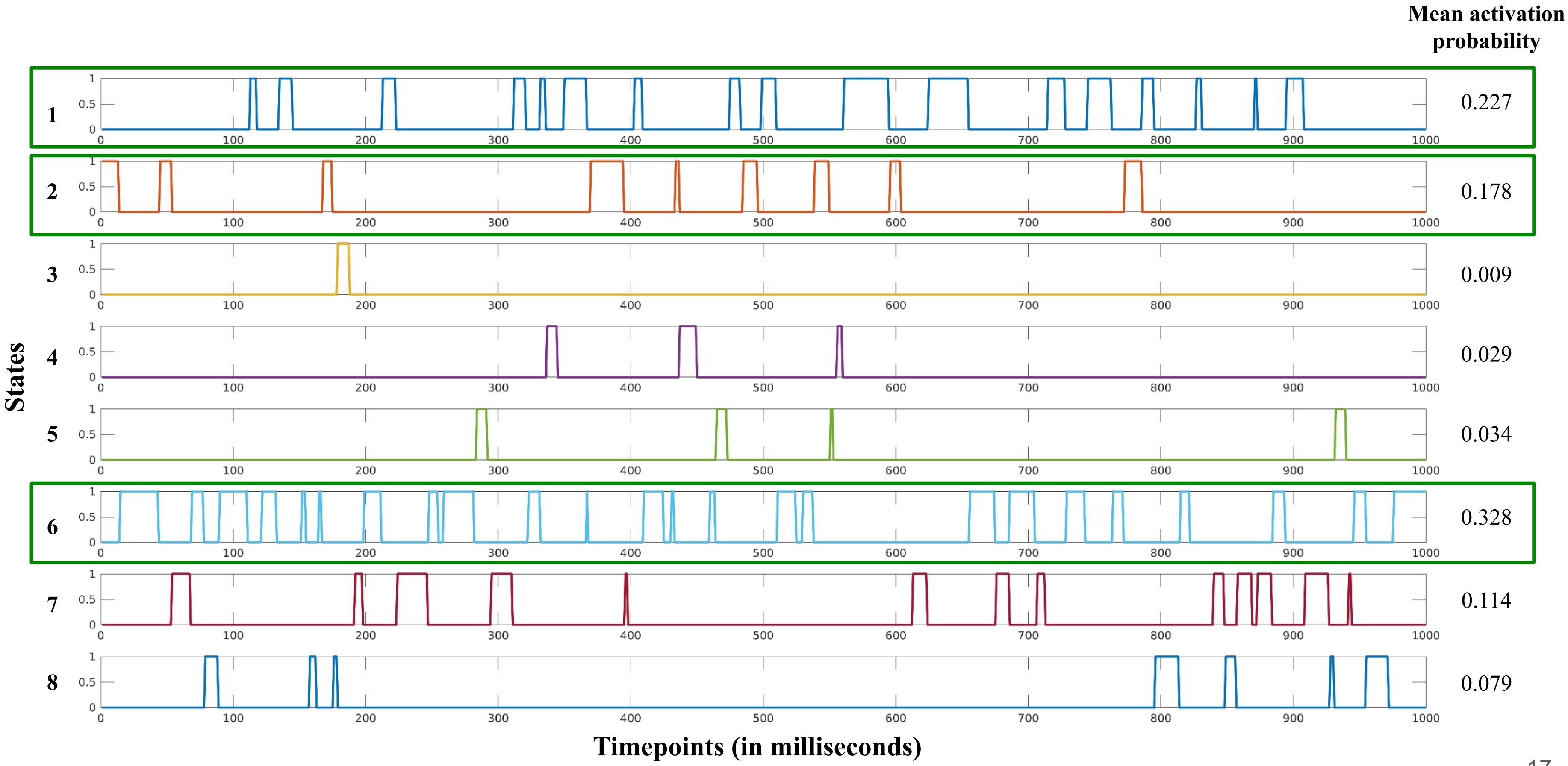
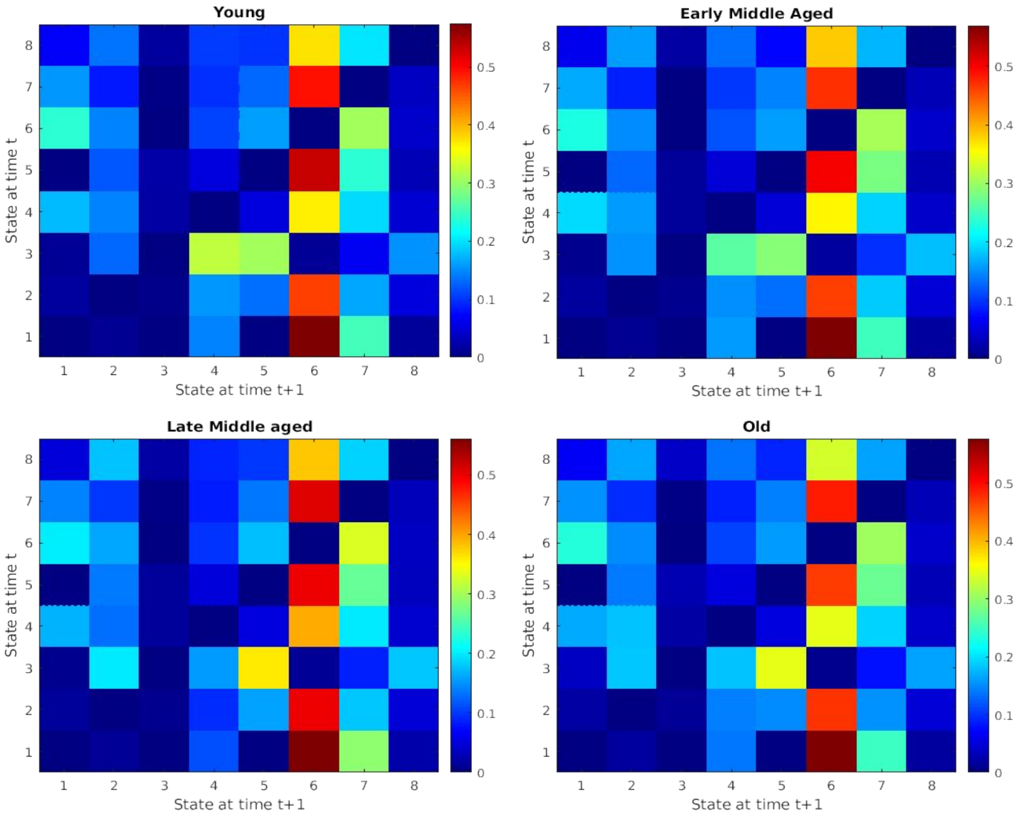
The probability of activation of the states resembling DMN is higher than other states



The brain tends to switch to the default state



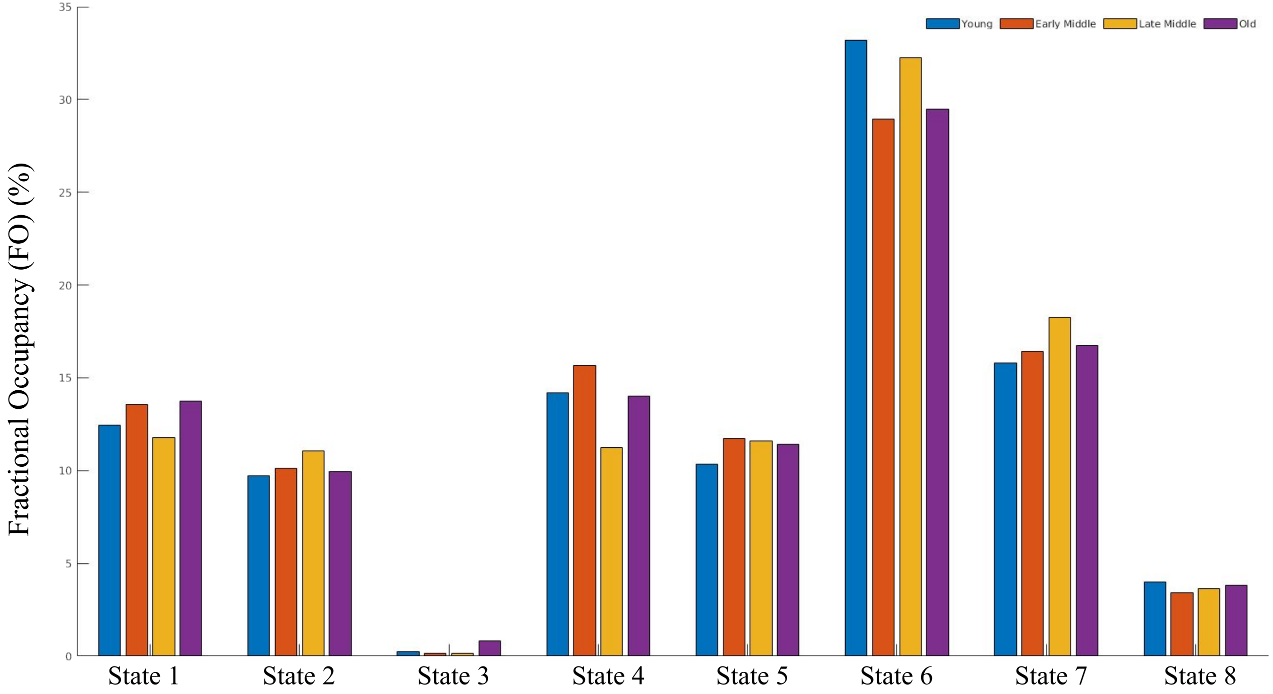
The probability of transitioning from one state (at time *t*) to the next (at time *t+1*)

Probability of transitioning to State 6 is the highest (M = 0.34, SD = 0.02)

Main effect of age group was not significant $F(3,255) = 7.5e\text{-}30$, $p > 0.5$

- The probability of switching from one state to another does not change significantly with age.

The brain tends to stay in the default state



The amount of time the brain spends on each state at each timepoint (averaged across all trials)

- There is no significant effect of age on the fractional occupancy of a state ($p > 0.05$)
- Stability of the default mode network in the resting state is much higher than all other networks (FO = 31%)

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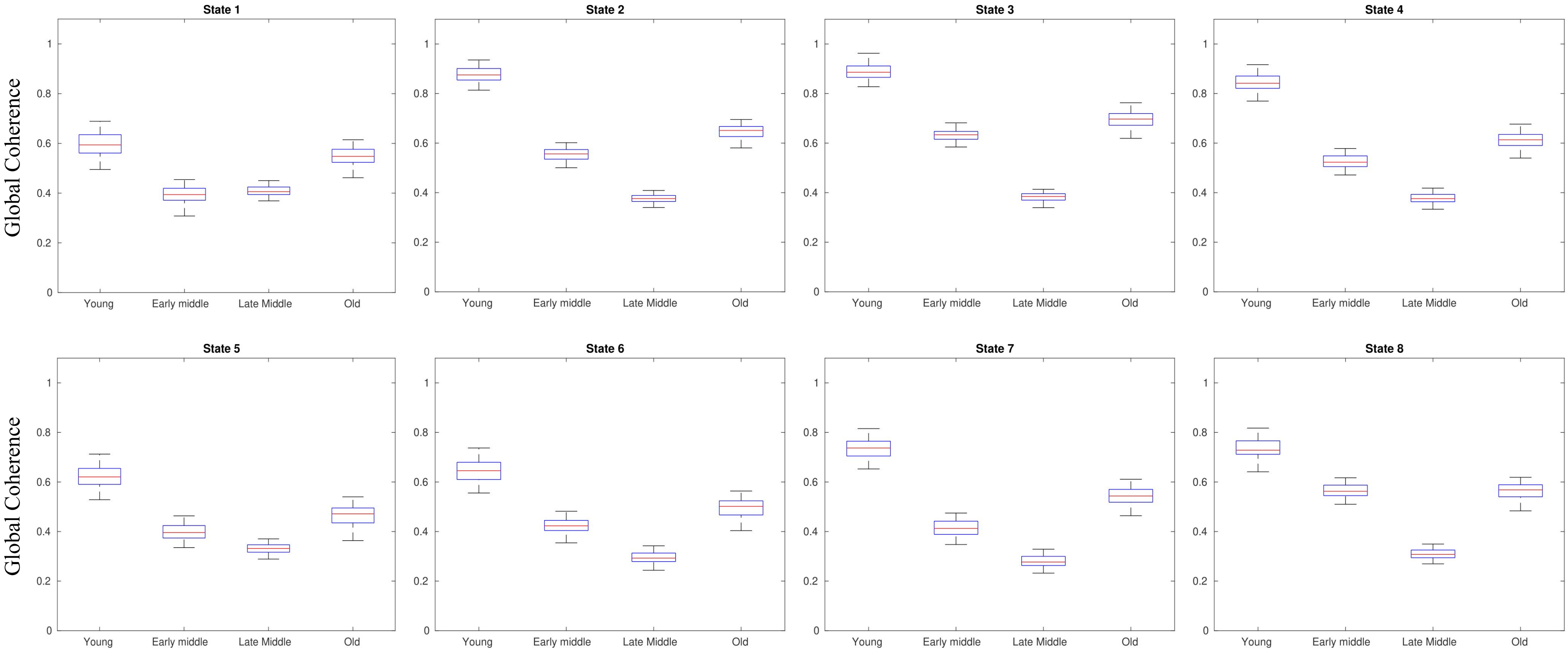
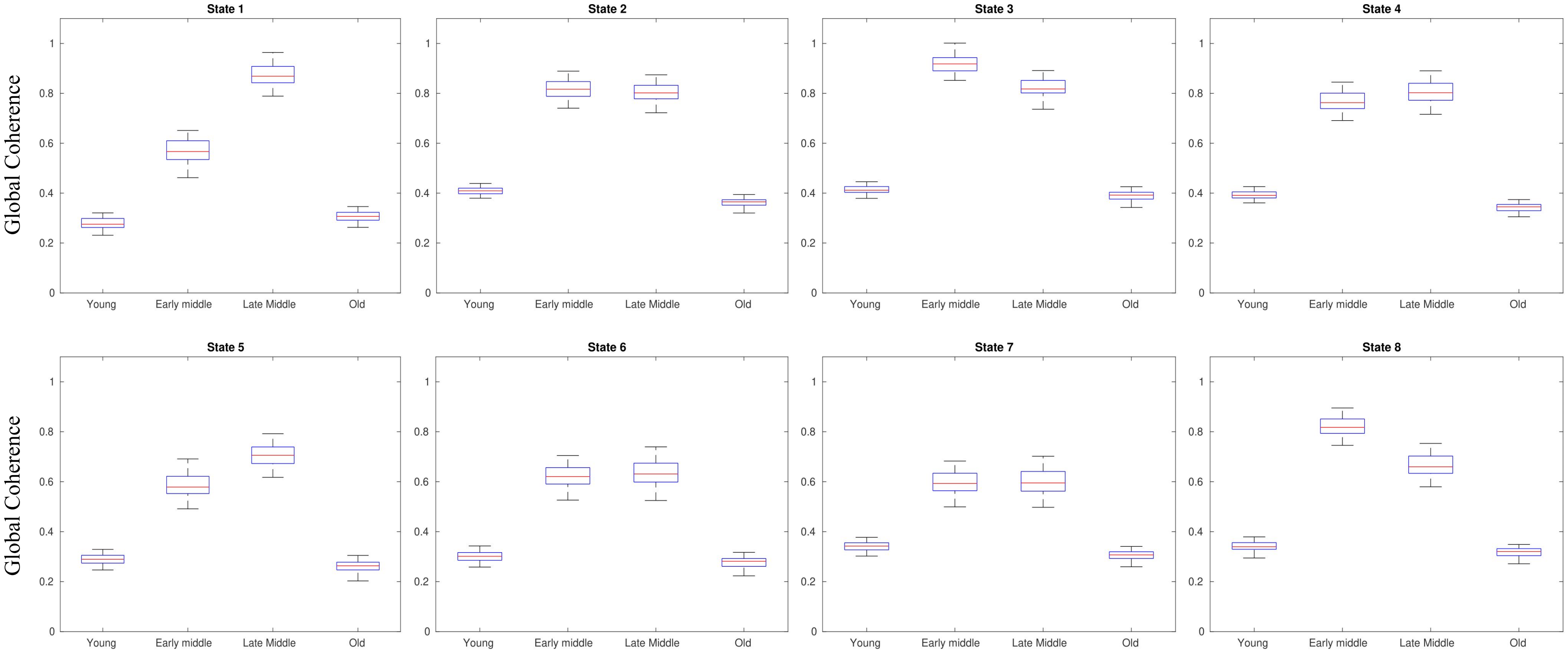
Coherence between all brain regions in the theta band



- Change in global coherence with age follows a U-shaped pattern in the theta band
- Significant main effects of both age group and frequency

Coherence between all brain regions in the alpha band



- Change in global coherence with age follows an inverse U-shaped pattern in the alpha band
- Significant main effects of both age group and frequency

Hypothesis

1. The inferred states will show some spatial overlap with established resting state networks and describe unique patterns of whole brain spontaneous activity.

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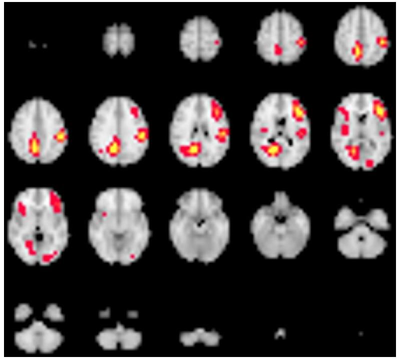
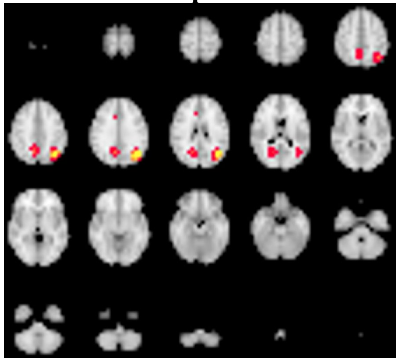
Cluster based analysis of coherence

Band limited power maps

Theta



Alpha



State 6

Common parcels

Common parcels

Coherence values between the clusters in a particular state are calculated

- Changes in coherence between regions within the cluster showed a significant main effect of age ($p < 0.001$).

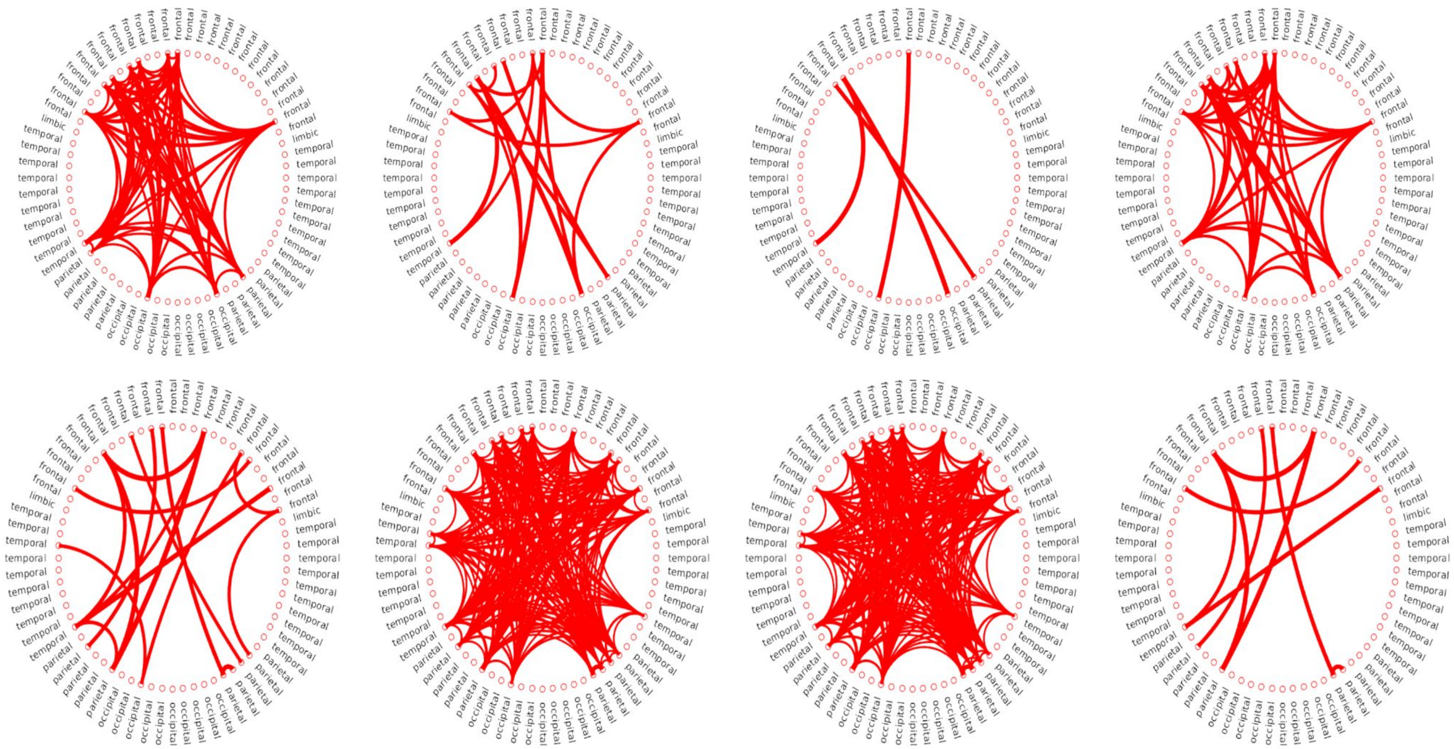
Connectivity patterns in different frequency bands

State 6

	Young	Early Middle	Late Middle	Old

Theta band

Alpha band



50% strongest connections between brain regions are shown both frequency bands

Summary

- Eight transient states which resembled fMRI RSNs were inferred from the source reconstructed MEG data of 200 participants.
- The states possibly overlapping with the DMN had an overall higher activation and showed a decreasing trend with age.
- There were no significant effects of age on the temporal characteristics of the HMM states.
- The brain tends to preferably switch to the default mode network. Temporal stability of the default mode network was also found to be much higher than all other networks.
- Coherence between brain regions in the theta and alpha bands show inverse patterns with age. This indicates that a compensatory mechanism might be in place to prevent age-related decline in cognitive performance.
- Connectivity between the anterior and posterior regions of the DMN is disrupted with advancing age. The connectivity between posterior regions was also affected as a consequence of aging.

Future Prospects

1. The data can be divided into training, testing and validation sets to ensure high accuracy and generalisability.
2. The sample size can be increased to include more subjects and a longer duration of data can be analysed.
3. Correlation analysis between the transient states and spatial ICA can provide a more robust correspondence between HMM states and resting state networks.
4. The subject-level differences between temporal and spectral measures can be studied to get a better idea of the inter-subject variability of the spontaneous brain states.
5. Communication between brain regions can be studied in the cross-frequency spectral scale.
6. Task-related data can be used to correlate the changes in the network to behavior.

Thank you!

Acknowledgement

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(Supervisor)

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Questions