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PATTERNS OF SPECTRAL AND FRACTAL CHANGES IN THE AGING BRAIN

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Background

Aging

A complex process and a risk factor for neurodegenerative diseases
Population aging is a social burden to be targeted

Fractal Dimension Analysis

Summarizes effects related to local oscillations and network topology with univariate measures [1]

Detrended Fluctuation Analysis (DFA)

Assesses the strength of long-range correlations in a time series by estimating the power-law scaling
Similar to Hurst Exponent (HE), but DFA is suitable for non-stationary time series

fractional Amplitude of Low-Frequency Fluctuations (fALFF)

The most used univariate spectral feature in fMRI analysis
Associated with the amplitude of spontaneous neural activity

Rationale

Aging impact on BOLD time series has hardly been addressed with FD analysis
It has been debated whether DFA provides additional information with respect to spectral analysis [2]

Goal

To investigate how aging alters resting-state fMRI network spectral and fractal features
To compare the predictive power of spectral (fALFF) and fractal (DFA) measures for aging

Methods

Dataset:

- Publicly available fMRI dataset (Cambridge Centre for Ageing and Neuroscience (CamCAN)
- 97 Young Adults (YA, 50 F, 47M, aged 28,38]) vs 114 Old Adults (OA, 51F, 53M, aged [68,78])
- Pre-processed resting-state functional MRI, eyes closed, + information on age, sex, handedness

Definition of 14 Functional Networks:

- Group Independent Component Analysis (GIFT software) – intensity normalization pre-processing, infomax algorithm for component estimation, standard PCA for data reduction, GICA algorithm for component grouping.
- Akaike Information Criterion (AIC) to estimate the number of sources at subject level. Number of Sources at group level assessed using the inter-subject mode.
- Identification of noisy Independent Components (ICs) as in [3]
- IC selection by maximizing the Dice's overlap coefficient with a set of 14 resting-state network templates

DFA

- Computed on time series of ICs back-projected to subject level
- Quadratic Detrending
- Matlab 2024b, Toolbox "Detrended fluctuation analysis (DFA)" [4]

Hypothesis testing

- Multivariate analysis of variance (MANOVA) to assess group effect on DFA and fALFF for at least one IC.
- Post hoc t-tests, FDR-controlled using Benjamini-Hochberg.

Machine Learning Classifier

- Goal: To assess the predictive power of DFA and fALFF for age grouping
- 100-tree random forest classifier
- Data splitting: 80% training, 20% test
- Features: one DFA feature and one fALFF feature for each selected IC
- Features Ranked by importance of the out-of-bag predictor
- Same classification model trained and evaluated using only DFA features and using only fALFF features.
- Comparison in terms of accuracies and confusion matrices

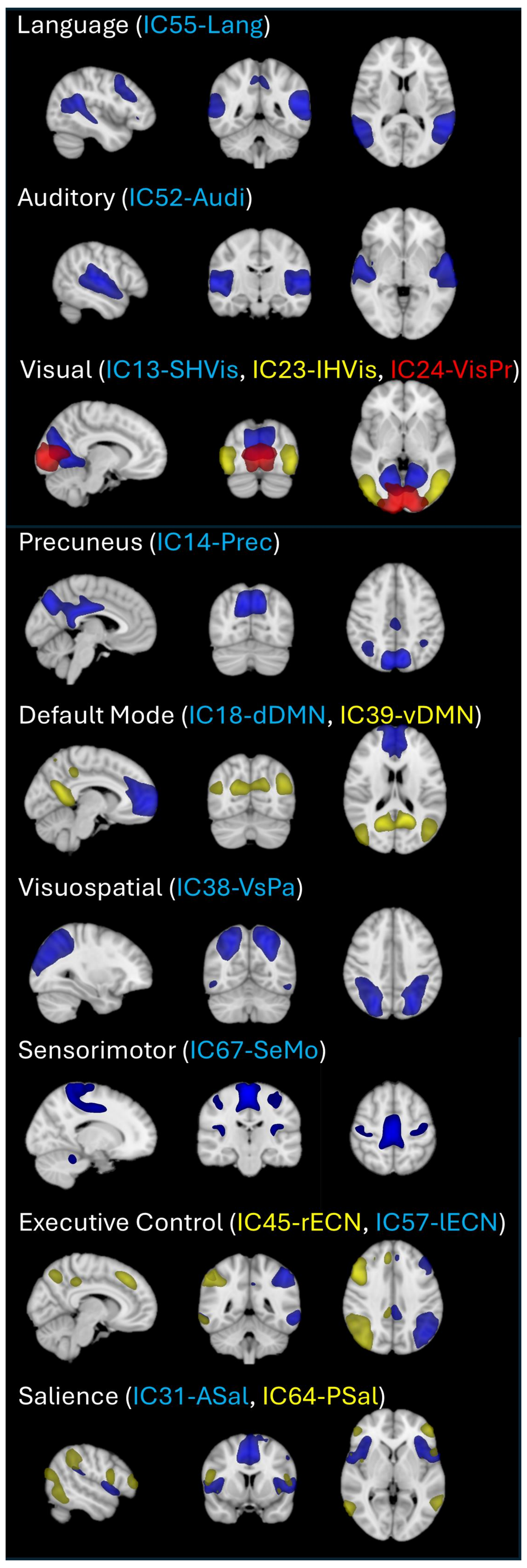


Fig. 1: Maps of selected group independent components, thresholded at Z-score≥2 and superimposed on the MNI template. Components are grouped by function, where appropriate, and displayed with different colormaps for visualization purposes.

Results

DFA – fALFF comparison

MANOVA: Group effect significant for both
DFA: F=6.92, p<10-10
fALFF: F=10.26, p<10-16

Post-hoc t-tests:

For DFA, statistically significant differences ($p<0.05$, Benjamini-Hochberg corrected) for
IC38- VsPa
IC52-Audi
IC18-dDMN
IC31-ASal
IC64-PSal.

In all these comparisons, OA showed lower DFA values compared to YA.

For fALFF, statistically significant differences ($p<0.05$, Benjamini-Hochberg corrected) for
IC45-rECN
IC57-lECN
IC38-VsPa
IC52-Audi
IC18-dDMN
IC23.IHVis
IC55-Lang
IC64-PSal.

All ICs showed lower average fALFF in OA, except for IC31-ASal which showed a slight increase.

Machine Learning

Features: DFA+fALFF
85% accuracy on the test set.
4 features have importance score > 0.4,
fALFF of IC39-VsPa
fALFF of IC18-dDMN
DFA of IC31-ASal
DFA of IC64-PSal.
Features: DFA only
62.5% accuracy on the test set
Features: fALFF only
75% accuracy on the test set.

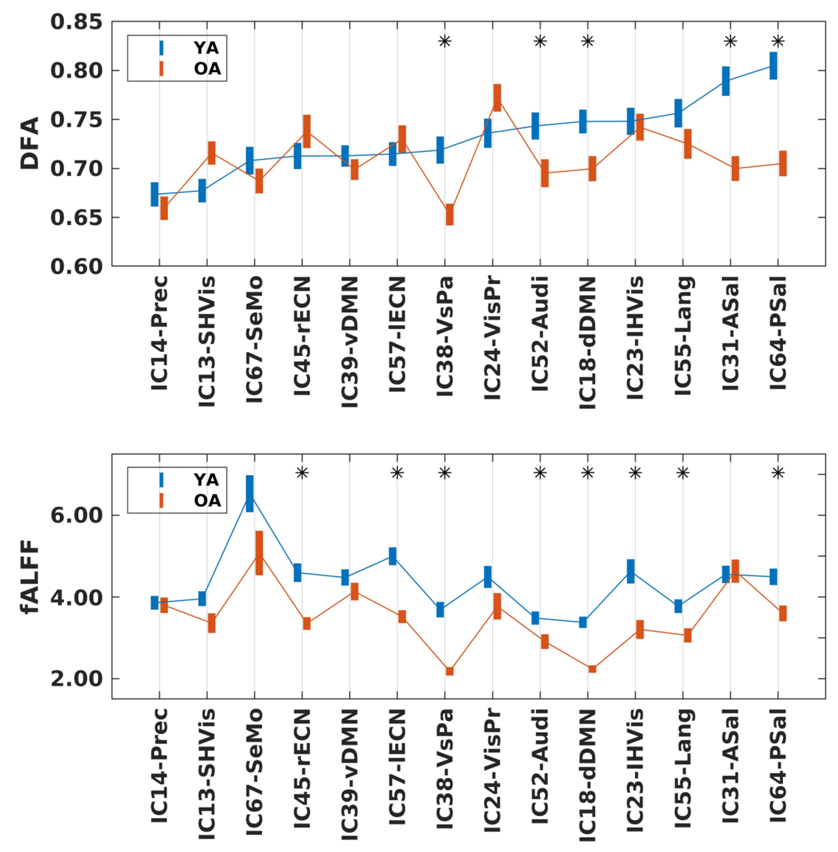


Fig. 2: Comparison between the values assumed in the YA group (blue) and in the OA group (red) for the DFA of the ICs (top) and the fALFF (of the ICs (bottom). Black asterisks indicate a significant difference as determined by two-tailed t-tests, significance threshold p≤0.05 and Benjamini-Hochberg FDR correction.

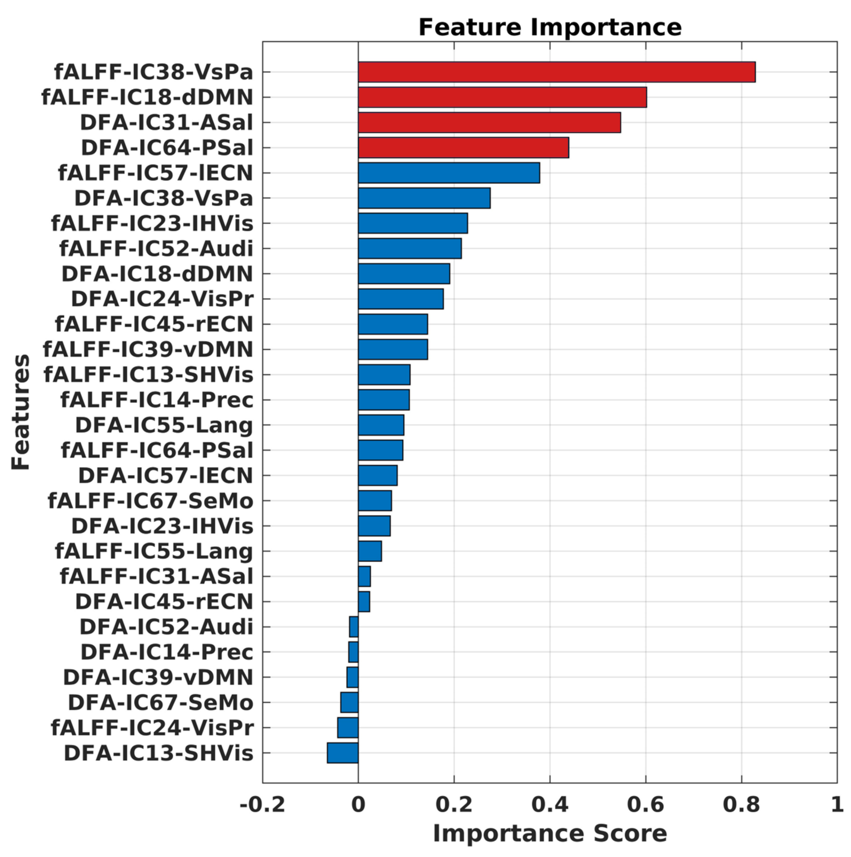
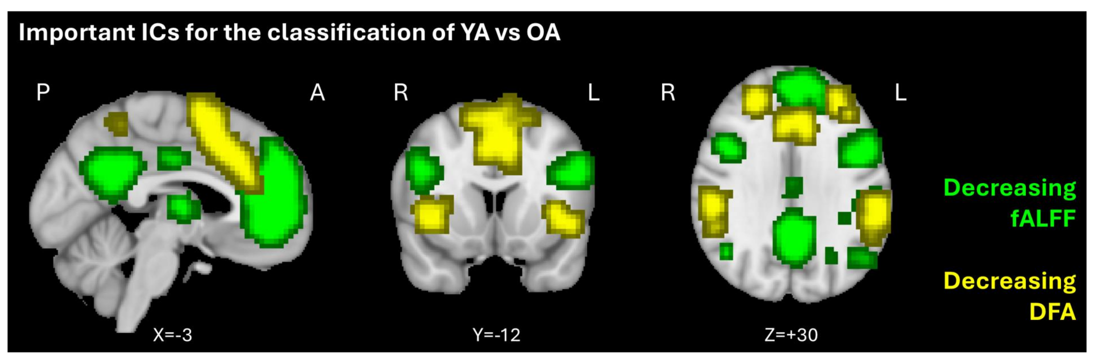


Fig. 3: Histogram of out-of-bag importance scores obtained for the model trained on fALFF and DFA values. Features that reach the 0.40 threshold are highlighted in red

Fig. 4: ICs maps, thresholded at Z-score≥2 and superimposed on the MNI template, for the components that showed an importance score ≥0.4 as determined by the out-of-bag importance ranking. Two components were selected for their fALFF values (IC18-dDMN and IC38-VsPa, both in green), and two components were selected for their DFA values (IC31-ASal and IC64-PSal, both in yellow).



Conclusion

- The use of both fALFF and DFA outperforms the use of fALFF alone and the use of DFA alone in predicting age
- The detrimental effects of aging on brain functions are most visible in visuospatial and default mode networks with fALFF, and in salience networks with DFA.
- We hypothesize here that changes in long-range connectivity previously reported [5] for salience networks are reflected by fractal properties but not necessarily by spectral properties.
- There is a complementarity relationship between fALFF and DFA in specific networks.
- While the default mode and the visuospatial networks have been extensively studied in aging using standard techniques, the insufficient literature on FD analysis in aging [1] may have missed important detrimental effects within the nodes of salience networks.

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