Leveraging **highly-comparative time-series analysis** to study properties of **neural activity** related to **amyloid-beta plaque burden**

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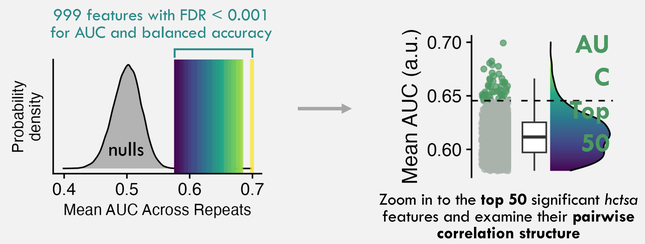
Background

Alzheimer's disease is characterized by diverse neuropathological changes like **neurodegeneration** and the aggregation of **amyloid-beta (Aβ) plaques** throughout the brain. Prior neuroimaging studies suggest a link between **Aβ plaque deposition** and **altered neural activity**, particularly in the **default mode network (DMN)**. However, such previous work has generally focused on just a **few statistical properties of neural activity data** like the fractional amplitude of low-frequency fluctuations or regional homogeneity, which could overlook **nuanced changes in activity dynamics** throughout the brain.

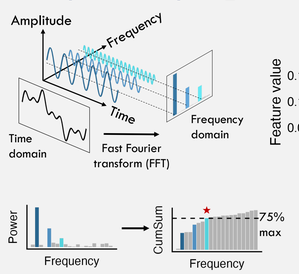
Here, we comprehensively analyse 6,639 univariate properties of **DMN activity dynamics** from resting-state functional magnetic resonance imaging (**rs-fMRI**) data. We compare these dynamics in high- versus low-amyloid individuals across the cognitive spectrum, revealing a **signature of disrupted activity** across the DMN characterized largely by changes in the **power spectrum shape** and time-series **correlation structure.**

Results 1. The feature-wise approach identifies **999 distinguishing *hctsa* features** across 4 DMN ICs

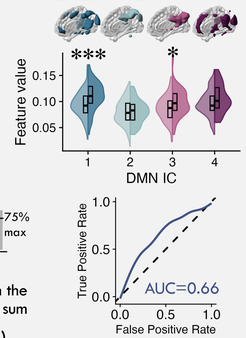


hctsa feature category examples:

Power spectrum shape: SP_Summaries_fft_wmax_75

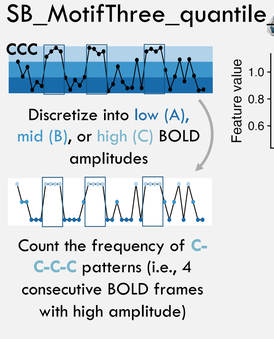


Find the **BOLD frequency** for which the **power spectral density** cumulative sum is at **75% of its maximum** (★)

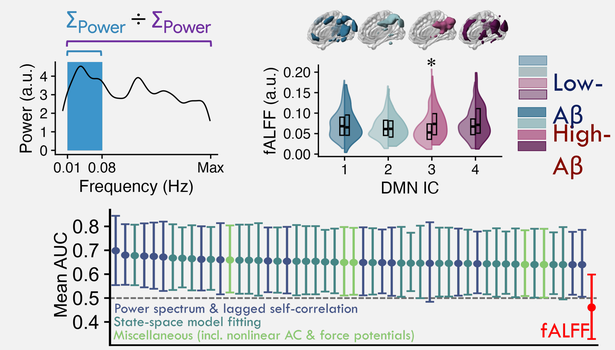


Lagged self-correlation structure:

SB_MotifThree_quantile

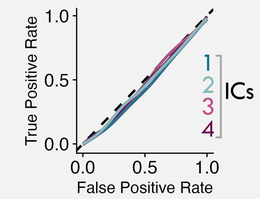


2. Many *hctsa* features **outperform** the fractional amplitude of low frequency fluctuations (**fALFF**)



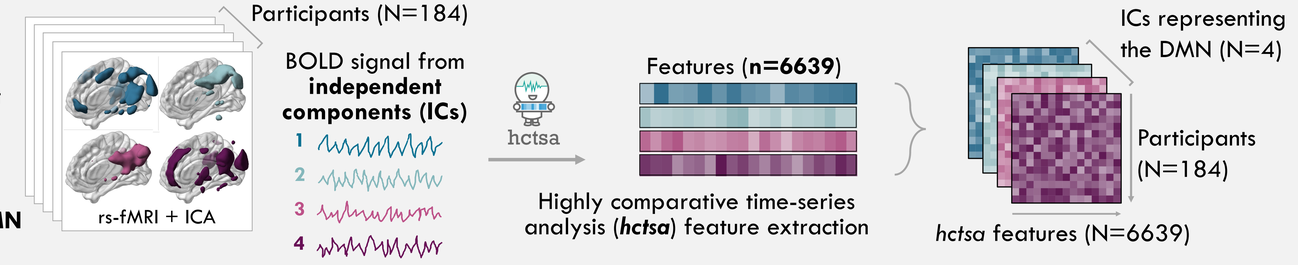
3. **Null results:**

Linear SVM with all **6,639 hctsa features** per DMN component **does not** perform well

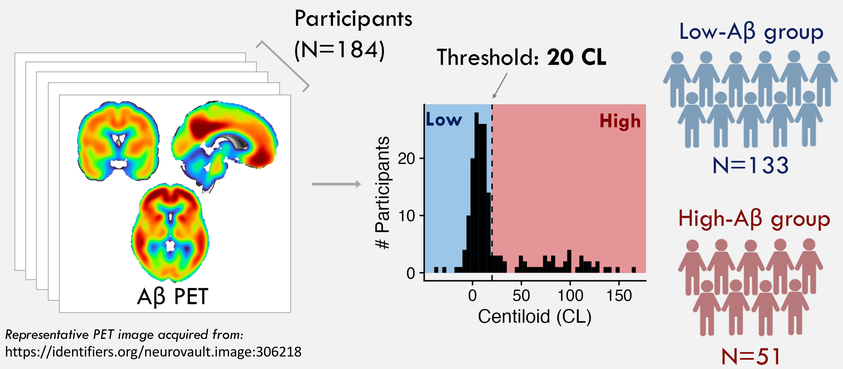


Methods

Step 1: Compute a comprehensive set of **6,639** from rs-fMRI blood oxygen level dependent **(BOLD) time series** across a set of four independent components (ICs) representing the **DMN**

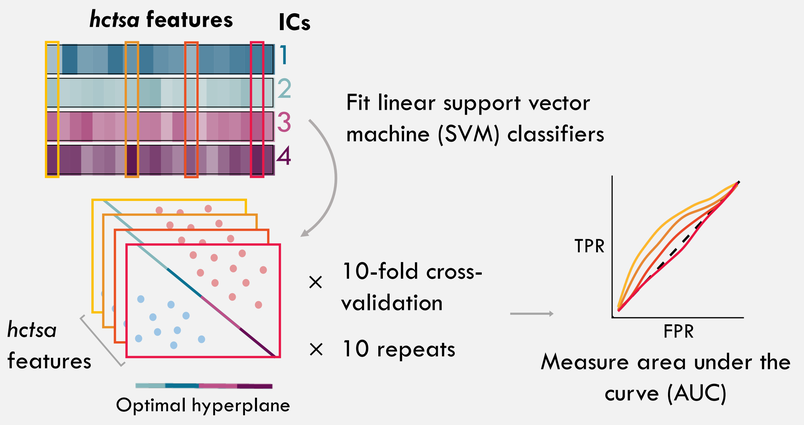


Step 2: Calculate **brain-wide Aβ centiloids (CL)** and classify participants as **low- or high-amyloid**



Representative PET image acquired from: https://identifiers.org/neurovault.image:306218

Step 3: Use **DMN neural activity properties** to predict low- vs. high-Aβ participants



Key Conclusions

- The DMN exhibits **diverse altered neural activity dynamics** in high- versus low-amyloid burden individuals
- **Power spectrum shape** and **lagged self-correlation structure** features are among top-performing discriminators
- Many *hctsa* features are **more sensitive at identifying high-amyloid participants** than the fALFF, a commonly-used biomarker for univariate neural activity alterations in AD

Next steps

- Incorporate **tau PET** given evidence for altered **excitation:inhibition balance** in the DMN, which can promote tau aggregation
- Expand analysis to bivariate domain to examine **functional connectivity** between the DMN and other parts of the brain as it relates to **AD neuropathology**
- **Dimensionality reduction** and **feature selection** to better understand how activity dynamics **relate to each other**

Acknowledgements

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Key References

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