Brain Hack School

Curt – Truc Nguyen

PhD Y3 in Neuroscience, NTU (TW) & Academia Sinica

June 10, 2025

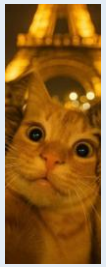
My PhD Thesis

"Multiple Levels of Investigation into Late-Life Cognitive Heterogeneity"

Between-person variability (Inter-individual)

- **Nguyen T**, Chang YL. *Journals of Gerontology Series B–Psychological Sciences & Social Sciences*. In Press.
- **Nguyen T**, ..., Lin MC. *Plos ONE*. **2023**.

Within-person variability (Intra-individual)



Neuropsychology

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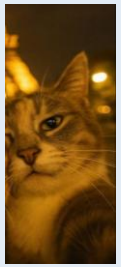

Neuroimaging (fMRI)

Precision functional mapping

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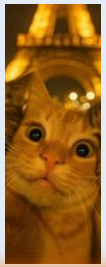

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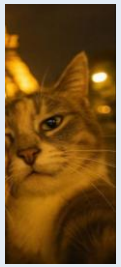

Neuroimaging (fMRI)

Precision functional mapping

Cognitive performance

- **Between-person (aka Inter-individu**
  - Young vs. Old
  - Alzheimer's disease vs. MCI vs. Cognitivel
  - Alzheimer's disease vs. Vascular dementia

Salthouse & Soubelet. *Neuropsychology* 2014

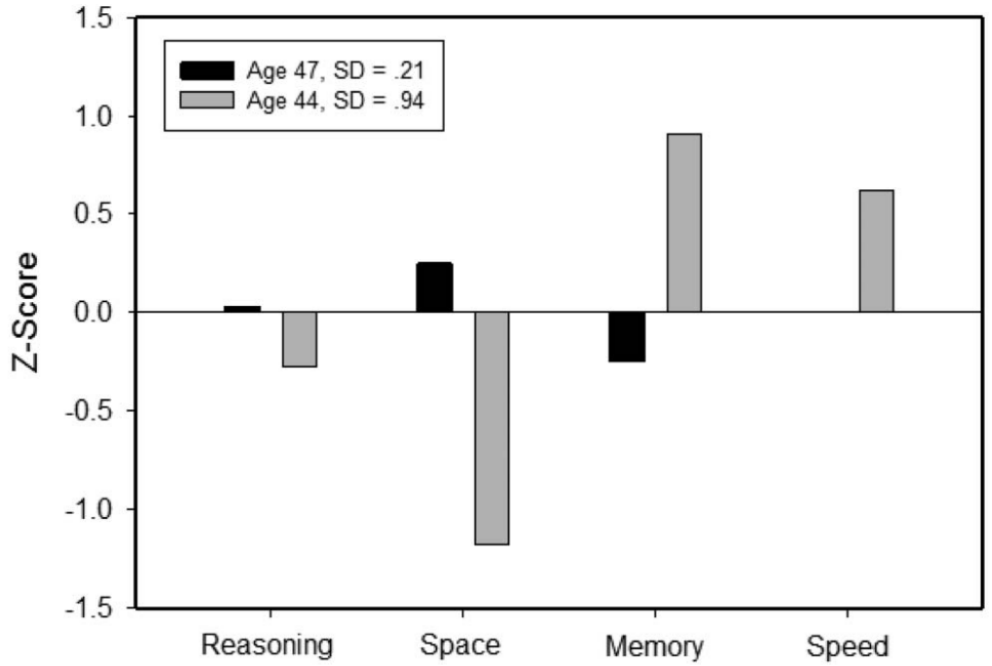

Figure 1. Illustration of ability profiles for two participants with nearly the same average level of cognitive performance. The *z* score for speed in the 47-year-old was 0, and thus the value is not apparent in the figure.

- **Within-person (aka Intra-individual variability)**
  - *Dispersion*: across multiple cognitive tasks, at a single time point
  - *Inconsistency*: Within one cognitive task, across multiple time points (trials, hours, days)

Is **cognitive dispersion** associated with **cognitive impairment**?

Greater cognitive dispersion has been found to be associated with:

- presence of **MCI or AD** vs. healthy controls (HC), and **APOE ε4+** vs. APOE ε4− HC (Aita et al., *Neuropsychol Rev* 2024);
- greater **dementia** incidence at follow-up (Watermeyer et al., *Age & Aging* 2021; Jabcobson et al., *Neurocase* 2009);
- faster rates of **medial temporal lobes** atrophy (Bangen et al., *Neuropsychology* 2019);
- reduced **cerebral blood flow** in inferior parietal and temporal regions (Holmqvist et al., *JINS* 2023);
- disruptions in **functional connectivity networks** (Meeker et al., *Neurobiol Aging* 2021; Mulet-Pons et al., *J Gerontol B Psychol Sci Soc Sci* 2023);
- more severe **neurofibrillary** tangle pathology (Malek-Ahmadi et al., *JAD* 2017).

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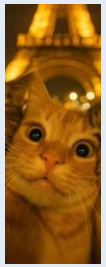

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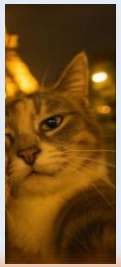
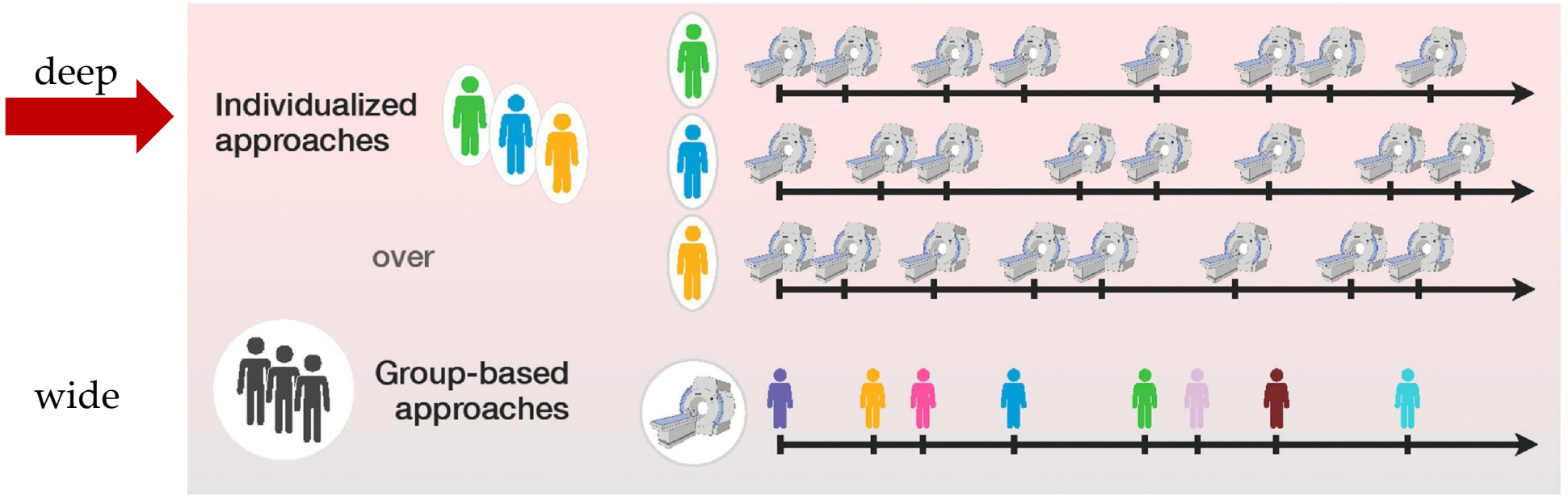


Neuroimaging (fMRI)

Precision functional mapping

Precision functional mapping
(Intensive fMRI, deep fMRI)

Data acquisition from **many hours** of data on **a few individuals** ("deep" fMRI), as opposed to a **few hours** of data on **many individuals** ("wide" fMRI).



Lee *et al.*, *Trends in Cognitive Sciences* 2025

Examples of **intensive fMRI** studies

Dataset name	**No. of participants**	**fMRI description**	**Ref.**
MyConnectome	1 (age 45)	15 sessions of diffusion MRI 84 sessions of rs-fMRI (10 min) 5–15 sessions of task fMRI	Poldrack et al., *Nat Comm* 2015 (Texas & Washington)
Midnight Scan Club	10 (age 24–34)	10 sessions of rs-fMRI (30 min) 10 sessions of task fMRI (35 min)	Gordon et al., *Neuron* 2017 (Missouri)
Natural Scenes Dataset	8 (age 19–32)	30–40 sessions of 7T task fMRI *each participant viewed 9,000–10,000 color natural scenes (22,000–30,000 trials)*	Allen et al., *Nat Neurosci* 2021 (Minnesota)
Serial Imaging of Major Depression	6 (age 29 ± 8)	2–62 sessions of fMRI (58–1,792 min)	Lynch et al., *Nature* 2024 (New York)

Use **deep fMRI** to examine **cognitive dispersion** ?

Use **deep fMRI** to examine **cognitive dispersion** ?

The Midnight Scan Club (MSC) dataset

The goal of the MSC project is to enable precise MRI-based characterization of individual humans by collecting large quantities of MRI and fMRI data on each of ten subjects. In each subject, we collected five hours of resting state fMRI, six hours of task fMRI across four different tasks, and four scans in each of four different anatomical modalities--T1, T2, MRA, and MRV. This dataset includes all raw data in all ten subjects. In addition, we have included hand-edited T1-derived cortical surfaces, fully preprocessed volumetric and surface-based resting-state data, and individualized cortical parcellations and large-scale networks derived from the resting-state data.

Data Associated with Revision:

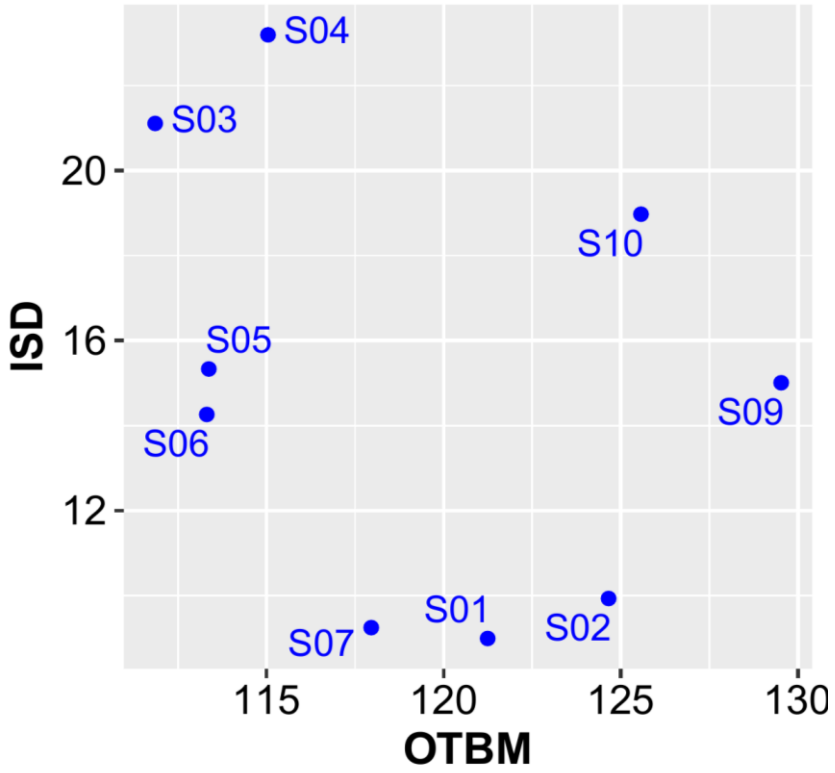
- Data for subjects 01-03 (7.6 GB)
- Data for subjects 04-06 (7.8 GB)
- Data for subjects 07-10 (10.5 GB)
- Metadata & Sourcedata (19.3 KB)
- MRIQC (2.3 GB)
- MRIQC anatomical T1w group report
- MRIQC anatomical T2w group report
- MRIQC functional group report
- Surface pipeline for subjects 01-03 (9.7 GB)
- Surface pipeline for subjects 04-06 (9.7 GB)
- Surface pipeline for subjects 07-10 (12.9 GB)
- Volume pipeline for subjects 01-05 (9.6 GB)
- Volume pipeline for subjects 06-10 (9.8 GB)

STEP 1. Calculate cognitive dispersion from MSC

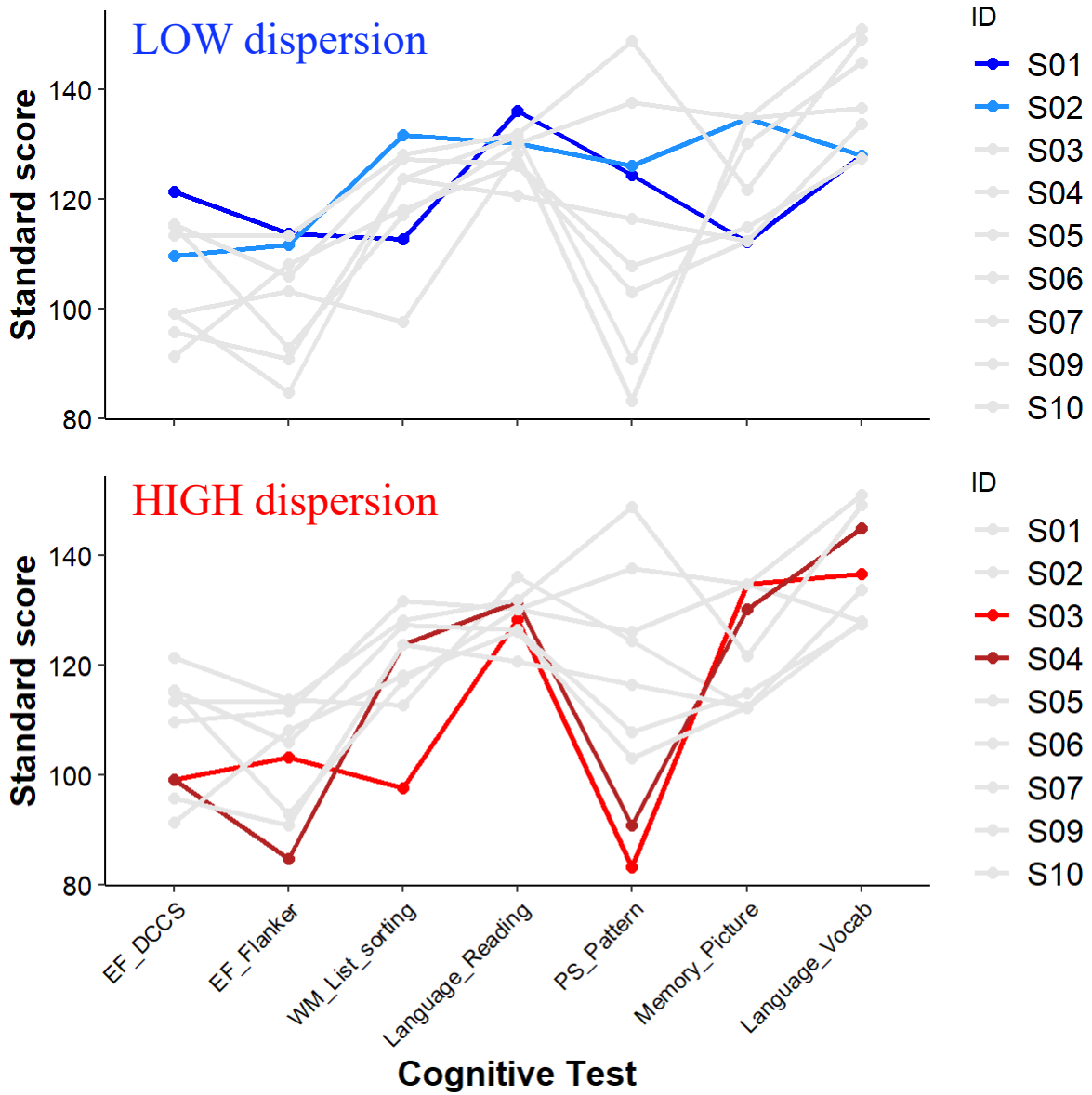
Table 1. Subject Demographic Information And Neuropsychological Assessment Scores

	01	02	03	04	05	06	07	08	09	10
Gender M = 5, F = 5	M	M	F	F	M	F	F		M	M
Age	34	34	29	28	27	24	31		26	31
Education (years)	22	28	18	22	20	17.5	20		19	19
NIH Toolbox										
Cognition Crystallized Composite										
9-Hole Pegboard Dexterity										
Dimensional Change Card Sort	121.4	109.7	99.2	99.1	95.7	91.4	115.5		113.4	115.1
Flanker Inhibitory Control & Attention	113.8	111.7	103.2	84.8	90.8	108.2	106.0		113.4	92.8
List Sorting Working Memory	112.7	131.8	97.6	123.7	123.7	118.1	127.4		128.2	117.2
Oral Reading Recognition ENG	136.1	130.3	128.3	131.6	120.7	126.2	126.5		131.9	130.3
Pattern Comparison Process Speed	124.4	126.2	83.2	90.9	116.5	103.1	107.9		148.9	137.7
Picture Sequence Memory	112.3	134.8	134.8	130.2	112.4	112.4	114.9		121.7	134.8
Picture Vocabulary	128.0	128.1	136.7	145.0	133.8	133.8	127.5		149.2	151.1
Mean	121.2	124.7	111.9	115.0	113.4	113.3	118.0		129.5	125.6
Dispersion (SD)	9.0	9.9	21.1	23.2	15.3	14.3	9.2		15.0	19.0

STEP 1. Calculate cognitive dispersion from MSC (cont.)



OTBM, overall test battery mean
ISD, intra-individual standard deviation (aka cognitive dispersion)



EF, executive function
DCCS, Dimensional Change Card Sort
WM, working memory
PS, processing speed

STEP 2. Resting state fMRI analysis

- **Attempt #1**: use Infomap to parcellate functional brain networks and calculate size of the default mode network (Lynch et al., *Nature* 2024)
  - Outcome: too many errors in Matlab
- **Attempt #2**: use another method to parcellate functional brain networks, i.e., multi-session hierarchical Bayesian modeling (MS-HBM; Kong et al., *Cereb Cortex* 2019)
  - Outcome: same as attempt #1
- **Attempt #3** (final): use CONN toolbox for functional connectivity analysis (Nieto-Castanon, 2020)

Errors from attempt #1

```
Error using  *
Requested 81407x81407 (49.4GB) array exceeds maximum array size preference (31.5GB). This
might cause MATLAB to become unresponsive.

Error in internal.stats.corrPearson (line 115)
        coef = x' * x; % 1/(n-1) doesn't matter, renormalizing anyway

Error in corr (line 248)
        coef = corrFun(rows,tail,wts,x);

Error in pfm_infomap (line 57)
m = corr(C.data(GoodVerts,:)');

Error in pfm_tutorial (line 116)
pfm_infomap(ConcatenatedCifti,DistanceMatrix,PfmDir,GraphDensities,NumberReps,DistanceCutc

Related documentation
```

Errors from attempt #1 (cont.)

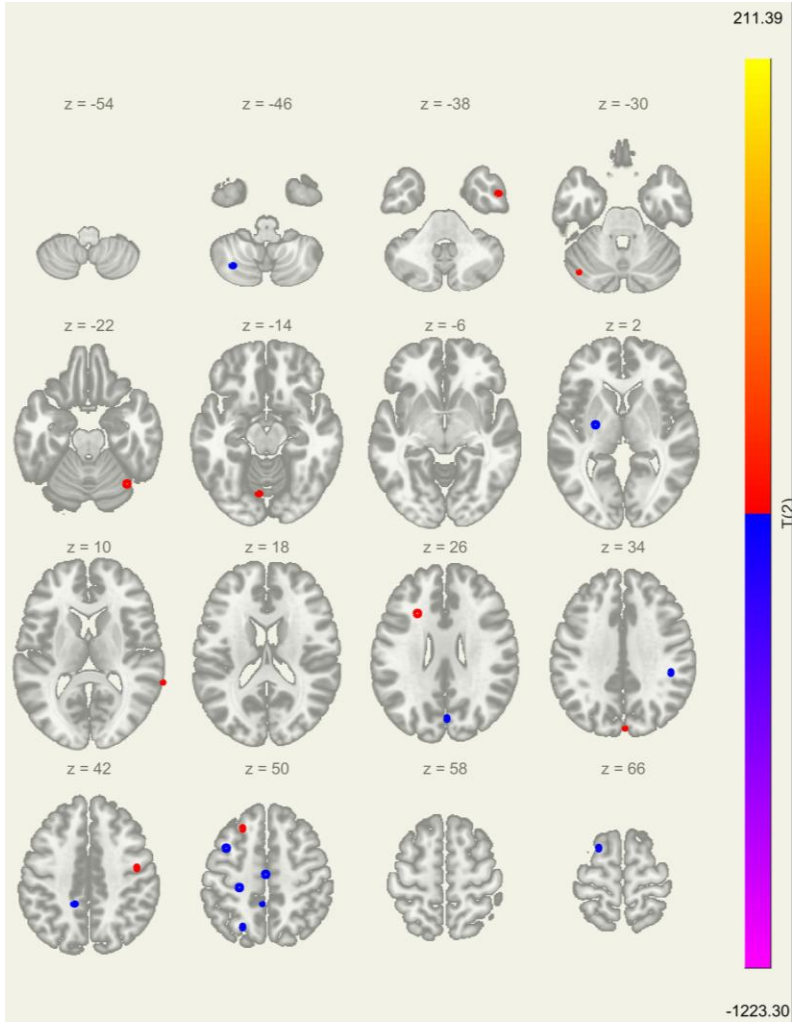
```
Out of memory.

Error in internal.stats.corrPearson (line 115)
        coef = x' * x; % 1/(n-1) doesn't matter, renormalizing anyway

Error in corr (line 248)
        coef = corrFun(rows,tail,wts,x);

Error in pfm_identify_networks (line 34)
m = corr(C.data(1:nCorticalVertices,:)');

Error in pfm_tutorial (line 144)
pfm_identify_networks(ConcatenatedCifti,Ic,MidthickSurfs,Column,Priors,Output,PfmDir,WorkbenchBinary);

Related documentation

>> memory
Maximum possible array:             46276 MB (4.85e+10 bytes) *
Memory available for all arrays:    46276 MB (4.85e+10 bytes) *
Memory used by MATLAB:              21735 MB (2.28e+10 bytes)
Physical Memory (RAM):              32231 MB (3.38e+10 bytes)

*  Limited by System Memory (physical + swap file) available.
```

CONN toolbox

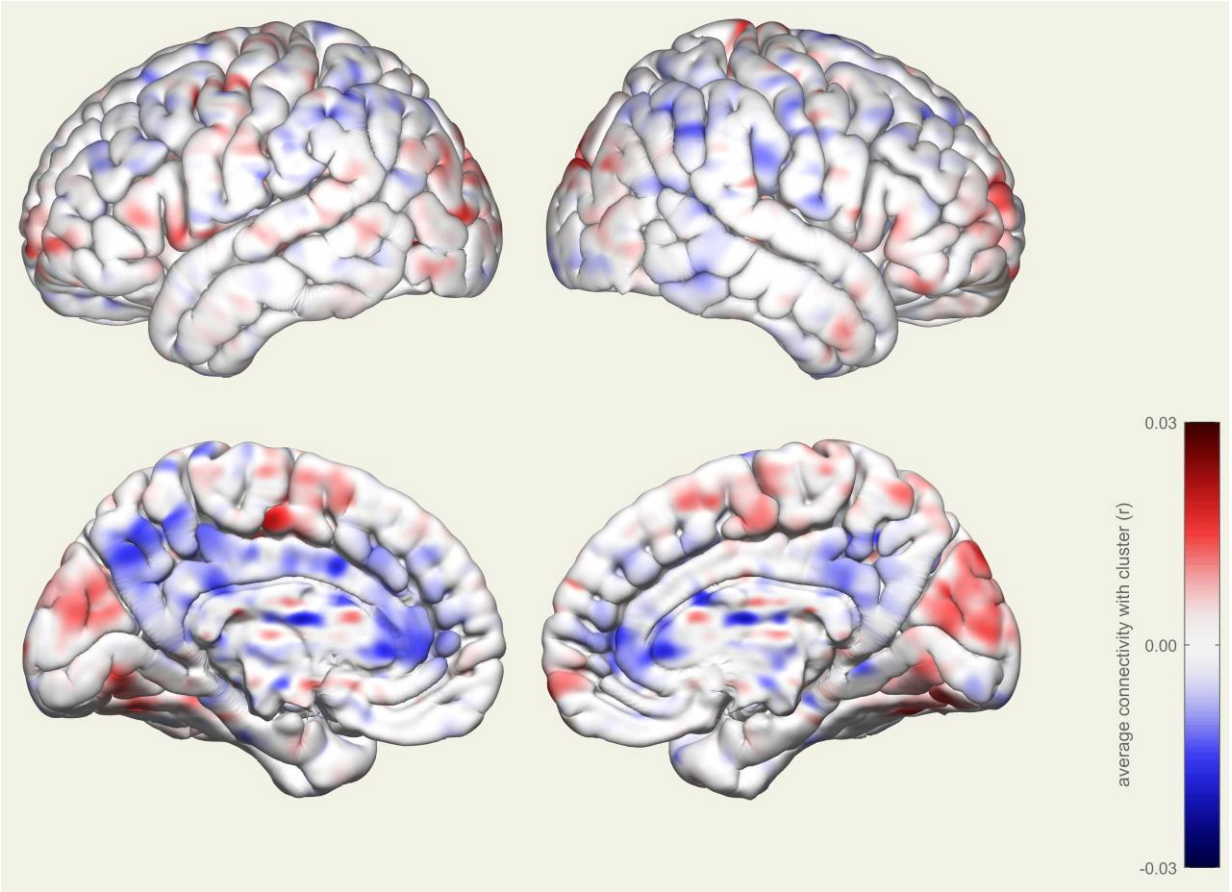
- **Data**: one resting state scan (~ 30 mins) from two individuals with high dispersion (S03, S04) and two with low dispersion (S01, S02).
- **First-level analysis**: Seed-based connectivity maps (SBC) to characterize functional connectivity between **default_mode_MFPC** and the rest of the brain.
- **Second-level analysis**:
    1. 'Does the average connectivity differ between HIGH and LOW DISPERSION subjects?' (two-sample t-test)
    2. 'Does the correlation between connectivity and DISPERSION differ from zero?' (bivariate regression analysis)

‘Does the correlation between connectivity and DISPERSION differ from zero?’

Slice display

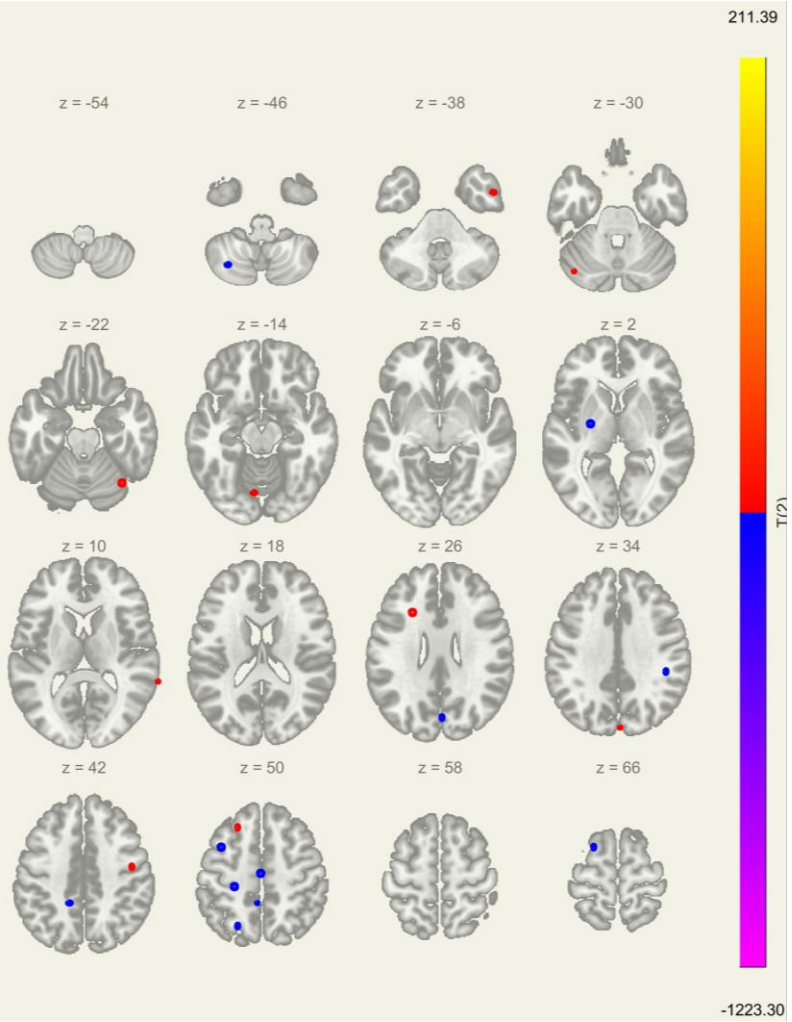


Network view



‘Does the correlation between connectivity and DISPERSION differ from zero?’

Slice display



Cluster	Coordinates	Voxels	*p*(unc.)
Left Middle Frontal Gyrus	-36 +8 +50	8	<.001
Left Precentral Gyrus	-2 -16 +50	16	<.001
Left Putamen	-26 -8 +4	5	<.001
Right Cerebelum	+36 -64 -22	4	<.001


謝謝

Appendix

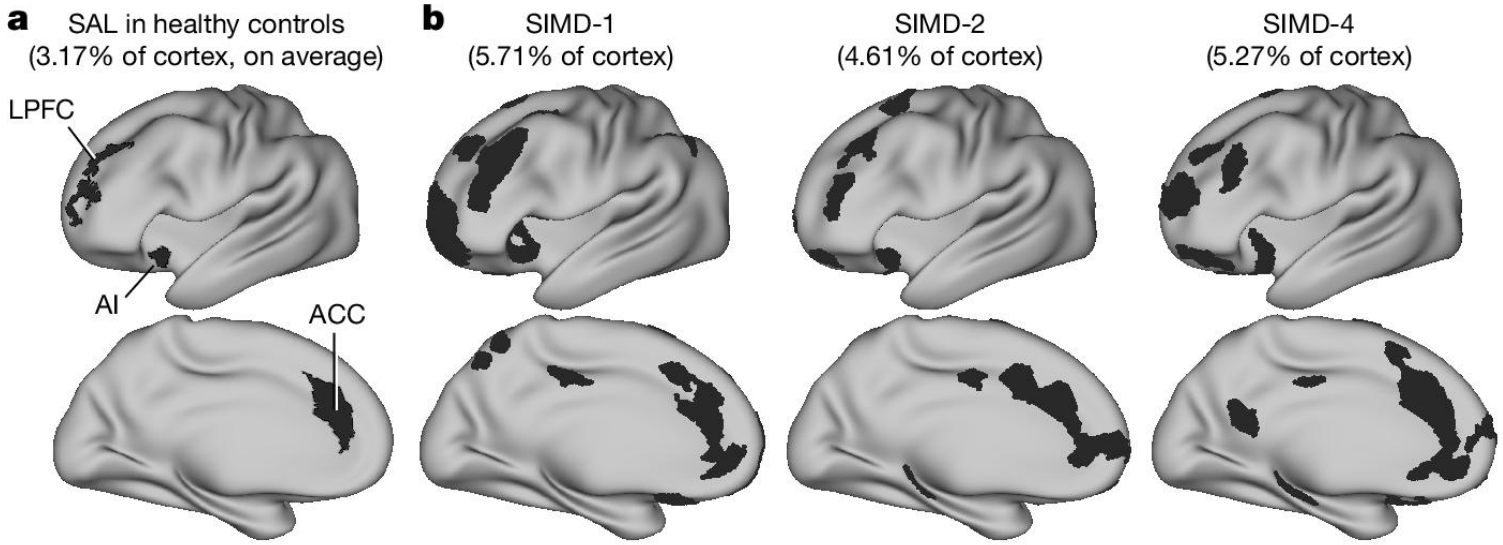
Frontostriatal salience network expansion in individuals in depression

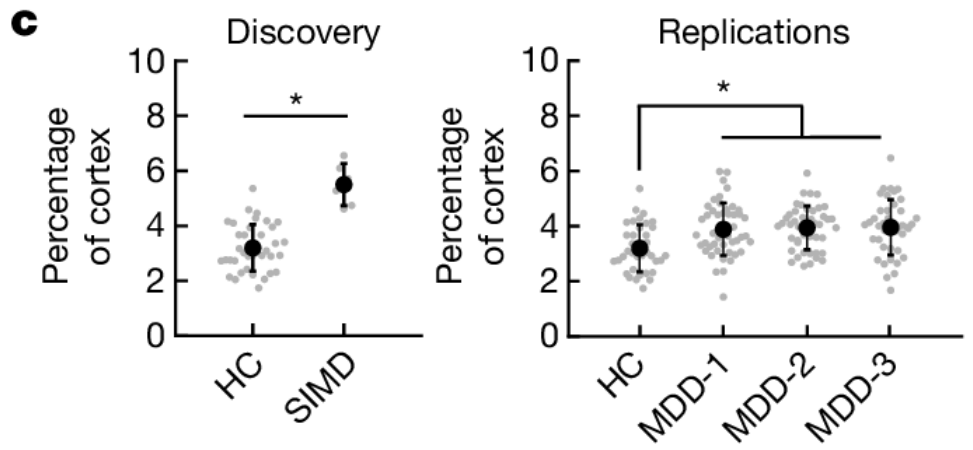
Charles J. Lynch[1]✉, Immanuel G. Elbau[1], Tommy Ng[1], Aliza Ayaz[1], Shasha Zhu[1], Danielle Wolk[1], Nicola Manfredi[1], Megan Johnson[1], Megan Chang[1], Jolin Chou[1], Indira Summerville[1], Claire Ho[1], Maximilian Lueckel[2,3], Hussain Bukhari[1], Derrick Buchanan[4], Lindsay W. Victoria[1], Nili Solomonov[1], Eric Goldwaser[1], Stefano Moia[5,6,7], Cesar Caballero-Gaudes[7], Jonathan Downar[8], Fidel Vila-Rodriguez[9], Zafiris J. Daskalakis[10], Daniel M. Blumberger[8,11,12], Kendrick Kay[13], Amy Aloysi[14], Evan M. Gordon[15], Mahendra T. Bhati[4], Nolan Williams[4], Jonathan D. Power[1], Benjamin Zebley[1], Logan Grosenick[1], Faith M. Gunning[1] & Conor Liston[1]✉

Nature **633**, 624–633 (2024) | Cite this article

[1]Department of Psychiatry, Weill Cornell Medicine, New York, NY, USA. [2]Leibniz Institute for Resilience Research, Mainz, Germany. [3]Neuroimaging Center (NIC), Focus Program Translational Neurosciences (FTN), Johannes Gutenberg University Medical Center, Mainz, Germany. [4]Department of Psychiatry and Behavioral Sciences, Stanford University, Stanford, CA, USA. [5]Neuro-X Institute, École Polytechnique Fédérale de Lausanne, Geneva, Switzerland. [6]Department of Radiology and Medical Informatics, Faculty of Medicine, University of Geneva, Geneva, Switzerland. [7]Basque Center on Cognition, Brain and Language, Donostia, Spain. [8]Department of Psychiatry and Institute of Medical Science, University of Toronto, Toronto, Ontario, Canada. [9]Department of Psychiatry, University of British Columbia, Vancouver, British Columbia, Canada. [10]Department of Psychiatry, University of California, San Diego, CA, USA. [11]Temerty Centre for Therapeutic Brain Intervention, Toronto, Ontario, Canada. [12]Centre for Addiction and Mental Health, Toronto, Ontario, Canada. [13]Center for Magnetic Resonance Research, University of Minnesota, Minneapolis, MN, USA. [14]Icahn School of Medicine at Mount Sinai, New York, NY, USA. [15]Department of Radiology, Washington University School of Medicine, St. Louis, MO, USA.

Salience network expansion in depression





ACC, anterior cingulate
AI, anterior insular cortex
LPFC, lateral prefrontal
MDD, major depressive disorder
SAL, salience network
SIMD, Serial Imaging of Major Depression

HC, n = 37 healthy controls
MDD-1, n = 48 from Cornell
MDD-2, n = 45 from Cornell
MDD-3, n = 42 from Stanford
SIMD, n = 6

- Data presented as mean ± s.d.
- Significance assessed using a permutation test, *P = 0.001, Bonferroni correction, Z-score = 6.19

cjl2007 / **PFM-Depression** Public

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cjl2007 Update README.md — 7a9c86a · last year — 39 Commits

Figure1	Add files via upload	last year
PFM-Tutorial	Add files via upload	last year
README.md	Update README.md	last year

README

This codebase contains code for delineating functional brain networks entirely within individual subjects, a procedure called precision functional mapping (PFM; see Gordon et al. 2017 Neuron).

The "pfm_tutorial.m" script (located in the ~/PFM-Depression/PFM-Tutorial) calls multiple Matlab scripts for performing PFM from ~/PFM-Depression/PFM-Tutorial/Utilities. This code can be run using an example PFM-style dataset we have uploaded to OpenNeuro.org (https://openneuro.org/datasets/ds005118/versions/1.0.0) and following step-by-step instructions outlined in the .pdf document "pfm_tutorial_instructions".

About

Code for implementing the precision functional mapping (PFM) routine used in "Frontostriatal salience network expansion in individuals with depression", Lynch et al. 2024 (Nature).

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