NeuroMark PET:
Towards a fully automated PET ICA pipeline

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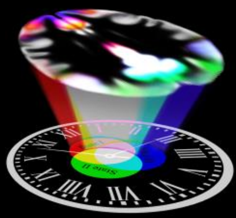

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Outline

- Motivation
- Preprocessing
- Blind ICA
- The NeuroMark framework
- NeuroMark PET (FBP and FBB)
- Multimodal comparison

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ROIs and brain networks

- Anatomy based atlases or fixed ROIs are often used to summarize positron emission tomography (PET) data.
- Fixed binary atlases do not capture variation among individuals and may average together voxels which are functionally distinct
- Functional boundaries do not correspond 1-1 with anatomic boundaries, and brain networks (and tissue types, e.g., white matter) can overlap

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A data-driven approach

- Independent component analysis (ICA) is one of the most widely used data-driven approaches in fMRI
- ICA allows extraction of maximally independent covarying sources which can overlap with one another
- ICA has been used successful in dozens of PET studies, but it can be challenging to compare as each study results in different components

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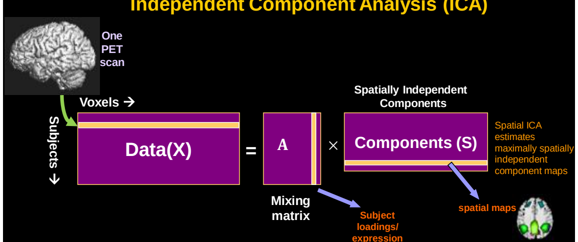
Independent Component Analysis (ICA)



Mixing equation: $X_{N\times V} = A_{N\times C} S_{C\times V}$

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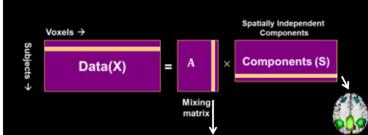
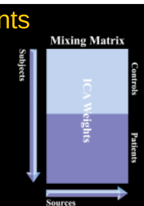
Loading Coefficients



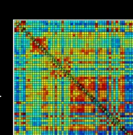


Loading coefficients (i.e., the mixing matrix): represent the relative degree each ICA component is 'expressed' in a given subject's PET data

Statistical tests (e.g., two sample test) can be applied to each colu of the mixing matrix to test differences between two groups.

The columns of the mixing mat can also be regressed agai other variable (e.g. age, site, etc.

PET FNC (functional network covariation): covariation among the columns of A.



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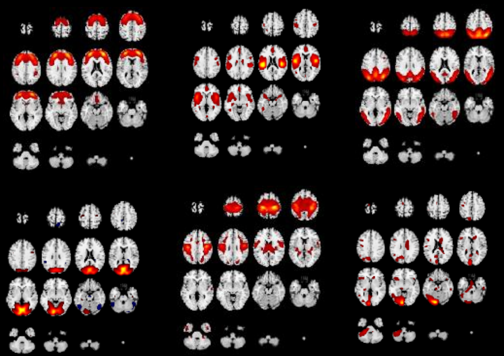
Data Driven (20 components)



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PET Data and Preprocessing

Data:
- FBP: N = 250, 76+/-8.2 yrs
- FBB: N = 175, ages: 70.8+/-7.47 yrs
- FDG: N = 220, ages 74+/- 6.4 yrs
- Each w/ four 5-minute frames/scans for each subject

Preprocessing:
- PET data converted to BIDS structure
- Motion correction (4 frames)
- FreeSurfer applied to T1 (create reference)
- PETSurfer: combine frames, transform the images into MNI space and extract cerebellar cortex size and intensities
- SUVR relative to cerebellum applied as below
- Data masked via a one-sample t-test to include the voxels that have significantly ($p < 0.0001$) more uptake than the reference (e.g., cerebellar cortex)

- *We use the following simplified SUVR equation (CB=cerebellum)*
- $ratio = \frac{Left\_CB\_cx\_vol}{left\_CB\_cx\_vol + right\_CB\_cx\_vol}$
- $SUVR = \frac{mean(frames\_voxel\_raw)}{left\_CB\_cx\_intensity \times ratio + right\_CB\_cx\_intensity \times (1 - ratio)}$

where cerebellar_cx_intensity is the average intensity of all the voxels inside the cerebellar cortex

https://github.com/trendscenter/gift-bids/tree/main/misc/pet/pipe/onp/example_fbb

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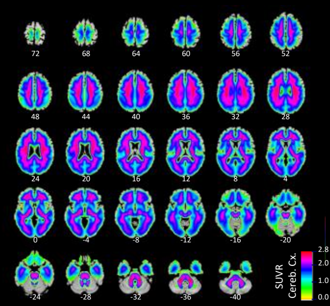
^{18}F-Florbetapir Uptake in Significant Regions



Masked regions show uptake > average(cerebellar cx), having significantly more uptake ($p < 0.0001$). cerebellar cx masked

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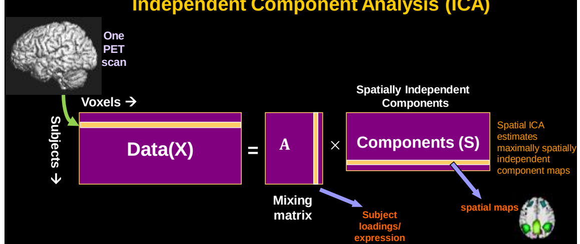
Independent Component Analysis (ICA)



Mixing equation: $X_{N \times V} = A_{N \times C} S_{C \times V}$

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Scaling (SUVR) does not impact ICA sources

Mixing equation: $X_{N\times V} = A_{N\times V} S_{C\times V}$

Subject specific (SUVR) scaling: $B_{N\times N} = \begin{bmatrix} b_1 & \cdots & b_N \\ b_1 & \cdots & b_N \\ b_1 & \cdots & b_N \end{bmatrix}$

Apply (SUVR) scaling to the data: $B_{N\times N}X_{N\times V} = B_{N\times N}A_{N\times C}S_{C\times V} = (B_{N\times N}A_{N\times C})S_{C\times V}$

$$(B_{T\times T}A_{T\times V}) = \begin{bmatrix} b_1 & \cdots & b_N \\ b_1 & \cdots & b_N \\ b_1 & \cdots & b_N \end{bmatrix}\begin{bmatrix} A_{11} & \cdots & A_{1V} \\ A_{21} & \cdots & A_{2V} \\ A_{N1} & \cdots & A_{NV} \end{bmatrix} = \begin{bmatrix} b_1A_{11} & \cdots & b_1A_{1V} \\ b_2A_{21} & \cdots & b_2A_{2V} \\ b_NA_{N1} & \cdots & b_NA_{NV} \end{bmatrix} = \begin{bmatrix} b_1A_1 \\ b_2A_2 \\ b_NA_N \end{bmatrix}$$

$$B_{N\times N}X_{N\times V} = B_{N\times N}A_{N\times C}S_{C\times V} = (B_{N\times N}A_{N\times C})S_{C\times V} = \begin{bmatrix} b_1A_1 \\ b_2A_2 \\ b_NA_N \end{bmatrix} S_{C\times V}$$

This tells us that the source maps are invariant to the scaling. It allow us to scale the loading parameters post ICA.

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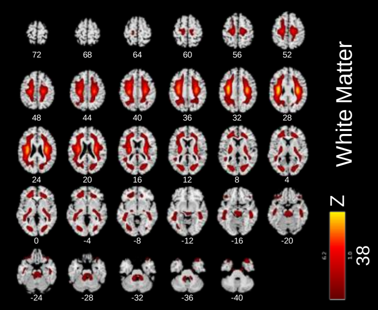
Example nuisance component



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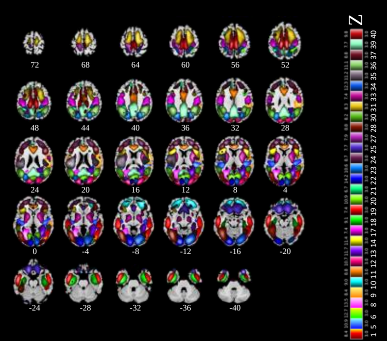
Non-Artifactual Components (30)



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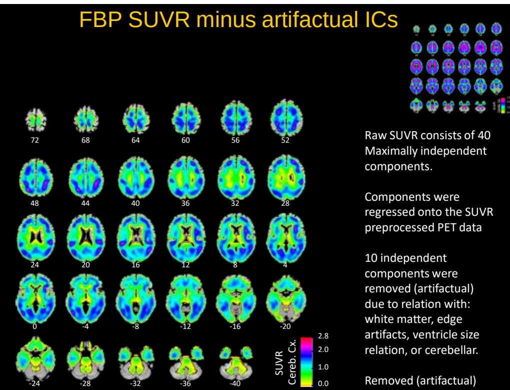
FBP SUVR minus artifactual ICs



Raw SUVR consists of 40 Maximally independent components.

Components were regressed onto the SUVR preprocessed PET data

10 independent components were removed (artifactual) due to relation with: white matter, edge artifacts, ventricle size relation, or cerebellar.

Removed (artifactual) ICs: 2, 3, 4, 7, 15, 16, 26, 29, 32, 38.

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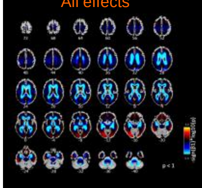
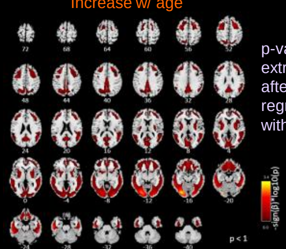
Non-ICA: FBP Age Regression p-values (+)

All effects



Increase w/ age



p-values extracted after SUVR regression with Age

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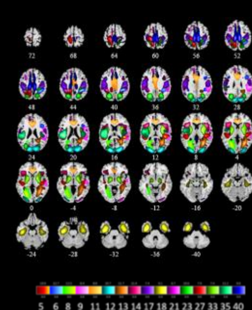
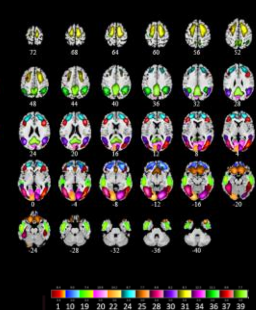
Age effects on (non-artifactual) components

Decreases w/ age



Increases w/ age



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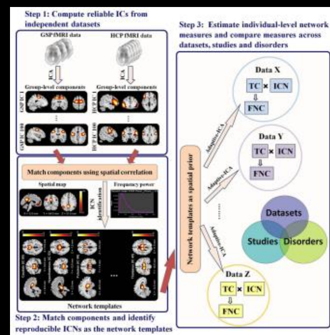
NeuroMark: A fully automated ICA pipeline



Source independence

$$max \begin{cases} J(S_l^k) = \{E[G(S_l^k)] - E[G(v)]\}^2 \\ F(S_l^k) = E[S_l S_l^k] \end{cases}$$

$$s.t. \|w_l^k\| = 1$$

$$S_l^k = (w_l^k)^T \cdot X^k$$

Similarity to template

Y. Du, et al., "NeuroMark: An automated and adaptive ICA based pipeline to identify reproducible fMRI markers of brain disorders," Neuroimage Clin, vol. 28, p. 102375, 2020, PMC7509081.

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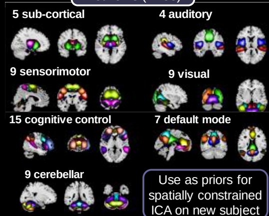
Neuromark pipeline (1.0) rsfMRI

HCP Data (N=823) 100 Components

GSS Data (N=1005) 100 Components

Common Rest Networks (N=58)

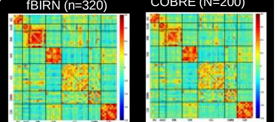


Use as priors for spatially constrained ICA on new subject

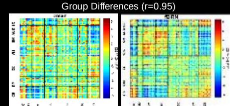
[adapts to individual subjects, preserves network labels, fuzzy parcellations]

Dataset 1: fBIRN (n=320)

Dataset 2: COBRE (N=200)



Group Differences (r=0.95)

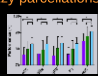


Y. Du, et al. "NeuroMark: An automated and adaptive ICA based pipeline to identify reproducible fMRI markers of brain disorders," NeuroImage Clin, 28, 2020.

A. Iraji, et al., "Canonical and Replicable Multi-Scale Intrinsic Connectivity Networks in 100k+ Resting-State fMRI Datasets," Human Brain Mapping, 2023.

W. Yan, et al, EBioMedicine 2019 Vol. 47.

Networks outperform fixed ROIs



https://trendscenter.org/software/gift

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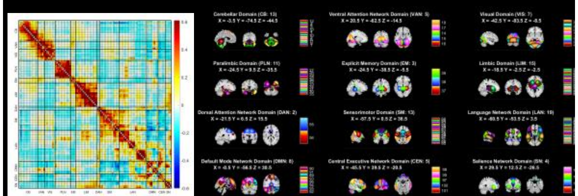
NeuroMark Multi-scale fMRI template

100K subjects, very broadly defined….

ICA model orders: 25, 50, 75, 100, 125, 150, 175, 200

Final template: 105 components across model orders



A. Iraji, et al., "Identifying canonical and replicable multi-scale intrinsic connectivity networks in 100k+ resting-state fMRI datasets," Hum Brain Mapp, vol. 44, pp. 5729-5748, 2023.

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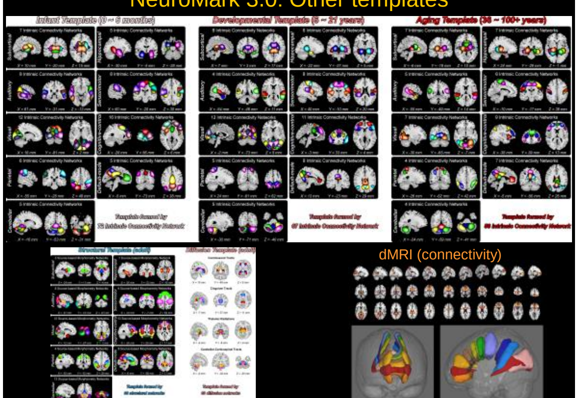
NeuroMark 3.0: Other templates



dMRI (connectivity)

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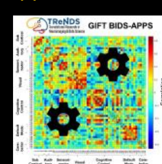
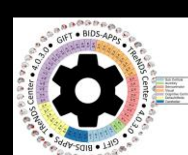
TReNDS GIFT BIDS-App

- GIFT BIDS-App includes a full suite of ICA tools
  - https://github.com/trendscenter/gift-bids
- Implements fully automated spatially constrained ICA
  - NeuroMark
    https://ncbi.nlm.nih.gov/pubmed/32961402
  - Enables single subject ICA, preserving component correspondence
  - Suppresses artifacts





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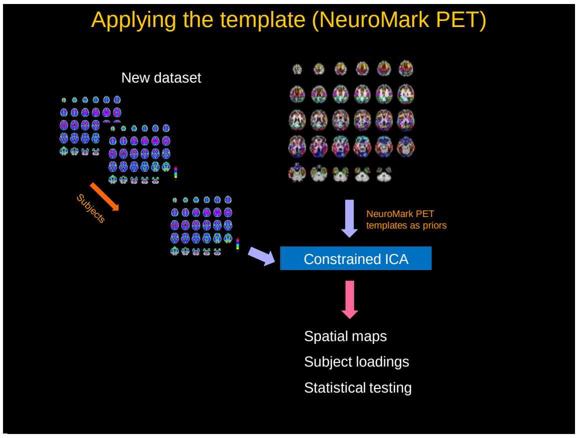

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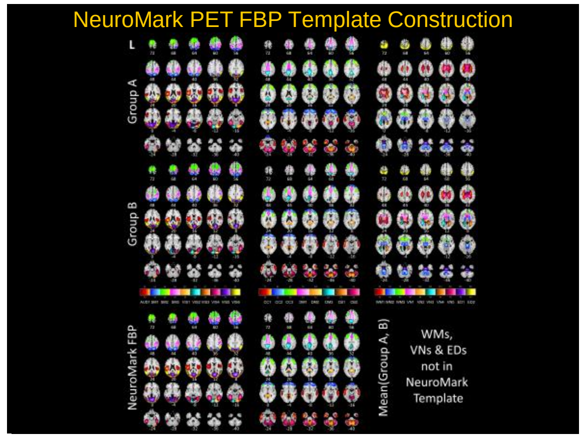

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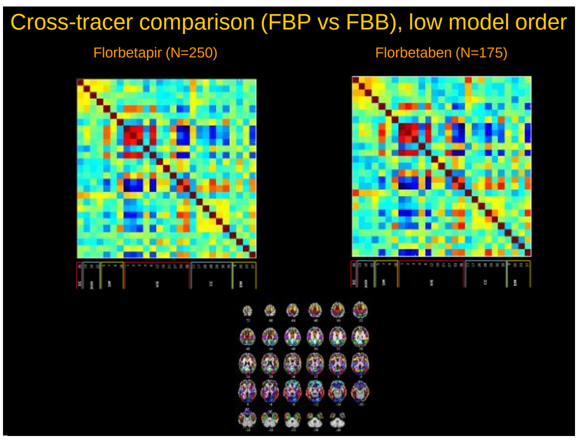

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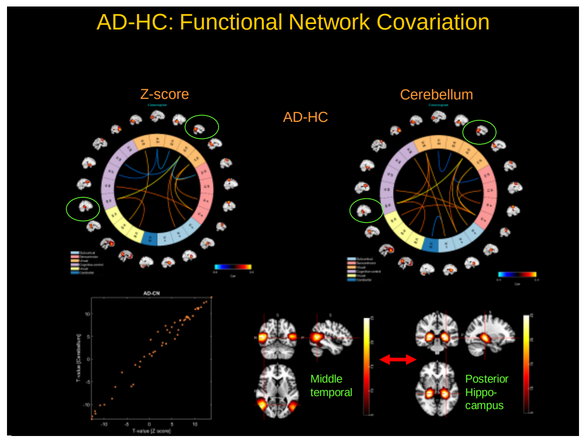

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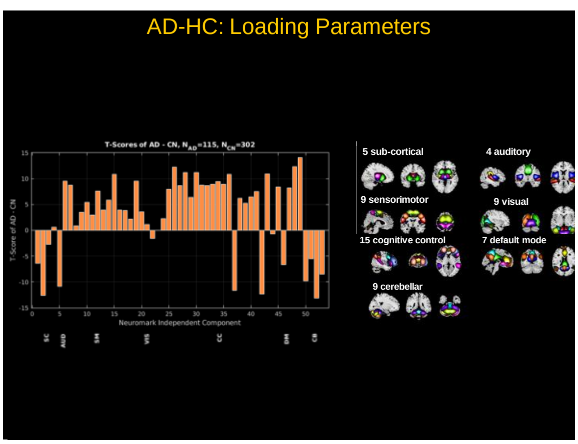

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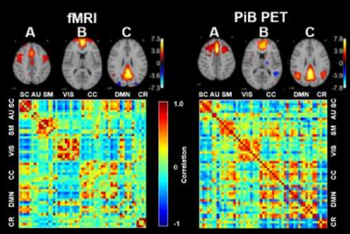
fMRI Informed PET



D. K. Saha, A. Bohsali, R. Saha, I. Hajjar, and V. D. Calhoun, "Neuromark PET: A multivariate method for Estimating and comparing whole brain functional networks and connectomes from fMRI and PET data," *bioRxiv, p. 2024.2001.2010.575131, 2024.*

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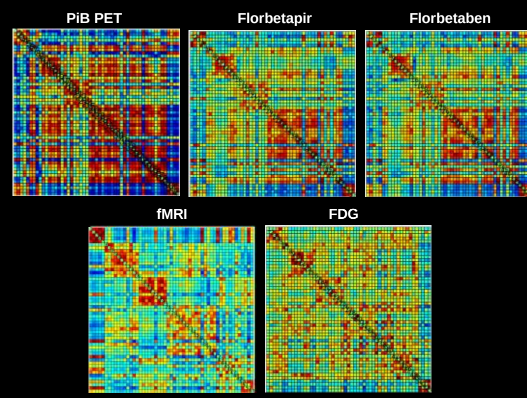
fMRI Informed PET connectome



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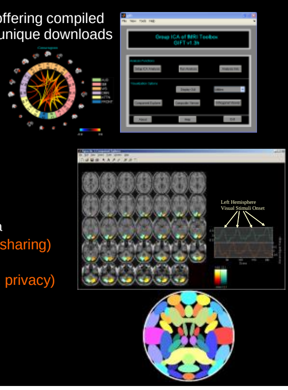
Software

- http://trendscenter.org/software
- freeware, written in MATLAB (also offering compiled versions), python, etc: over 25,000 unique downloads
- GIFT (Group ICA of fMRI Toolbox)
  - Single subject/Group ICA
  - MANCOVA testing framework
  - Source based morphometry
  - ICASSO (clustering/stability)
  - Dynamic FNC/Coherence
- FIT (Fusion ICA Toolbox)
  - Parallel ICA, jICA
  - mCCA+jICA & much more!
- Simulation Toolbox (SimTB)
  - Flexible generation of fMRI-like data
- COINS (data management/capture/sharing)
  - http://coins.trendscenter.org
- COINSTAC (decentralized analysis, privacy)
  - https://coinstac.org
- CORTEX (deep learning)
  - https://github.com/rdevon/cortex



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TReNDS Center for Translational Research in Neuroimaging and Data Science (TReNDS)

OpenNeuroPET team (+ more)

http://trendscenter.org

R01EB005846 , R01EB006841, P20GM103472, 1U01NS082074, 5R41MH100070, R01MH094524, 1R01MH104680

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