THE HONG KONG POLYTECHNIC UNIVERSITY
香港理工大學

Language, Cognition, and Neuroscience

Analysis of structural and resting-state functional MRI data using FreeSurfer

UBDA workshop.

Manson C-M. Fong
PhD in Electronic Engineering (CUHK)
Department of Chinese & Bilingual Studies
Research Centre for Language, Cognition, and Neuroscience
December 21, 2021

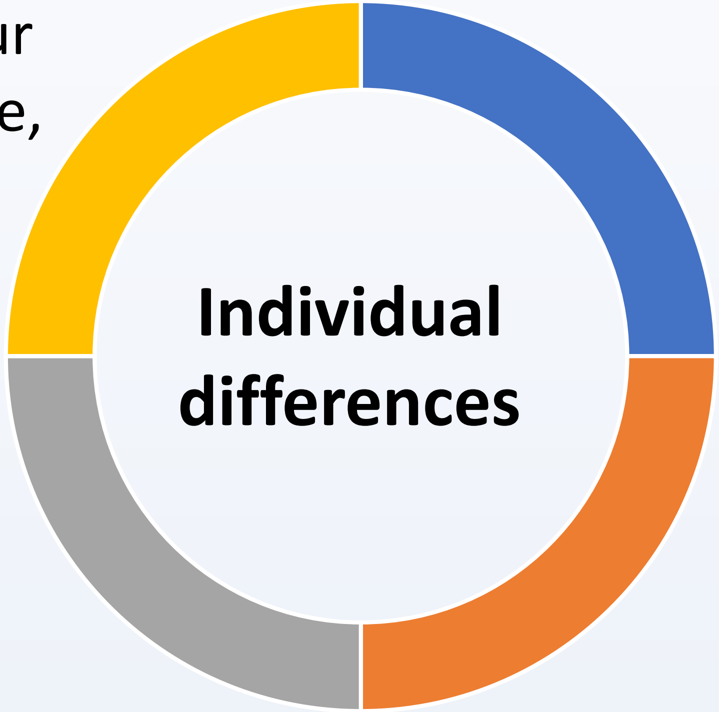
My research

Aging

- How does aging affect our brain, cognition, language, & vice versa?

Cognition

- Attention & inhibitory control
- Working memory
- Long term memory
- Fluid intelligence
- …



Individual differences

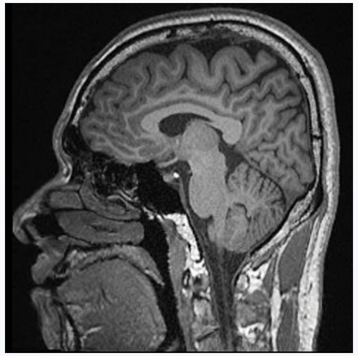
Brain

- Structural anatomy
- Functional connectivity
- Neurophysiology

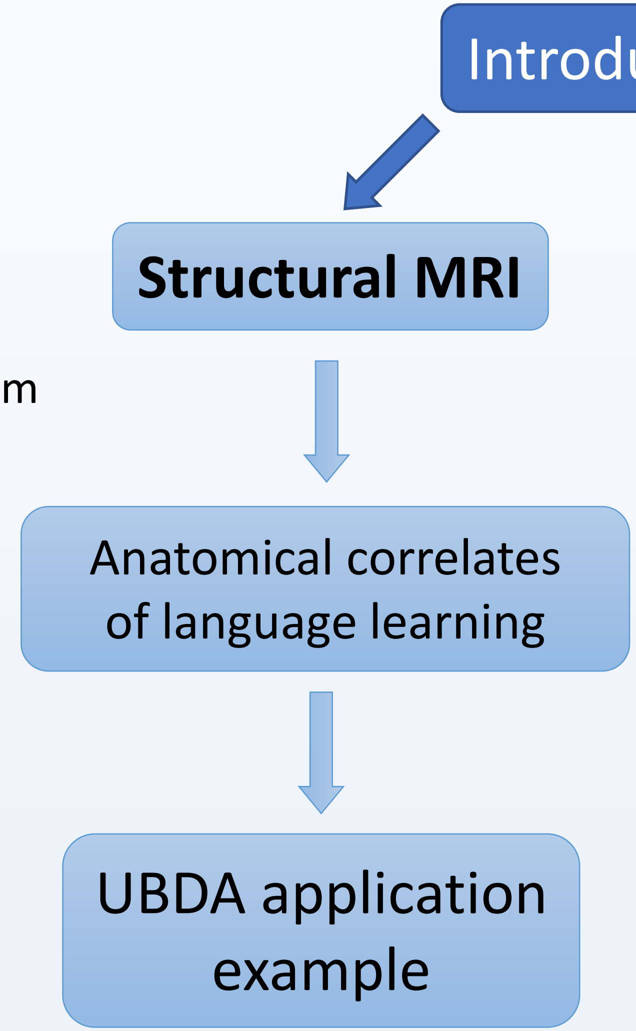
Language

- Word recognition
- Semantic processing
- Topics in bilingualism

Outline



Can structural MRI inform cognitive & language functions?



Introduction

Structural MRI

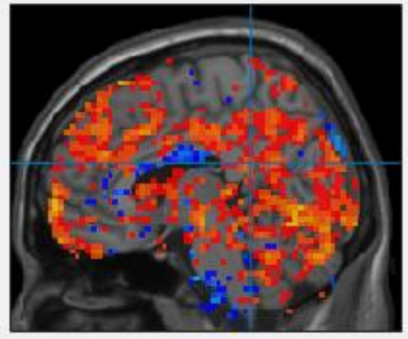
Anatomical correlates of language learning

UBDA application example

Resting-state fMRI

Brain age estimation

Ongoing analysis



Can we estimate cognitive age from resting-state fMRI?

Basic sub-divisions of the brain

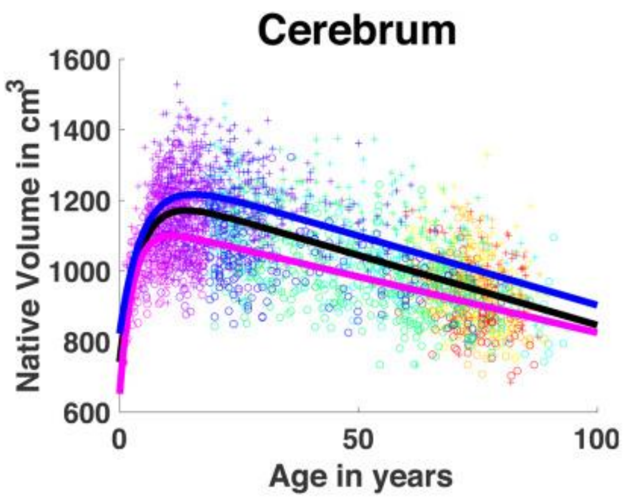
Corpus callosum (fibres connecting both hemispheres)

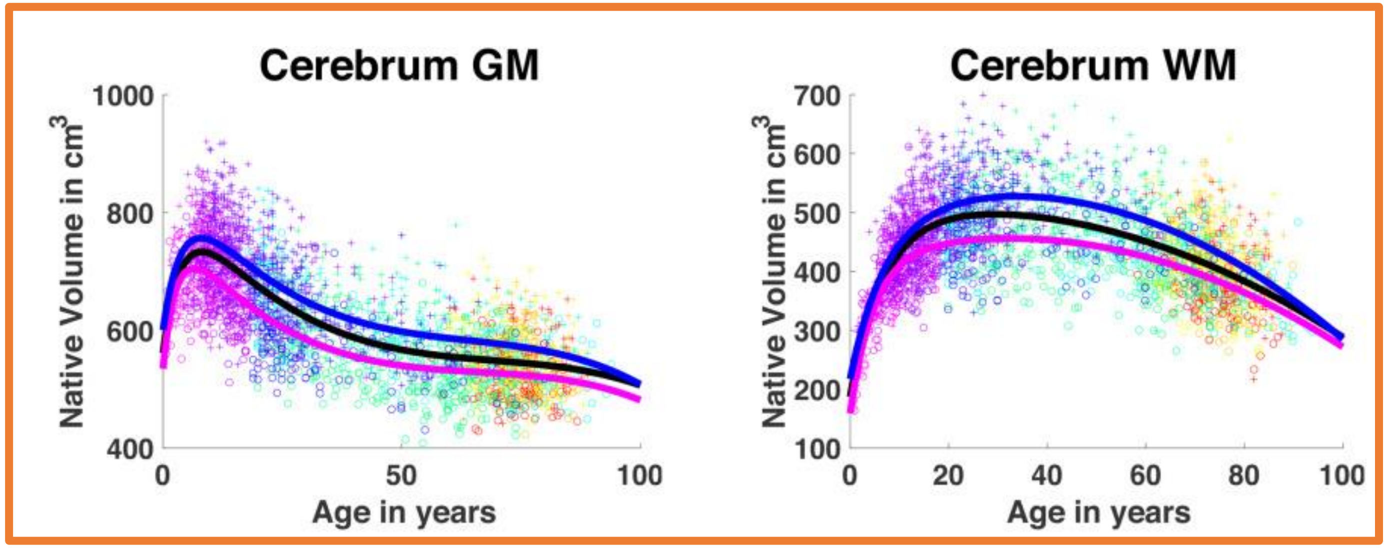
Brainstem

Cerebrum

Cerebellum

Age-related brain changes



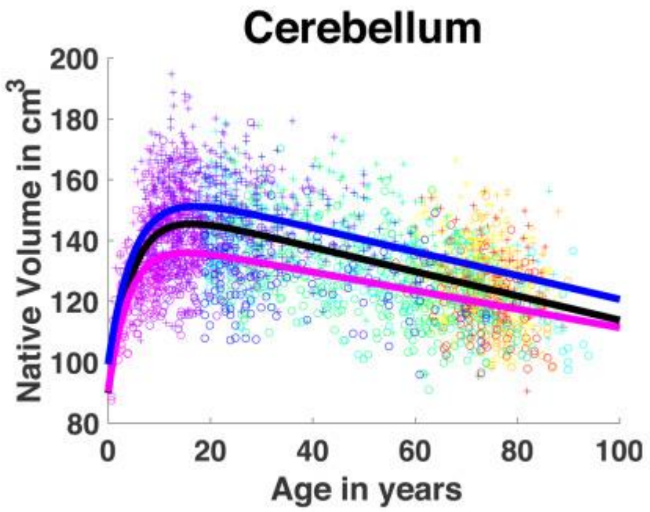


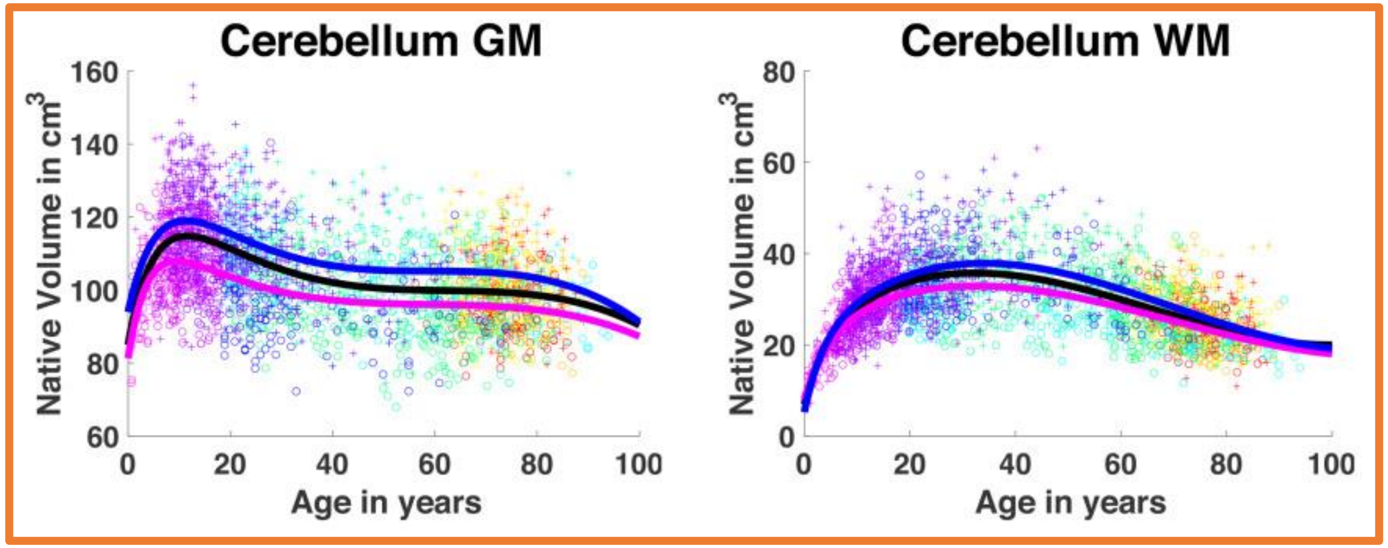
Grey matter (GM)

- Massive pruning of early on

White matter (WM)

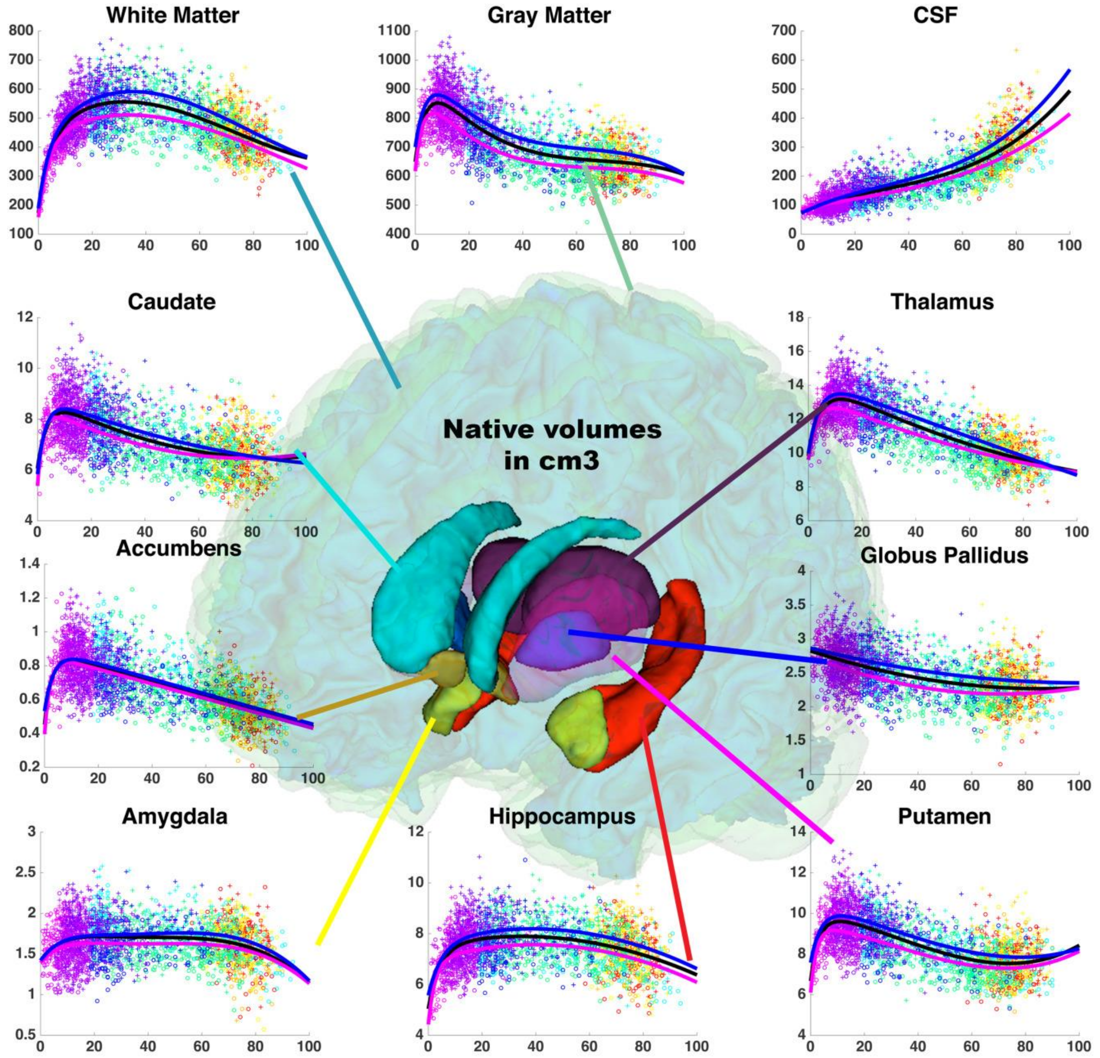
- Peak in early middle age





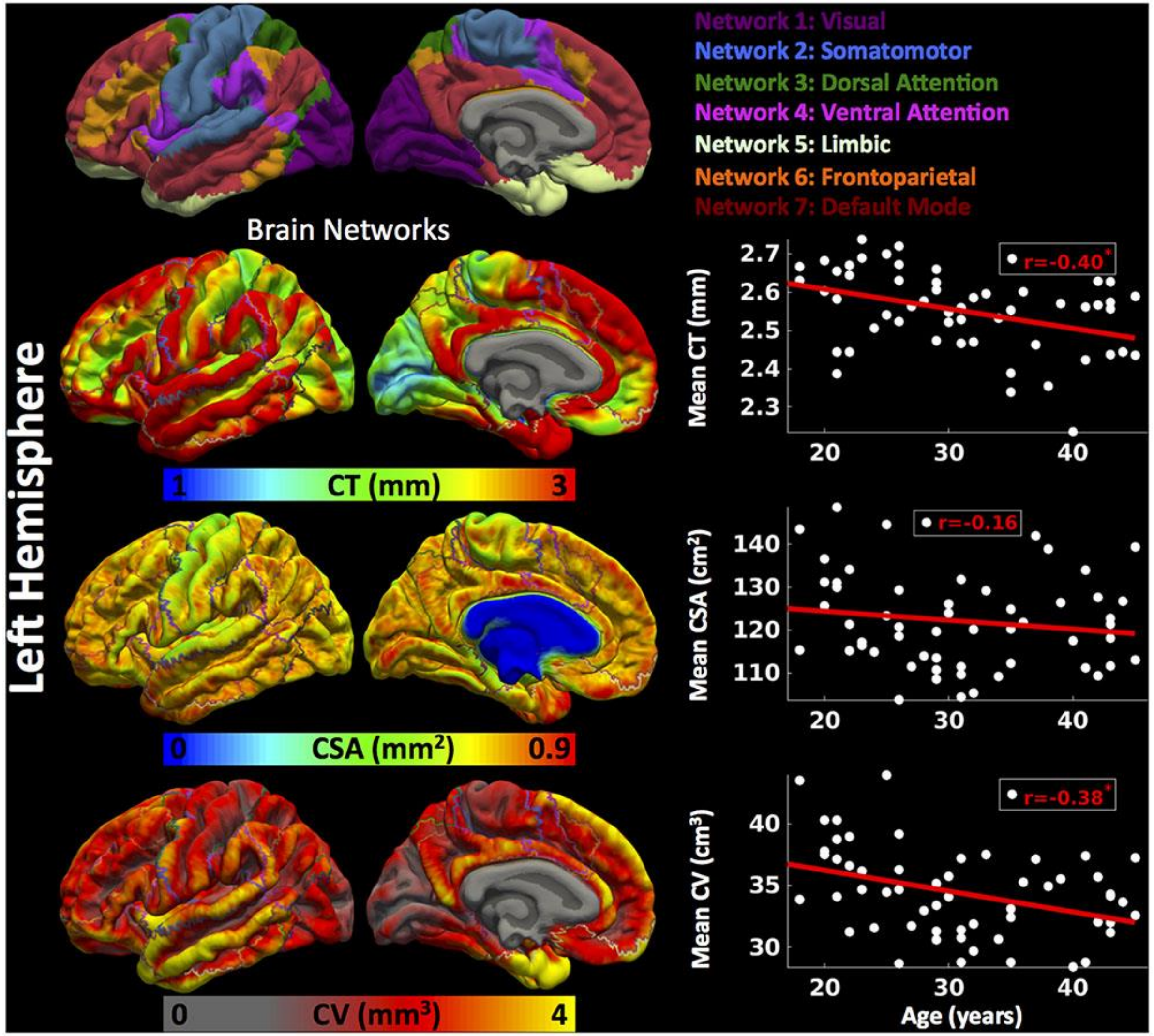
Human Brain Mapping, Volume: 38, Issue: 11, Pages: 5501-5518, First published: 24 July 2017, DOI: (10.1002/hbm.23743)

Subcortical changes



Human Brain Mapping, Volume: 38, Issue: 11, Pages: 5501-5518, First published: 24 July 2017, DOI: (10.1002/hbm.23743)

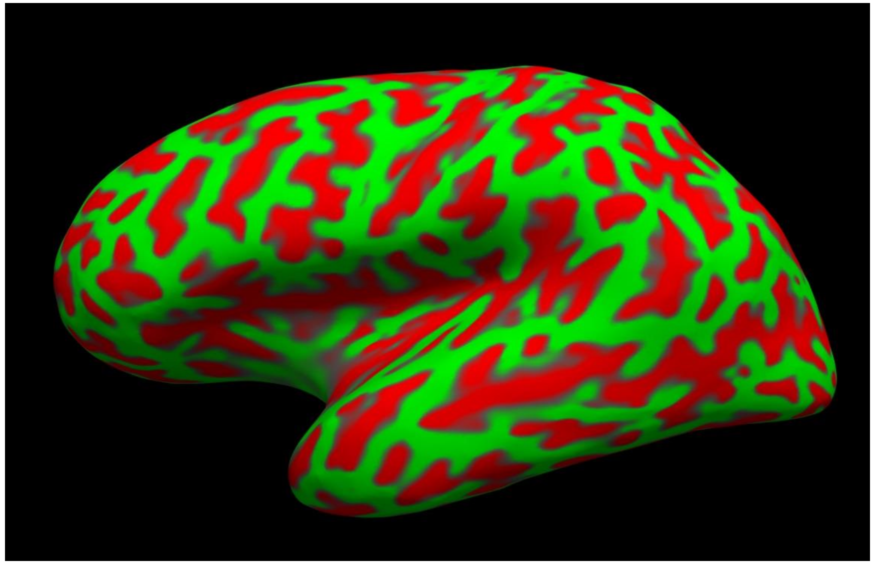
Cortical changes



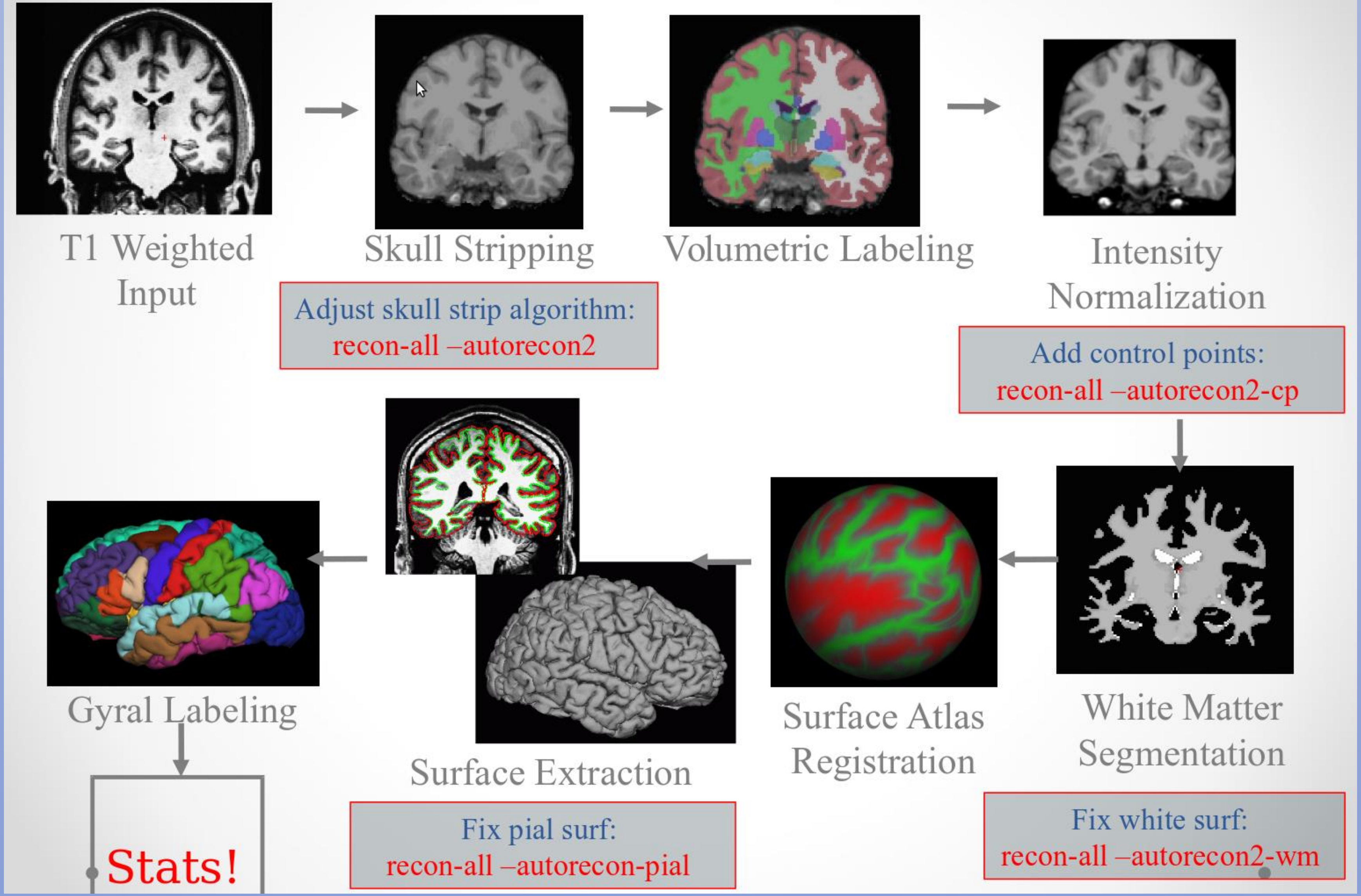
Bajaj et al. 2017. *Frontiers in Aging Neuroscience.*

FreeSurfer

- A package for automatically calculating the anatomical parameters of the brain
- Developed at MGH Martinos Center (Boston) over the past 20-25 years
- Main functions
  - Sub-cortical volume
  - Surface-based analysis of the cortex
    - Cortical thickness
    - Cortical surface area
    - Cortical volume
    - Mean curvature (also known as gyrification ratio)



FreeSurfer processing pipeline



T1 Weighted Input

Skull Stripping

Adjust skull strip algorithm:
recon-all –autorecon2

Volumetric Labeling

Intensity Normalization

Add control points:
recon-all –autorecon2-cp

White Matter Segmentation

Fix white surf:
recon-all –autorecon2-wm

Surface Atlas Registration

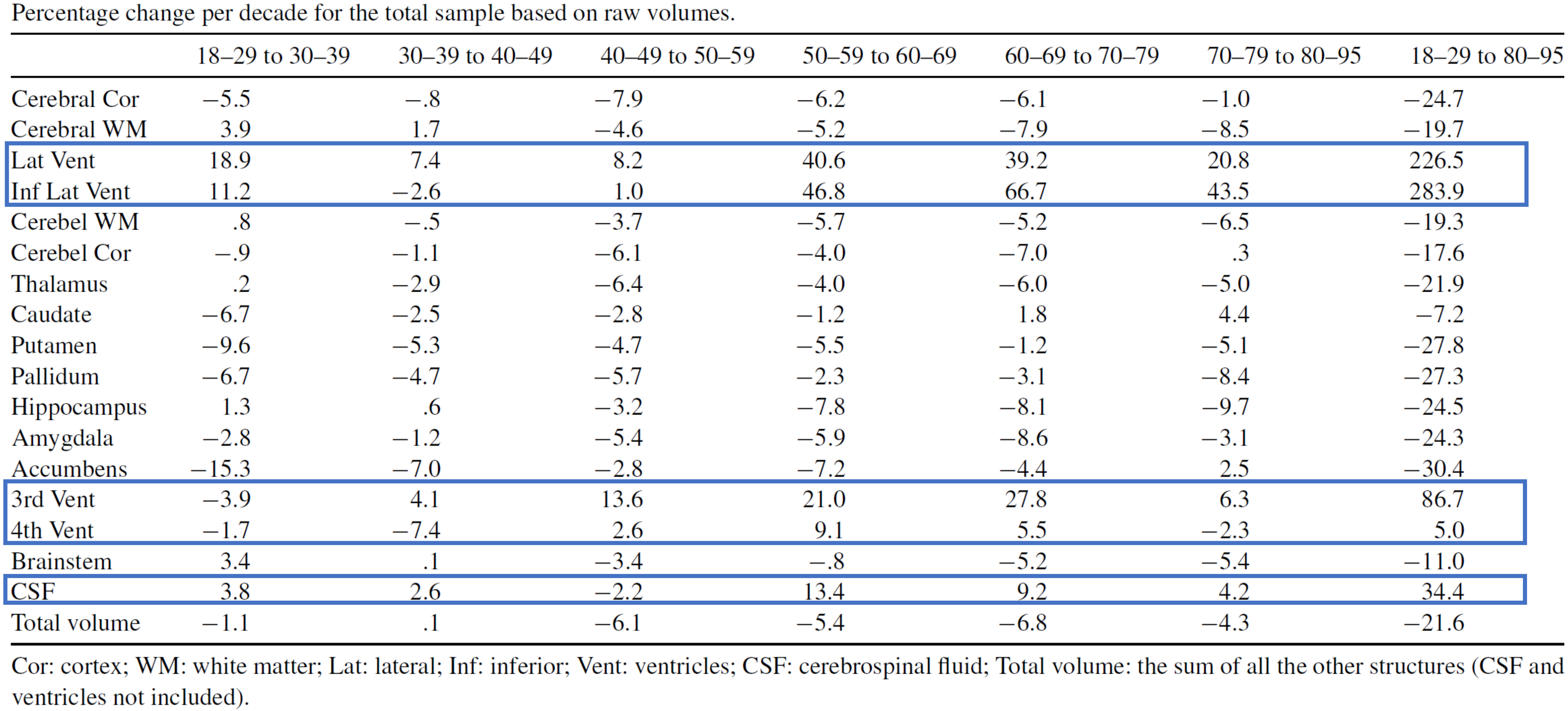
Surface Extraction

Fix pial surf:
recon-all –autorecon-pial

Gyral Labeling

Stats!

Percentage change per decade (both gender)



Percentage change per decade for the total sample based on raw volumes.

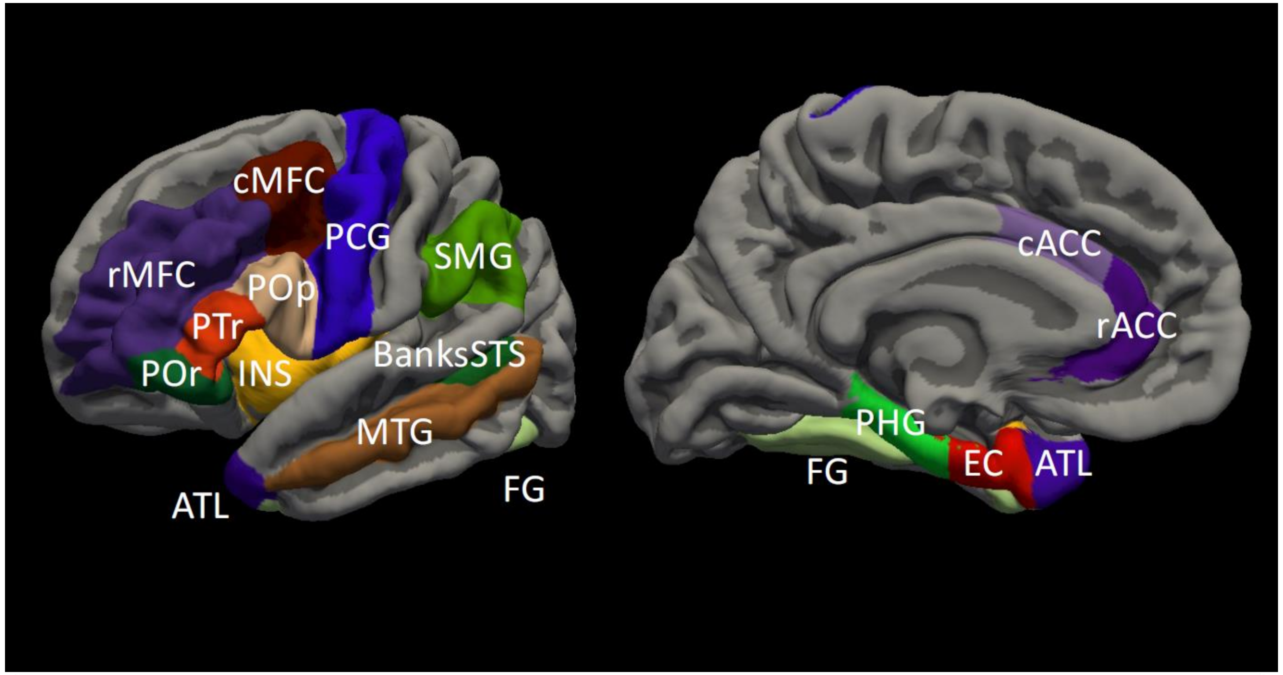
	18–29 to 30–39	30–39 to 40–49	40–49 to 50–59	50–59 to 60–69	60–69 to 70–79	70–79 to 80–95	18–29 to 80–95
Cerebral Cor	−5.5	−.8	−7.9	−6.2	−6.1	−1.0	−24.7
Cerebral WM	3.9	1.7	−4.6	−5.2	−7.9	−8.5	−19.7
Lat Vent	18.9	7.4	8.2	40.6	39.2	20.8	226.5
Inf Lat Vent	11.2	−2.6	1.0	46.8	66.7	43.5	283.9
Cerebel WM	.8	−.5	−3.7	−5.7	−5.2	−6.5	−19.3
Cerebel Cor	−.9	−1.1	−6.1	−4.0	−7.0	.3	−17.6
Thalamus	.2	−2.9	−6.4	−4.0	−6.0	−5.0	−21.9
Caudate	−6.7	−2.5	−2.8	−1.2	1.8	4.4	−7.2
Putamen	−9.6	−5.3	−4.7	−5.5	−1.2	−5.1	−27.8
Pallidum	−6.7	−4.7	−5.7	−2.3	−3.1	−8.4	−27.3
Hippocampus	1.3	.6	−3.2	−7.8	−8.1	−9.7	−24.5
Amygdala	−2.8	−1.2	−5.4	−5.9	−8.6	−3.1	−24.3
Accumbens	−15.3	−7.0	−2.8	−7.2	−4.4	2.5	−30.4
3rd Vent	−3.9	4.1	13.6	21.0	27.8	6.3	86.7
4th Vent	−1.7	−7.4	2.6	9.1	5.5	−2.3	5.0
Brainstem	3.4	.1	−3.4	−.8	−5.2	−5.4	−11.0
CSF	3.8	2.6	−2.2	13.4	9.2	4.2	34.4
Total volume	−1.1	.1	−6.1	−5.4	−6.8	−4.3	−21.6

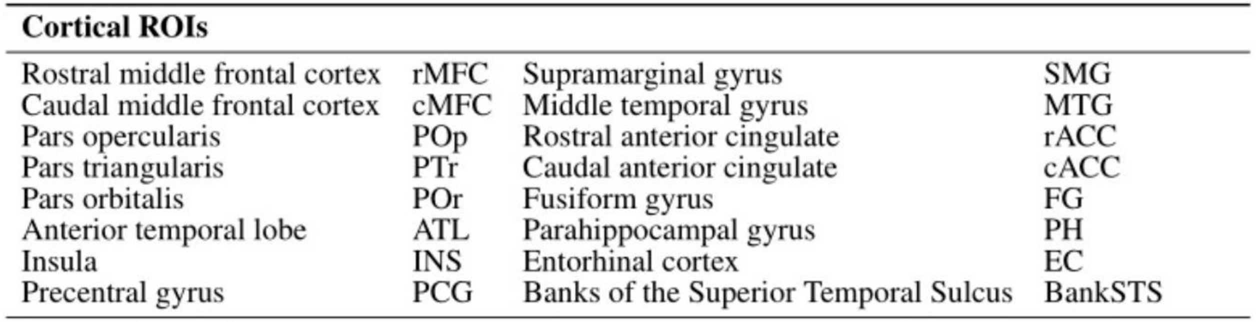
Cor: cortex; WM: white matter; Lat: lateral; Inf: inferior; Vent: ventricles; CSF: cerebrospinal fluid; Total volume: the sum of all the other structures (CSF and ventricles not included).

Walhovd et al. 2011. *Neurobio Aging*.

Foreign language learning as *cognitive training*

- Sep 2020 to May 2021
- Research participants
  - 25 older participants aged 58-69
- Italian vocabulary learning sessions
- Longitudinally follow their foreign language (Italian) learning performance for about 5 weeks

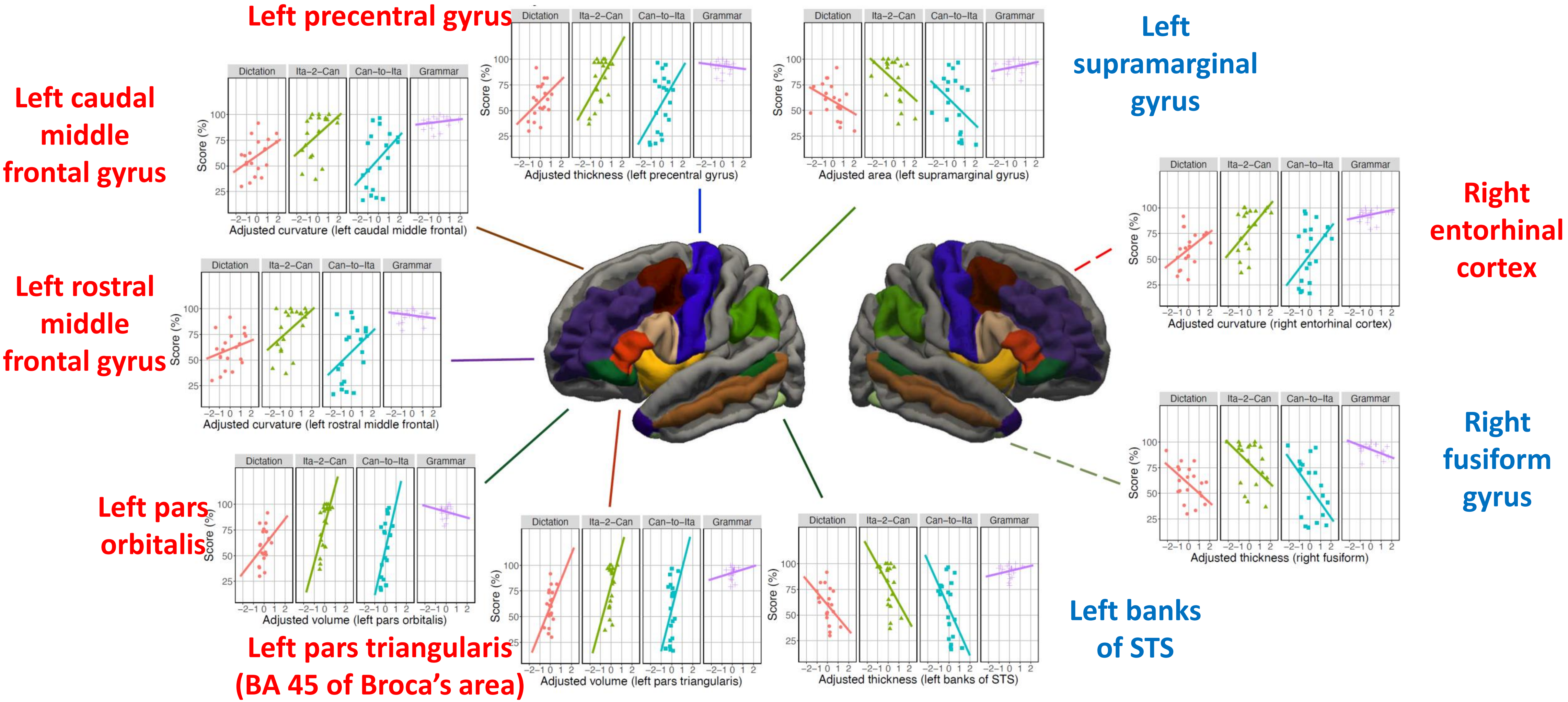




Cortical ROIs			
Rostral middle frontal cortex	rMFC	Supramarginal gyrus	SMG
Caudal middle frontal cortex	cMFC	Middle temporal gyrus	MTG
Pars opercularis	POp	Rostral anterior cingulate	rACC
Pars triangularis	PTr	Caudal anterior cingulate	cACC
Pars orbitalis	POr	Fusiform gyrus	FG
Anterior temporal lobe	ATL	Parahippocampal gyrus	PH
Insula	INS	Entorhinal cortex	EC
Precentral gyrus	PCG	Banks of the Superior Temporal Sulcus	BankSTS

Fong, Ma, Chui, Law, Hui, Au, & Wang (under review).

Language retention performance post-learning



Left precentral gyrus

Left caudal middle frontal gyrus

Left supramarginal gyrus

Right entorhinal cortex

Left rostral middle frontal gyrus

Right fusiform gyrus

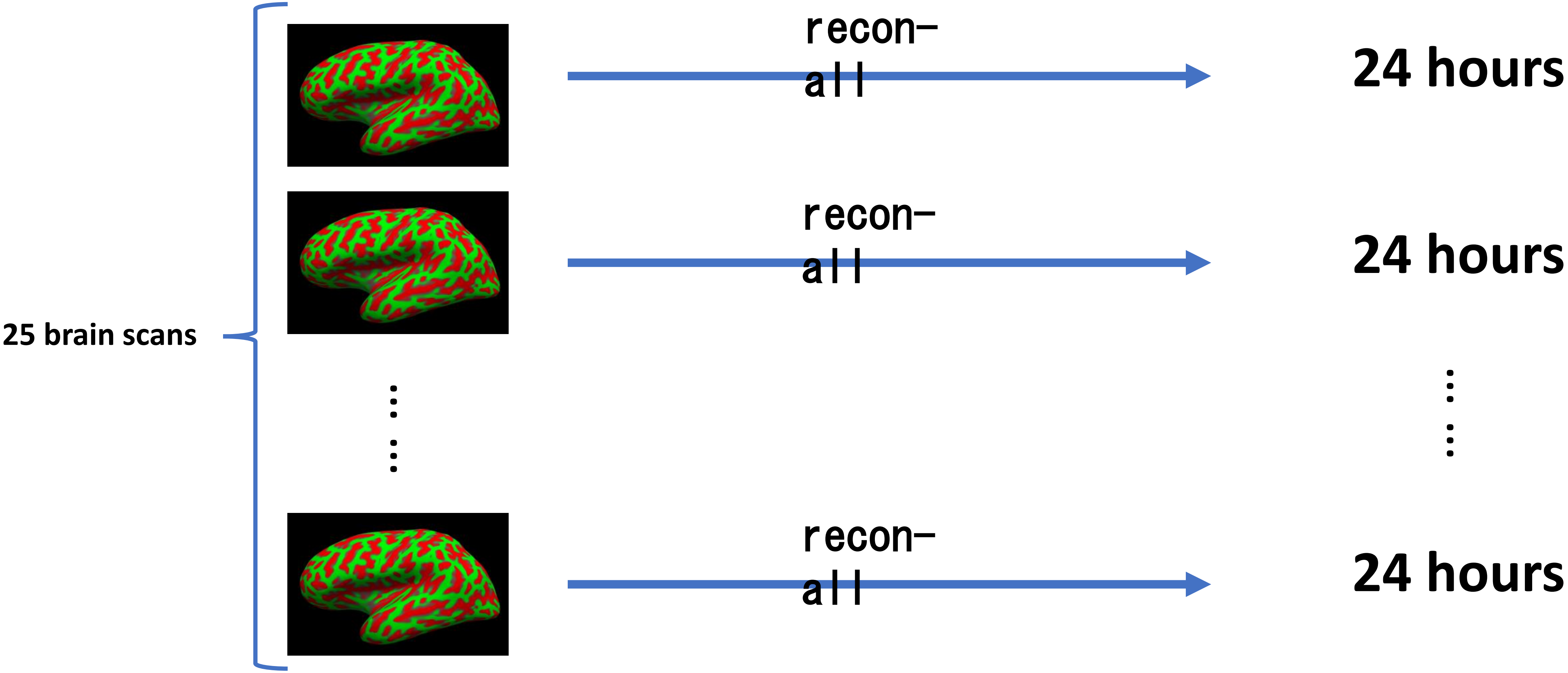
Left pars orbitalis

Left pars triangularis (BA 45 of Broca's area)

Left banks of STS

<u>Fong</u>, Ma, Chui, Law, Hui, Au, & Wang (under review).

UBDA application example: *brain segmentation*



25 brain scans

recon-all → 24 hours

recon-all → 24 hours

⋮

recon-all → 24 hours

UBDA example: *brain segmentation using FreeSurfer*

- Command-line analysis pipeline (**`recon-all`**)

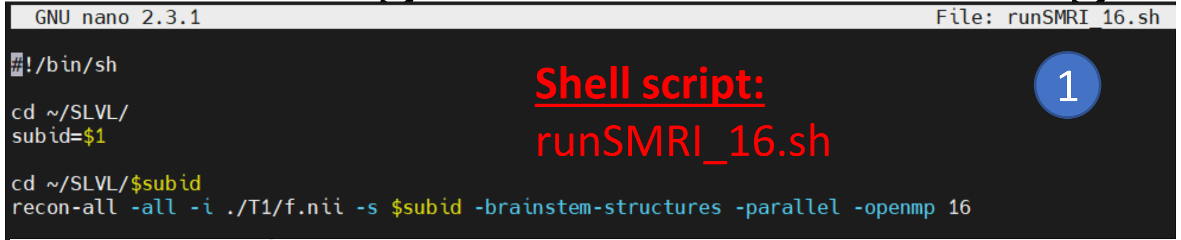
- `recon-all -all -i ./T1/f.nii -s L101 -brainstem-structures -parallel -openmp 6`

options of the command

options related to parallel processing (here, we used 6 processors or threads)

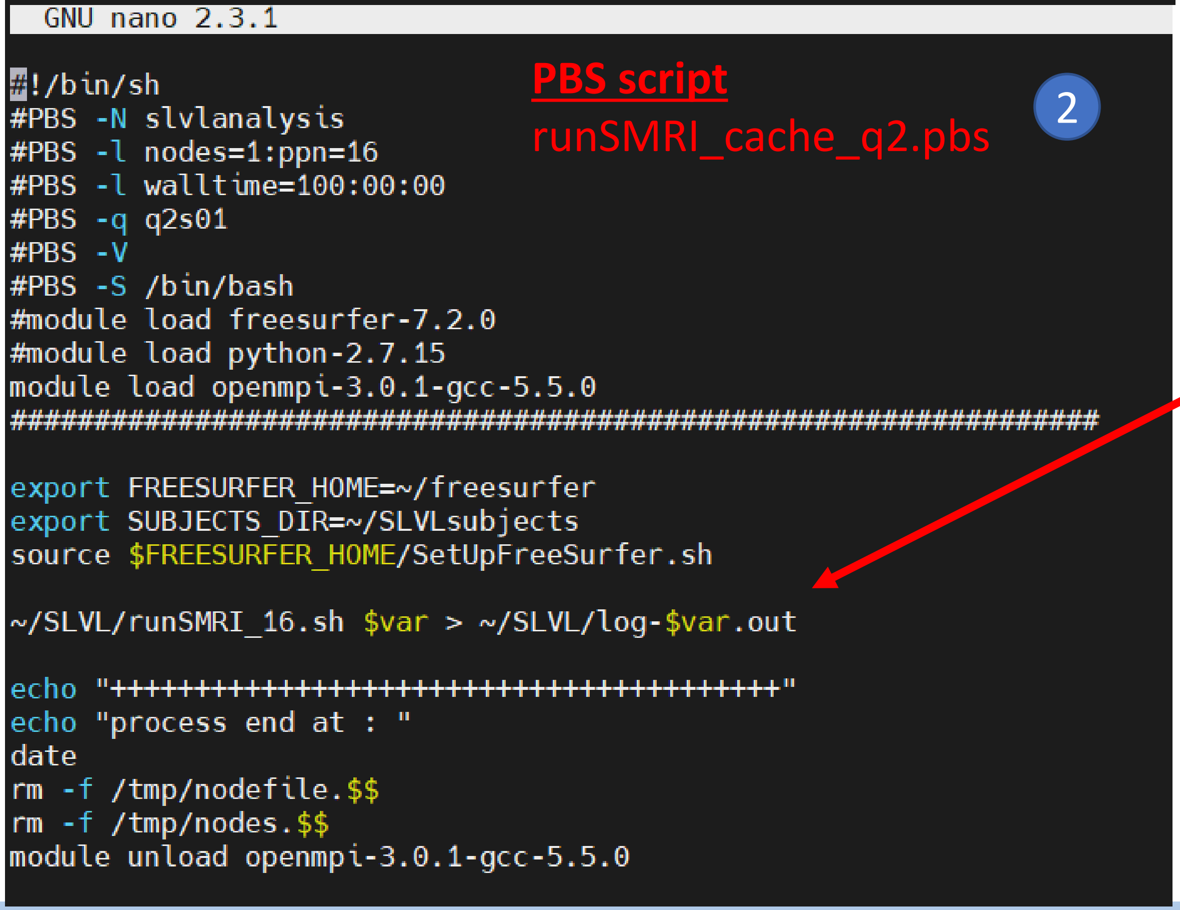
- With parallel computing, significant speedup to **~ 6 hours per brain scan**

UBDA example: *brain segmentation using FreeSurfer*



Shell script:
runSMRI_16.sh

```
#!/bin/sh

cd ~/SLVL/
subid=$1

cd ~/SLVL/$subid
recon-all -all -i ./T1/f.nii -s $subid -brainstem-structures -parallel -openmp 16
```



PBS script
runSMRI_cache_q2.pbs

```
#!/bin/sh
#PBS -N slvlanalysis
#PBS -l nodes=1:ppn=16
#PBS -l walltime=100:00:00
#PBS -q q2s01
#PBS -V
#PBS -S /bin/bash
#module load freesurfer-7.2.0
#module load python-2.7.15
module load openmpi-3.0.1-gcc-5.5.0
#################################################################

export FREESURFER_HOME=~/freesurfer
export SUBJECTS_DIR=~/SLVLsubjects
source $FREESURFER_HOME/SetUpFreeSurfer.sh

~/SLVL/runSMRI_16.sh $var > ~/SLVL/log-$var.out

echo "++++++++++++++++++++++++++++++++++++++++"
echo "process end at : "
date
rm -f /tmp/nodefile.$$
rm -f /tmp/nodes.$$
module unload openmpi-3.0.1-gcc-5.5.0
```

PBS setting

Use q2s01

Nodes=1:ppn=16

- Request 1 node
- 16 processors per node

Setup environment

- Setup Home directory (~/freesurfer)
- Setup Subject directory (~/SLVLsubjects)

Timekeeping & log

- Display the end time
- Remove some log files

Call the shell script

③ **Submit the job**

qsub -v "var=L101" runSMRI_cache_q2.pbs

Brief summary and tips (for absolute beginners)

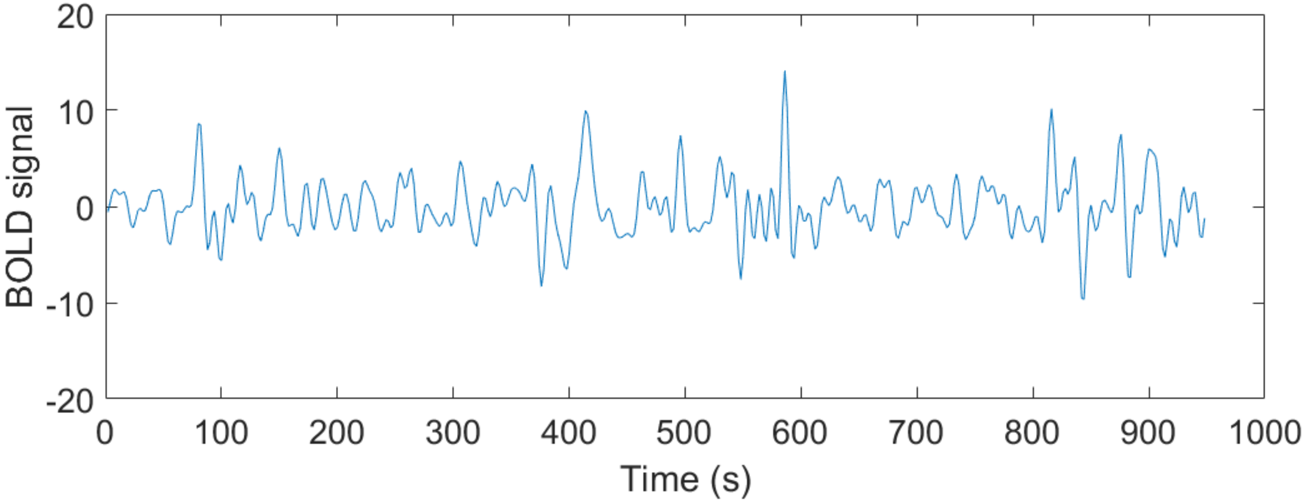
- **Procedure**
  - In the home directory (cd ~), install the required software or your own scripts
  - **Write the shell script**
  - **PBS (Portable Batch System) script (.pbs)**
    - **Setup number of nodes**
      - #PBS -l nodes=1:ppn=16
    - **Select the queue (q2s01, q4s01, qgpu01, qmic01)**
    - **Setup environmental variables**
    - **Call the shellscript (.sh)**
  - **Submit the job to the queue**

- **Useful software**
  - **Terminal software: MobaXterm (Windows)** or **Hyper (Mac)**
  - **FileZilla:** file transfer between local computer and server
- **Most useful commands**
  - history | grep "qsub"
    - to keep track of the submitted jobs
  - qstat
    - to see what jobs are currently running

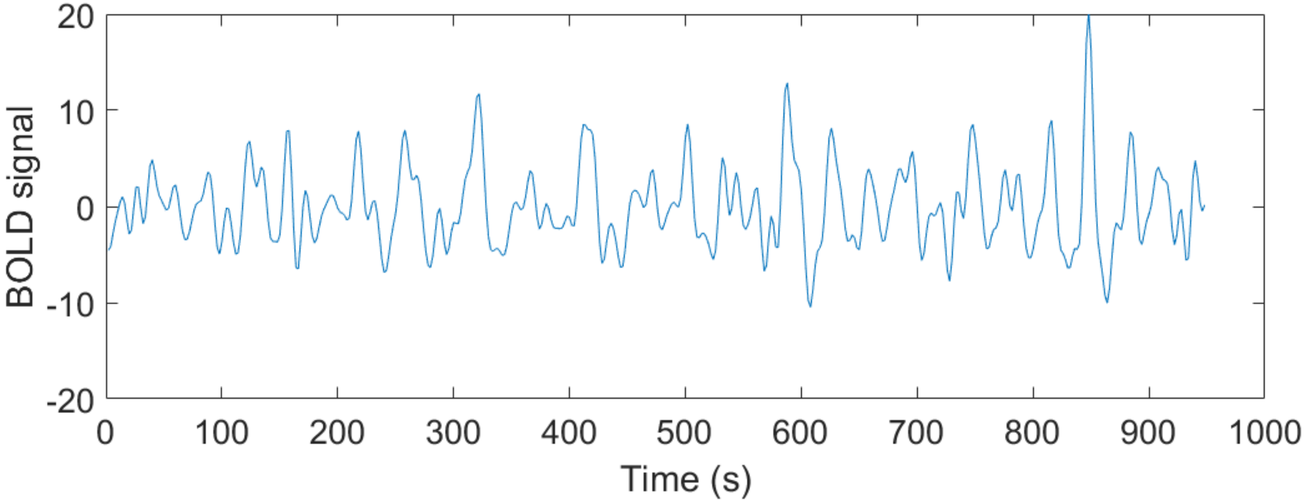
Functional connectivity

Temporal correlations between remote neurophysiological events (Friston,K. J.)

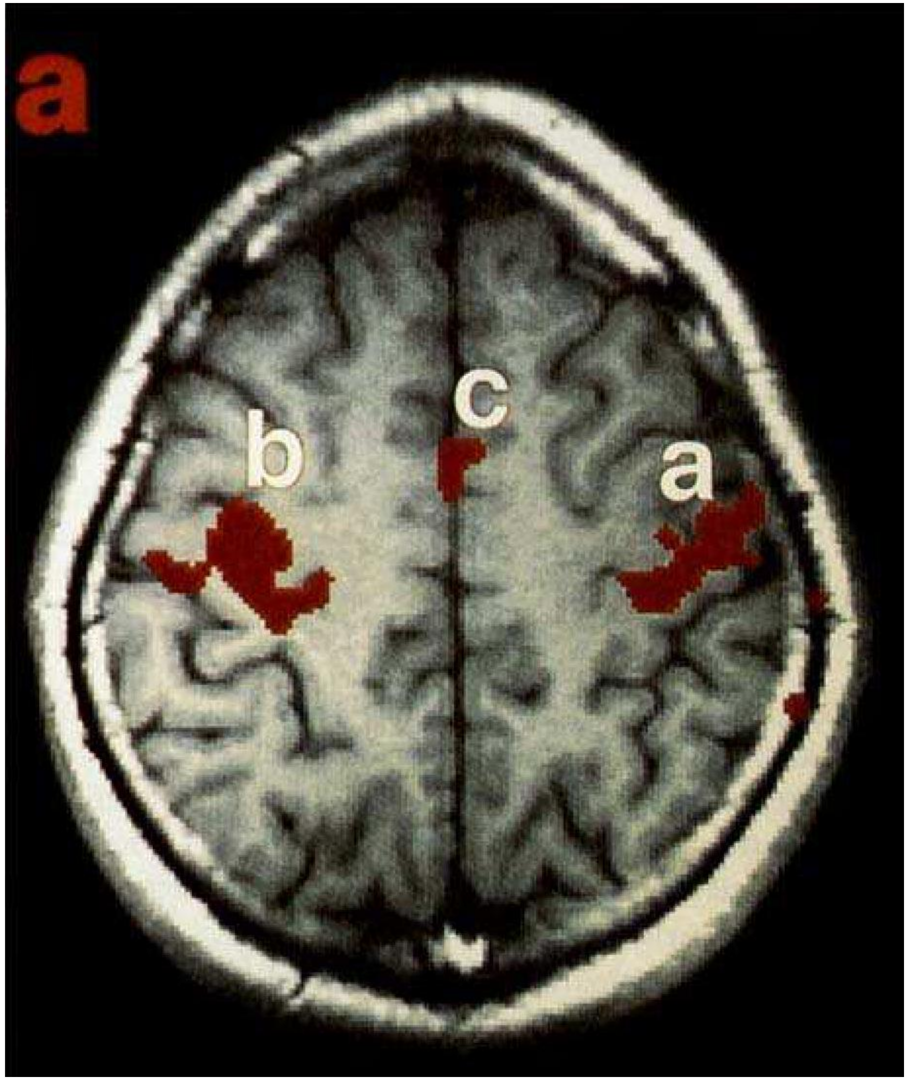
ROI1: Left precentral gyrus (primary motor cortex, controls right hand)



ROI2: Right precentral gyrus (primary motor cortex, controls left hand)



Resting-state functional connectivity



Biswal et al.

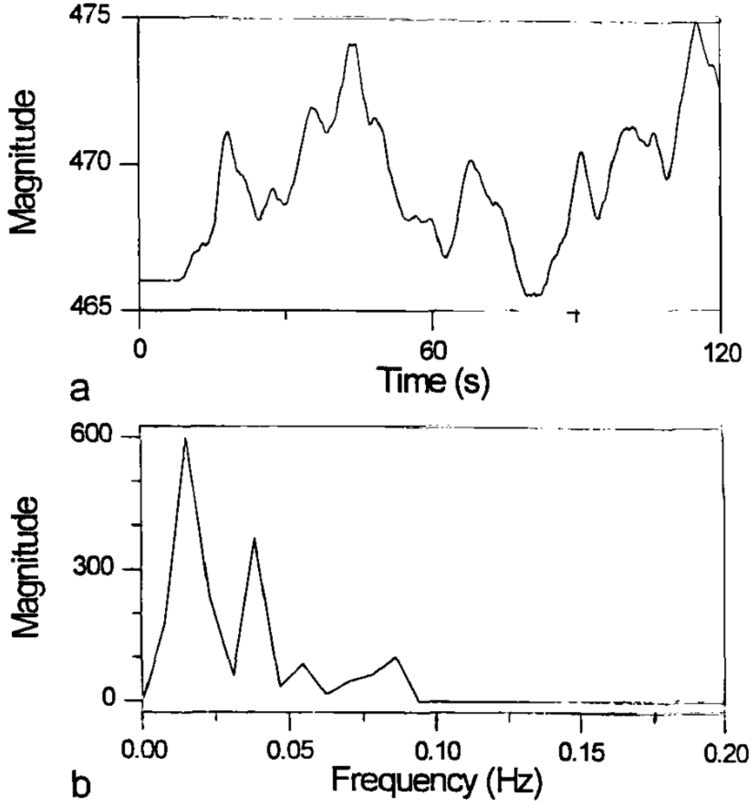
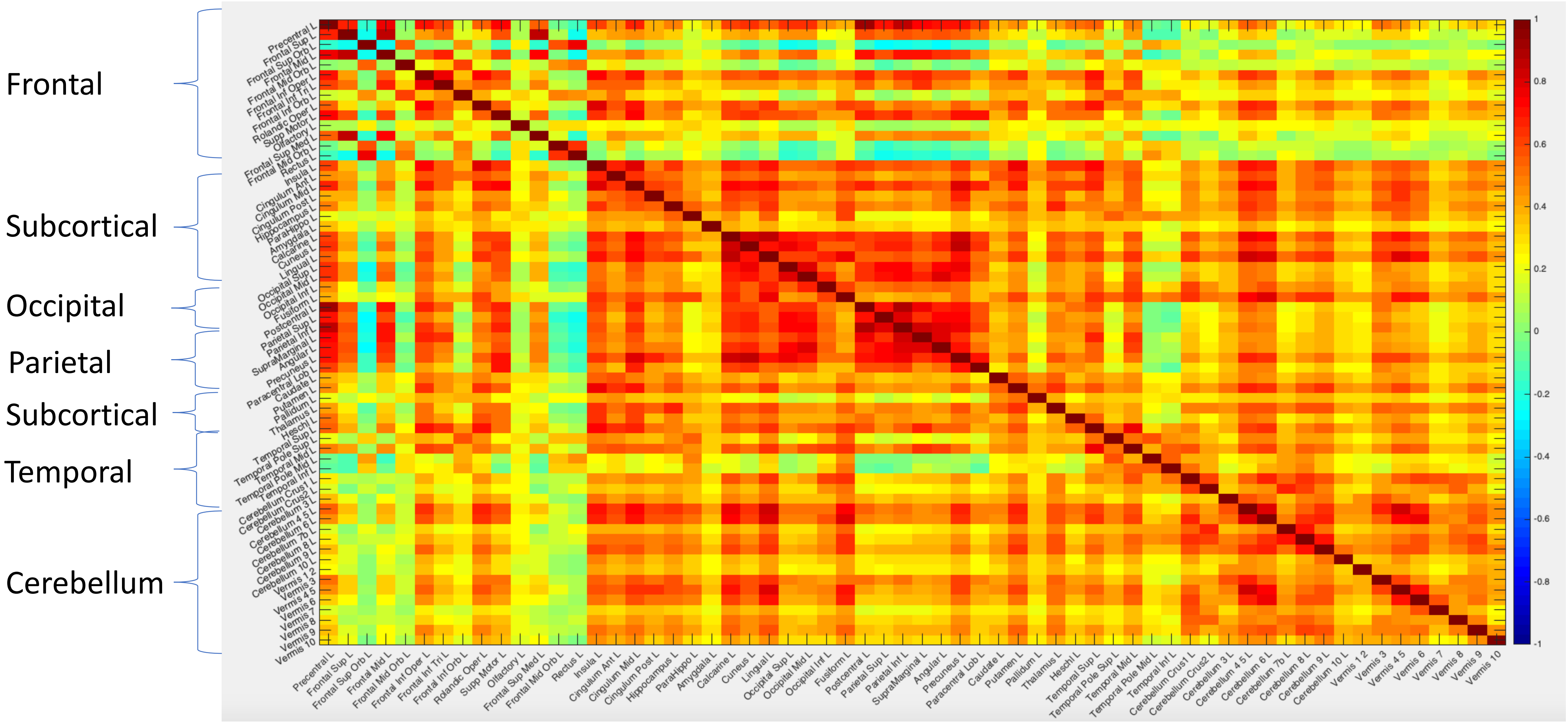


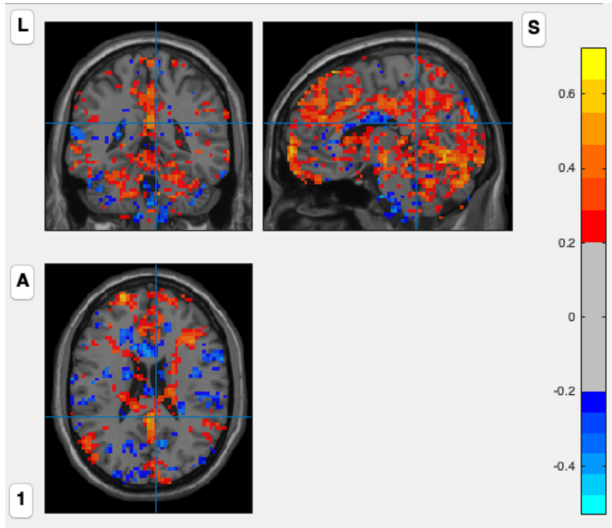
FIG. 1. (a) Representative time course of motor cortex physiological fluctuations after FIR filtering that passes frequencies <0.08 Hz. (b) Fourier transform of the time course.

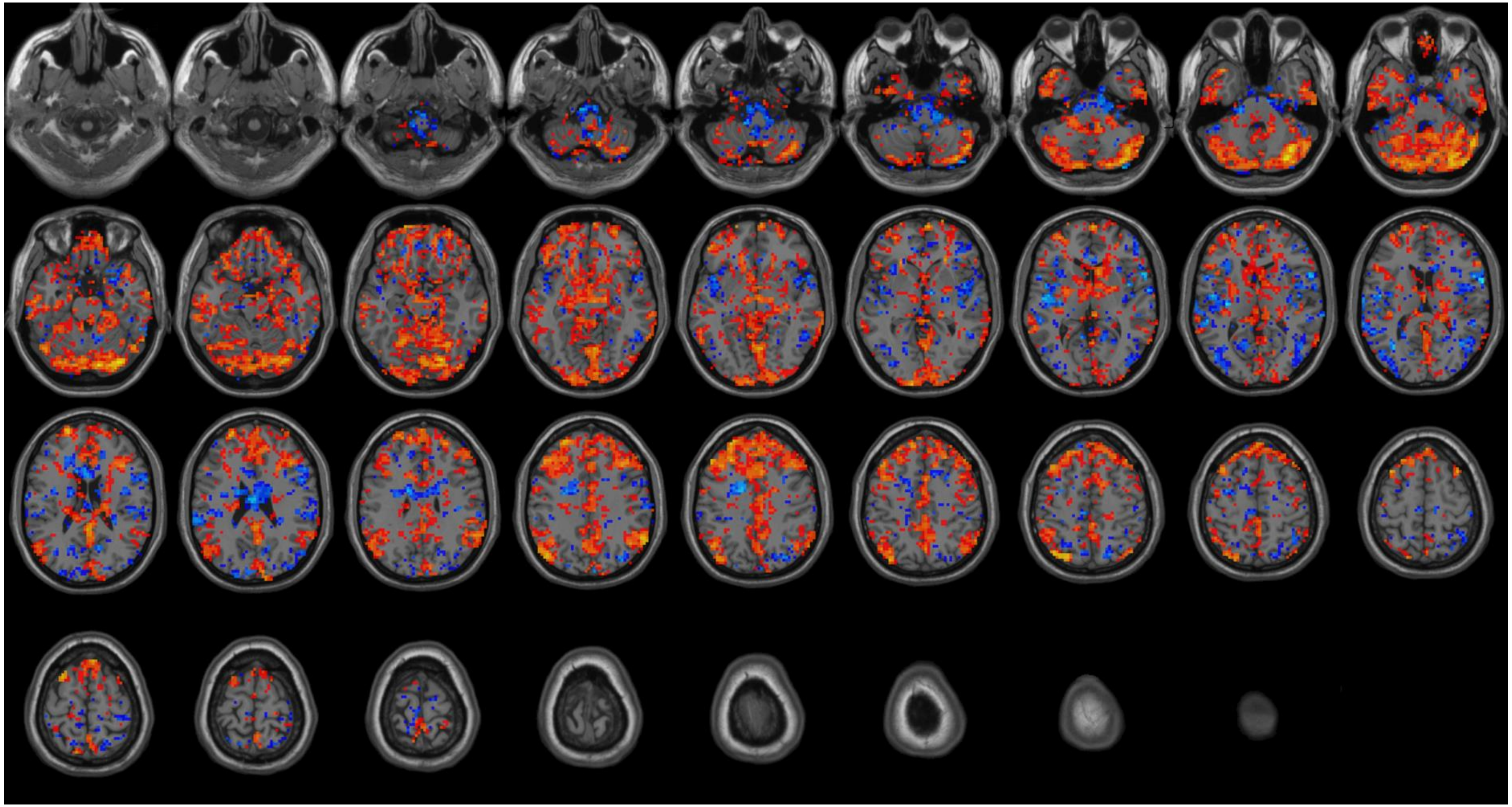
Biswal et al. (1995). *Magnetic Resonance in Medicine.*

Functional connectivity matrix



Example of functional connectivity pattern





UBDA application example: *brain segmentation*

PBS setting

Use q2s01

Nodes=1:ppn=16

- Request 1 node
- 16 processors per node

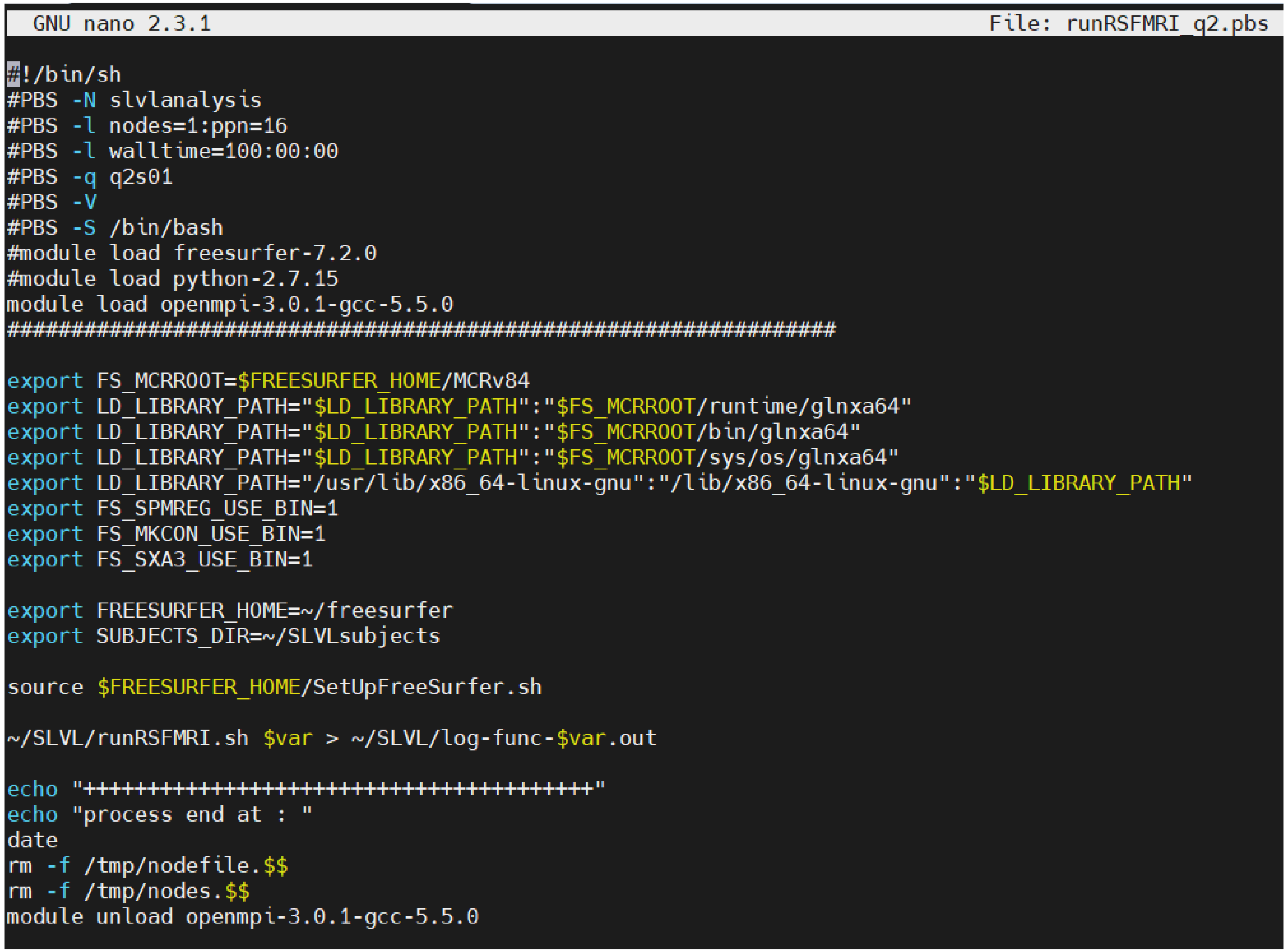
Setup environmental variables

- Load FreeSurfer
- Setup Home directory (~/freesurfer)
- Setup Subject directory (~/SLVLsubjects)
- Source to set path

Call the shell script

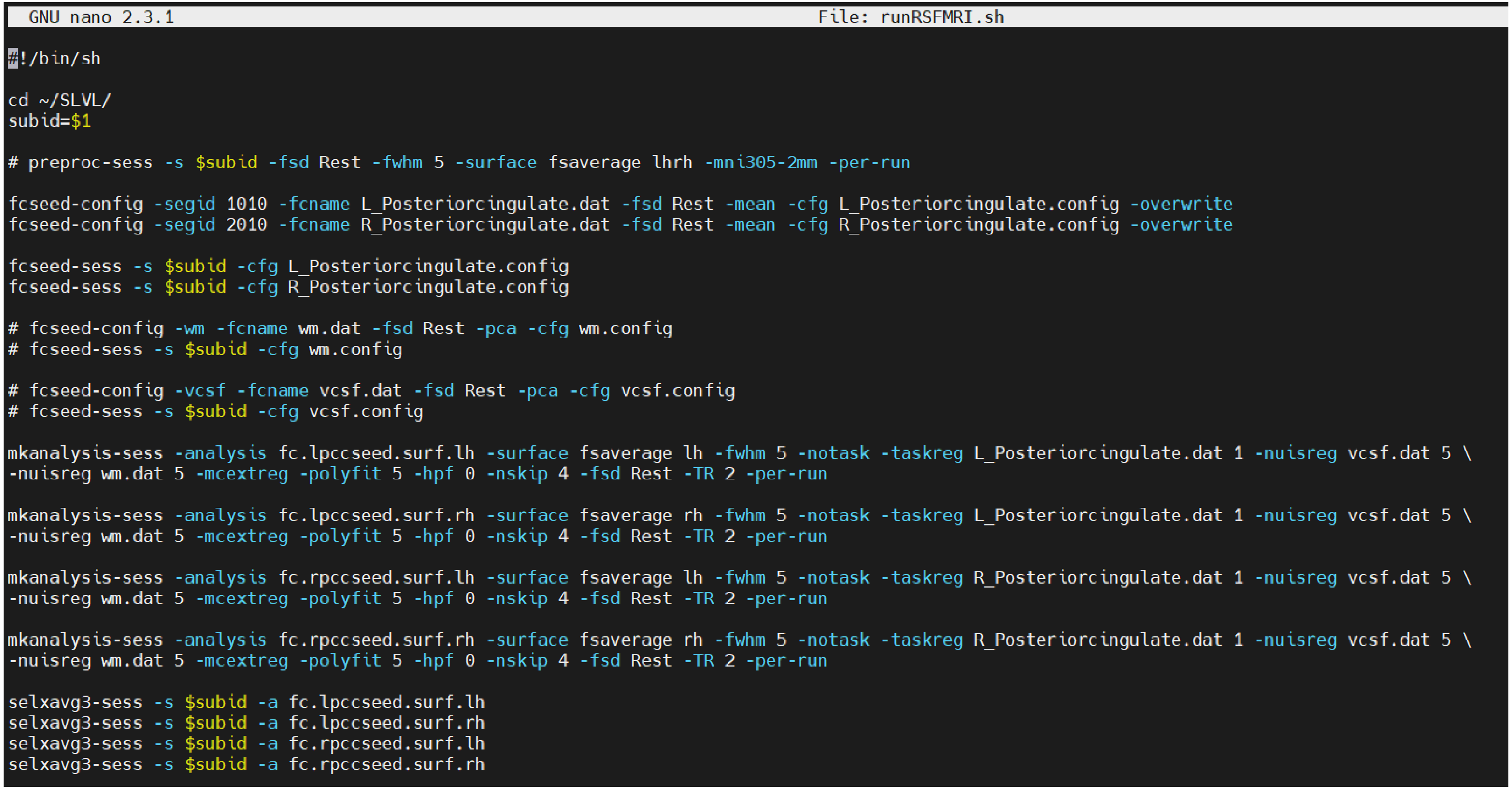
Timekeeping & log

- Display the end time
- Remove some log files



```
  GNU nano 2.3.1                                                     File: runRSFMRI_q2.pbs

#!/bin/sh
#PBS -N slvlanalysis
#PBS -l nodes=1:ppn=16
#PBS -l walltime=100:00:00
#PBS -q q2s01
#PBS -V
#PBS -S /bin/bash
#module load freesurfer-7.2.0
#module load python-2.7.15
module load openmpi-3.0.1-gcc-5.5.0
#################################################################

export FS_MCRROOT=$FREESURFER_HOME/MCRv84
export LD_LIBRARY_PATH="$LD_LIBRARY_PATH":"$FS_MCRROOT/runtime/glnxa64"
export LD_LIBRARY_PATH="$LD_LIBRARY_PATH":"$FS_MCRROOT/bin/glnxa64"
export LD_LIBRARY_PATH="$LD_LIBRARY_PATH":"$FS_MCRROOT/sys/os/glnxa64"
export LD_LIBRARY_PATH="/usr/lib/x86_64-linux-gnu":"/lib/x86_64-linux-gnu":"$LD_LIBRARY_PATH"
export FS_SPMREG_USE_BIN=1
export FS_MKCON_USE_BIN=1
export FS_SXA3_USE_BIN=1

export FREESURFER_HOME=~/freesurfer
export SUBJECTS_DIR=~/SLVLsubjects

source $FREESURFER_HOME/SetUpFreeSurfer.sh

~/SLVL/runRSFMRI.sh $var > ~/SLVL/log-func-$var.out

echo "++++++++++++++++++++++++++++++++++++++++"
echo "process end at : "
date
rm -f /tmp/nodefile.$$
rm -f /tmp/nodes.$$
module unload openmpi-3.0.1-gcc-5.5.0
```

RunRSFMRI.sh



```
#!/bin/sh

cd ~/SLVL/
subid=$1

# preproc-sess -s $subid -fsd Rest -fwhm 5 -surface fsaverage lhrh -mni305-2mm -per-run

fcseed-config -segid 1010 -fcname L_Posteriorcingulate.dat -fsd Rest -mean -cfg L_Posteriorcingulate.config -overwrite
fcseed-config -segid 2010 -fcname R_Posteriorcingulate.dat -fsd Rest -mean -cfg R_Posteriorcingulate.config -overwrite

fcseed-sess -s $subid -cfg L_Posteriorcingulate.config
fcseed-sess -s $subid -cfg R_Posteriorcingulate.config

# fcseed-config -wm -fcname wm.dat -fsd Rest -pca -cfg wm.config
# fcseed-sess -s $subid -cfg wm.config

# fcseed-config -vcsf -fcname vcsf.dat -fsd Rest -pca -cfg vcsf.config
# fcseed-sess -s $subid -cfg vcsf.config

mkanalysis-sess -analysis fc.lpccseed.surf.lh -surface fsaverage lh -fwhm 5 -notask -taskreg L_Posteriorcingulate.dat 1 -nuisreg vcsf.dat 5 \
-nuisreg wm.dat 5 -mcextreg -polyfit 5 -hpf 0 -nskip 4 -fsd Rest -TR 2 -per-run

mkanalysis-sess -analysis fc.lpccseed.surf.rh -surface fsaverage rh -fwhm 5 -notask -taskreg L_Posteriorcingulate.dat 1 -nuisreg vcsf.dat 5 \
-nuisreg wm.dat 5 -mcextreg -polyfit 5 -hpf 0 -nskip 4 -fsd Rest -TR 2 -per-run

mkanalysis-sess -analysis fc.rpccseed.surf.lh -surface fsaverage lh -fwhm 5 -notask -taskreg R_Posteriorcingulate.dat 1 -nuisreg vcsf.dat 5 \
-nuisreg wm.dat 5 -mcextreg -polyfit 5 -hpf 0 -nskip 4 -fsd Rest -TR 2 -per-run

mkanalysis-sess -analysis fc.rpccseed.surf.rh -surface fsaverage rh -fwhm 5 -notask -taskreg R_Posteriorcingulate.dat 1 -nuisreg vcsf.dat 5 \
-nuisreg wm.dat 5 -mcextreg -polyfit 5 -hpf 0 -nskip 4 -fsd Rest -TR 2 -per-run

selxavg3-sess -s $subid -a fc.lpccseed.surf.lh
selxavg3-sess -s $subid -a fc.lpccseed.surf.rh
selxavg3-sess -s $subid -a fc.rpccseed.surf.lh
selxavg3-sess -s $subid -a fc.rpccseed.surf.rh
```

RISA project: Brain age estimation

1. **Construct brain age models using large public datasets**

http://adni.loni.usc.edu/

ADNI
Alzheimer's Disease
Neuroimaging Initiative

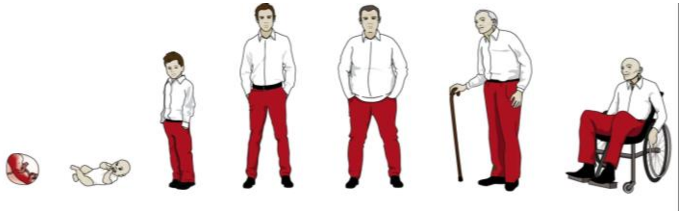
https://www.ukbiobank.ac.uk/

biobank uk
Enabling scientific discoveries that improve human health

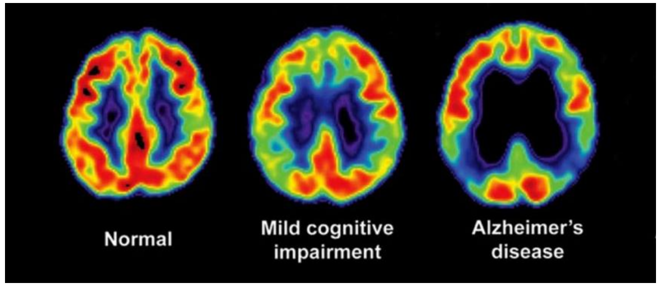
http://www.humanconnectomeproject.org/

Human Connectome Project

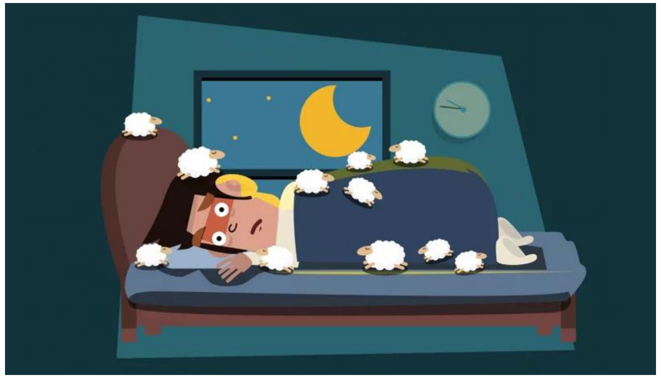
2. **Collect our own data to construct localized brain age models, & test their predictive powers for brain functions & prospective brain changes**



3. **Apply the brain age models in two clinical populations**

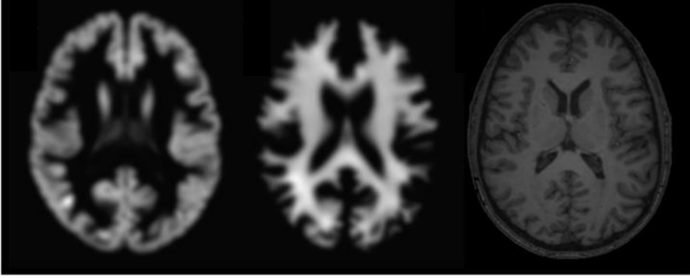


Mild cognitive impairment



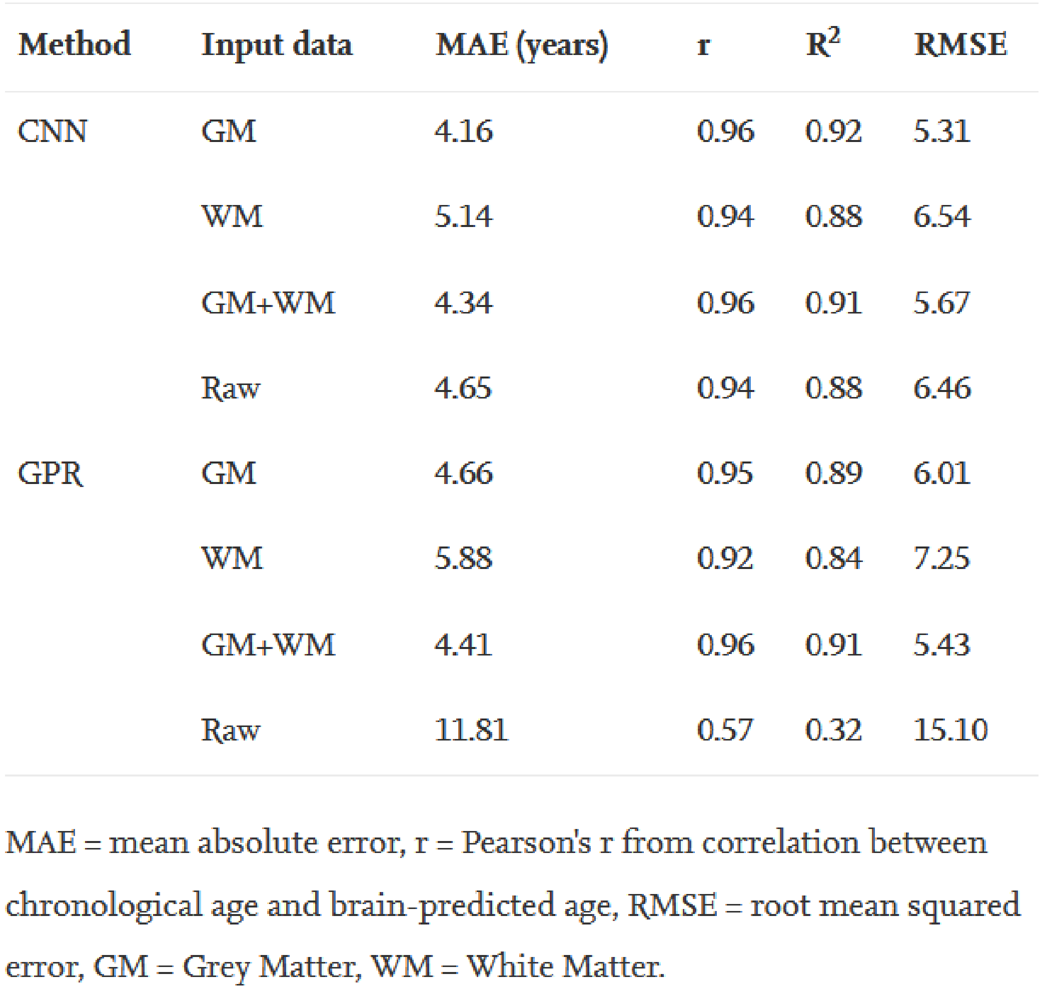
Insomnia disorder

Brain age (structural neuroimaging)



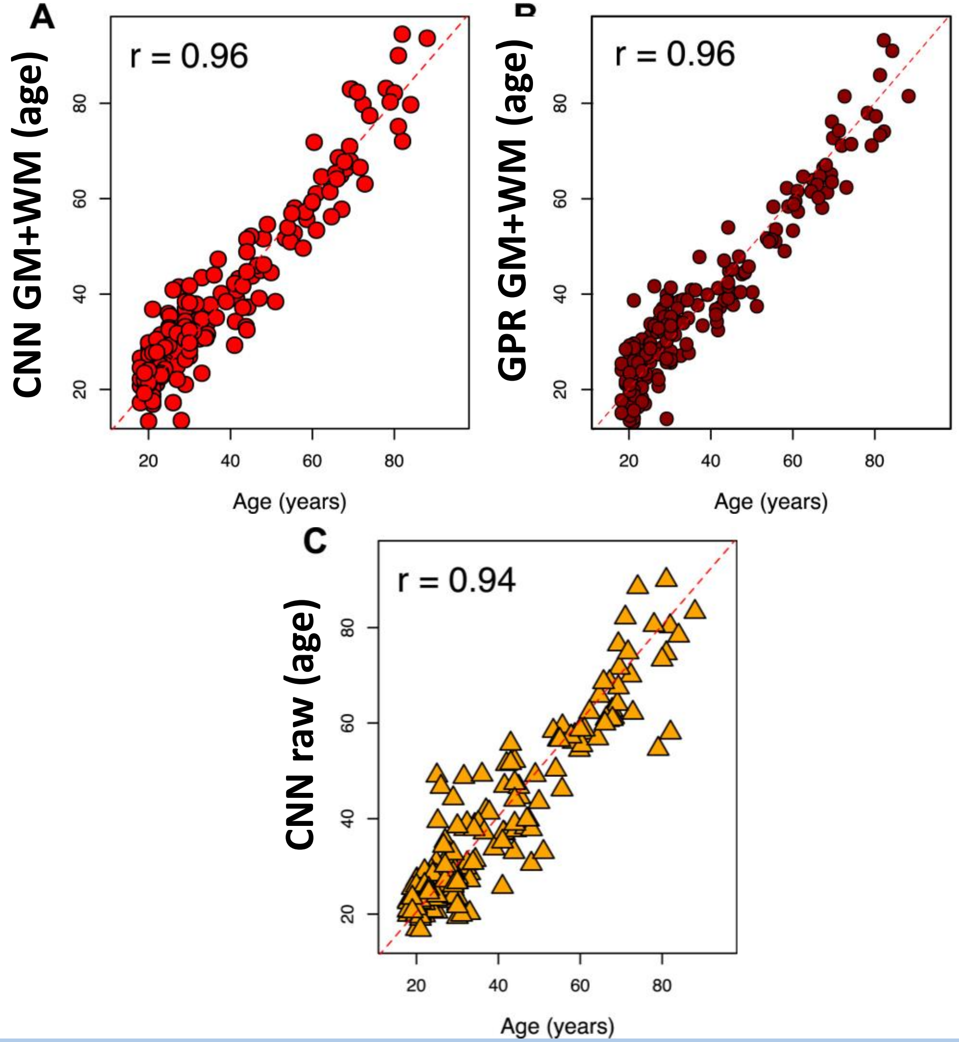
Convolutional neural network

Gaussian Process Regression



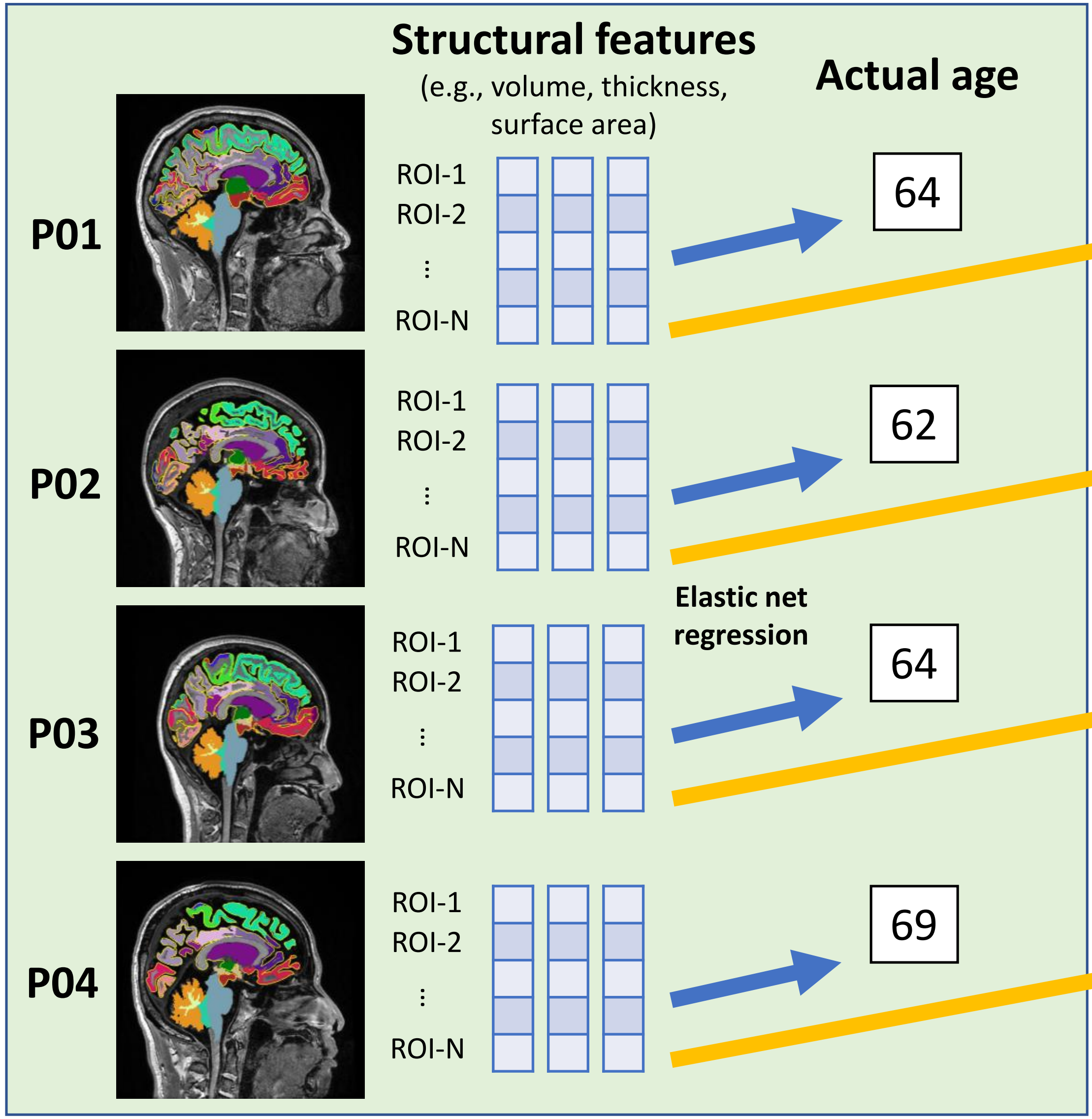
Method	Input data	MAE (years)	r	R^2	RMSE
CNN	GM	4.16	0.96	0.92	5.31
	WM	5.14	0.94	0.88	6.54
	GM+WM	4.34	0.96	0.91	5.67
	Raw	4.65	0.94	0.88	6.46
GPR	GM	4.66	0.95	0.89	6.01
	WM	5.88	0.92	0.84	7.25
	GM+WM	4.41	0.96	0.91	5.43
	Raw	11.81	0.57	0.32	15.10

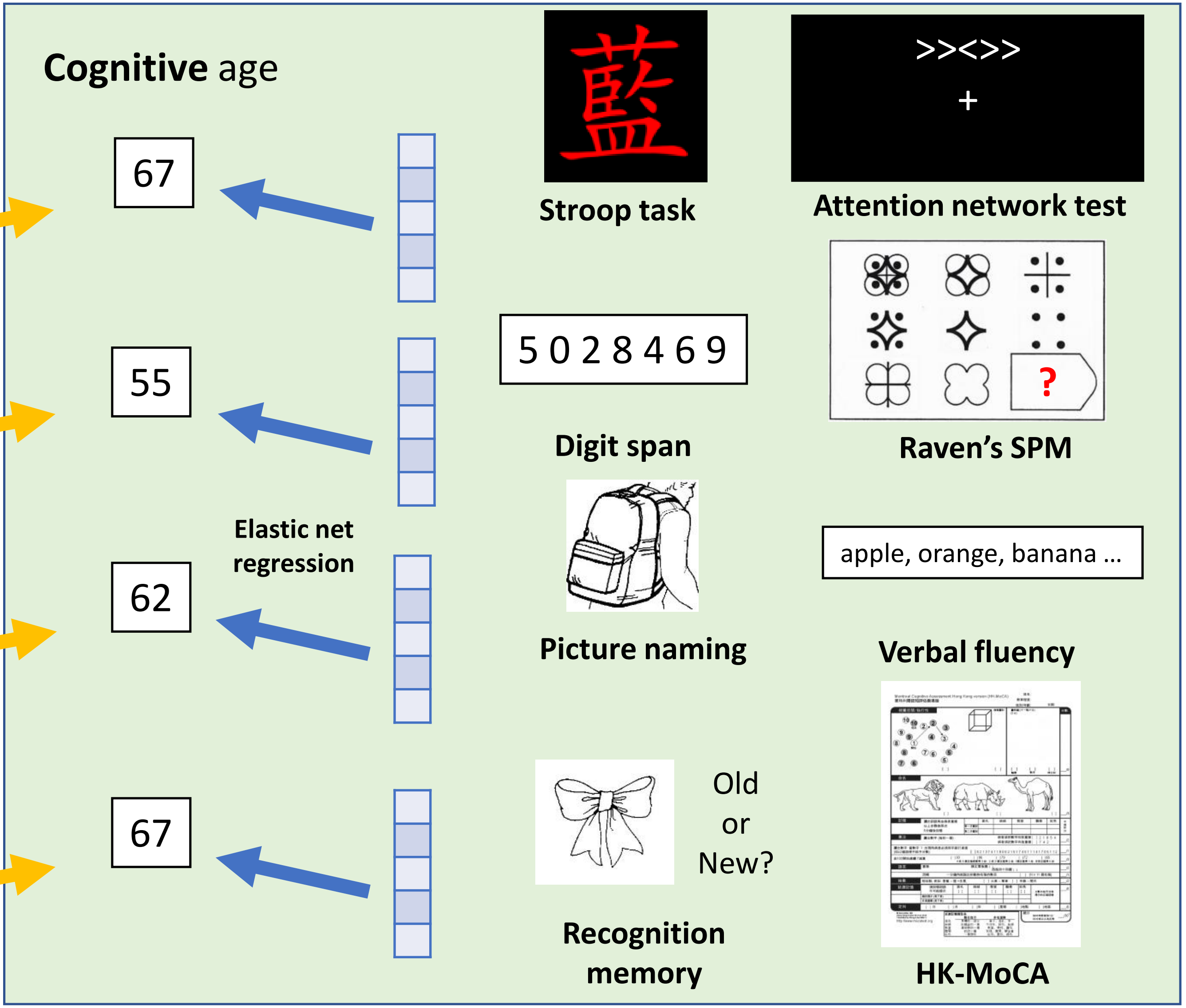
MAE = mean absolute error, r = Pearson's r from correlation between chronological age and brain-predicted age, RMSE = root mean squared error, GM = Grey Matter, WM = White Matter.



Cole et al. (2017). *NeuroImage*.

Aim 1: predicting cognitive age with brain measures

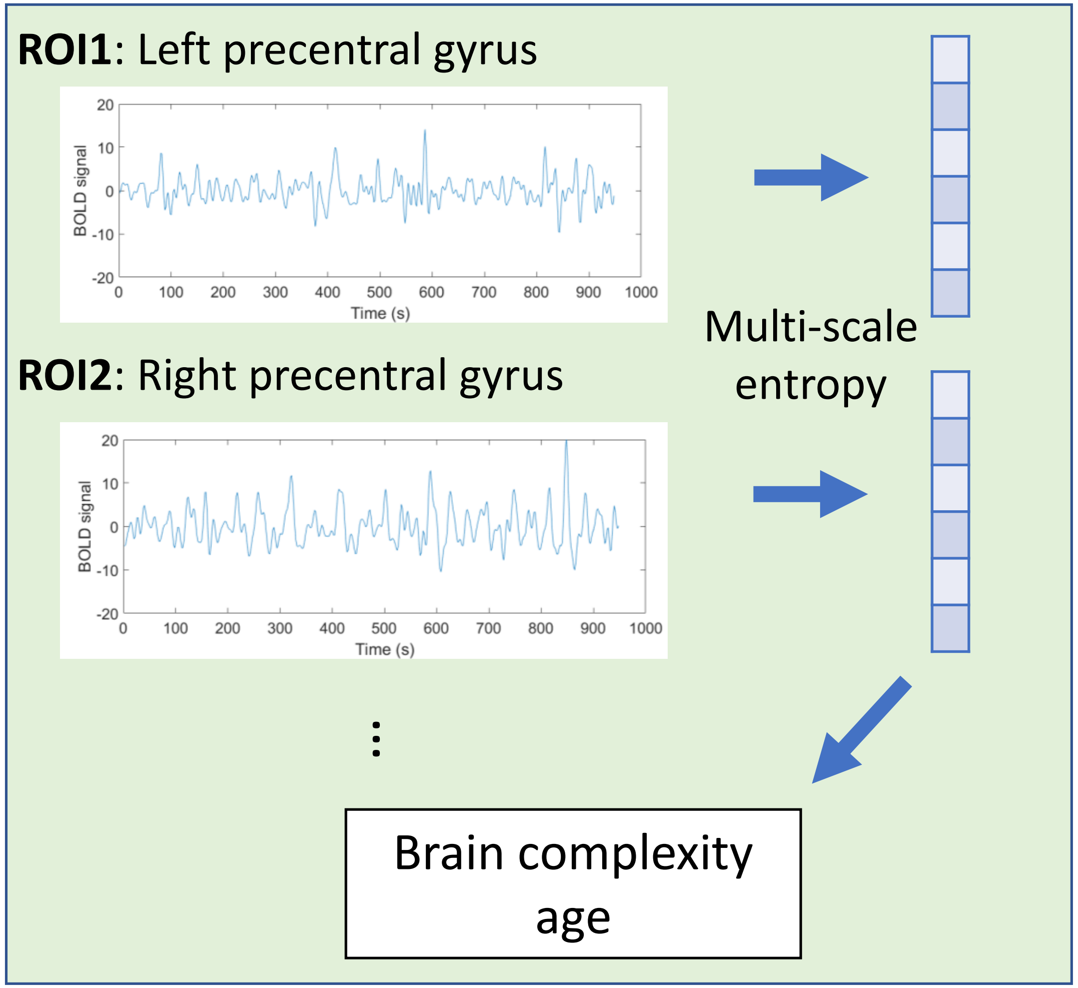




Fong, Hui, Fung, Ma, Law, Wang, & **Wang** (2020). *Quarterly Journal of Experimental Psychology*.
Fong, Law, Ma, Hui, & **Wang** (2021). *Brain and Language*.

Aim 2:

brain complexity age (temporal)



ROI1: Left precentral gyrus

ROI2: Right precentral gyrus

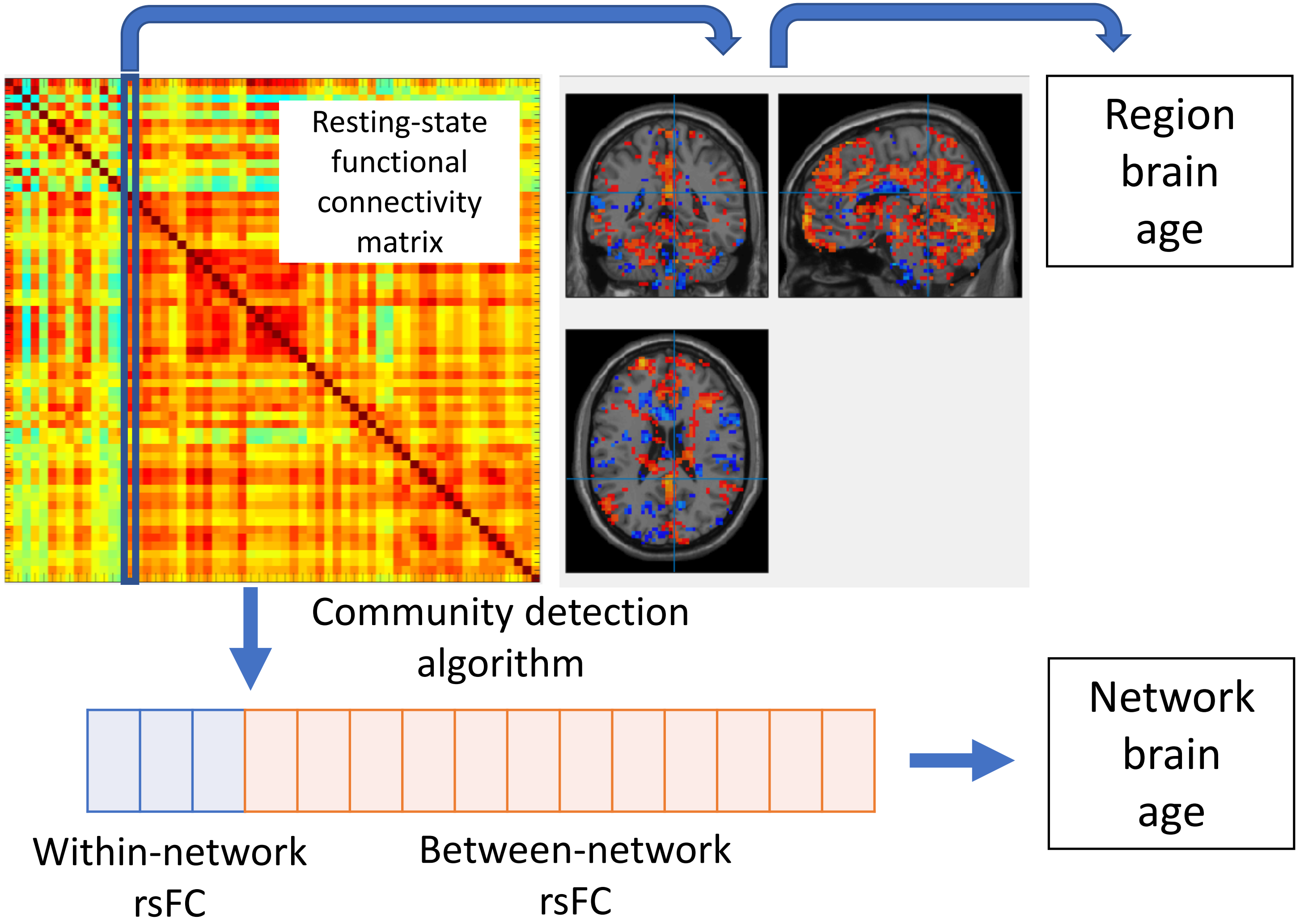
Multi-scale entropy

⋮

Brain complexity age

Aim 3:

region & network brain age (spatial)



Resting-state functional connectivity matrix

Region brain age

Community detection algorithm

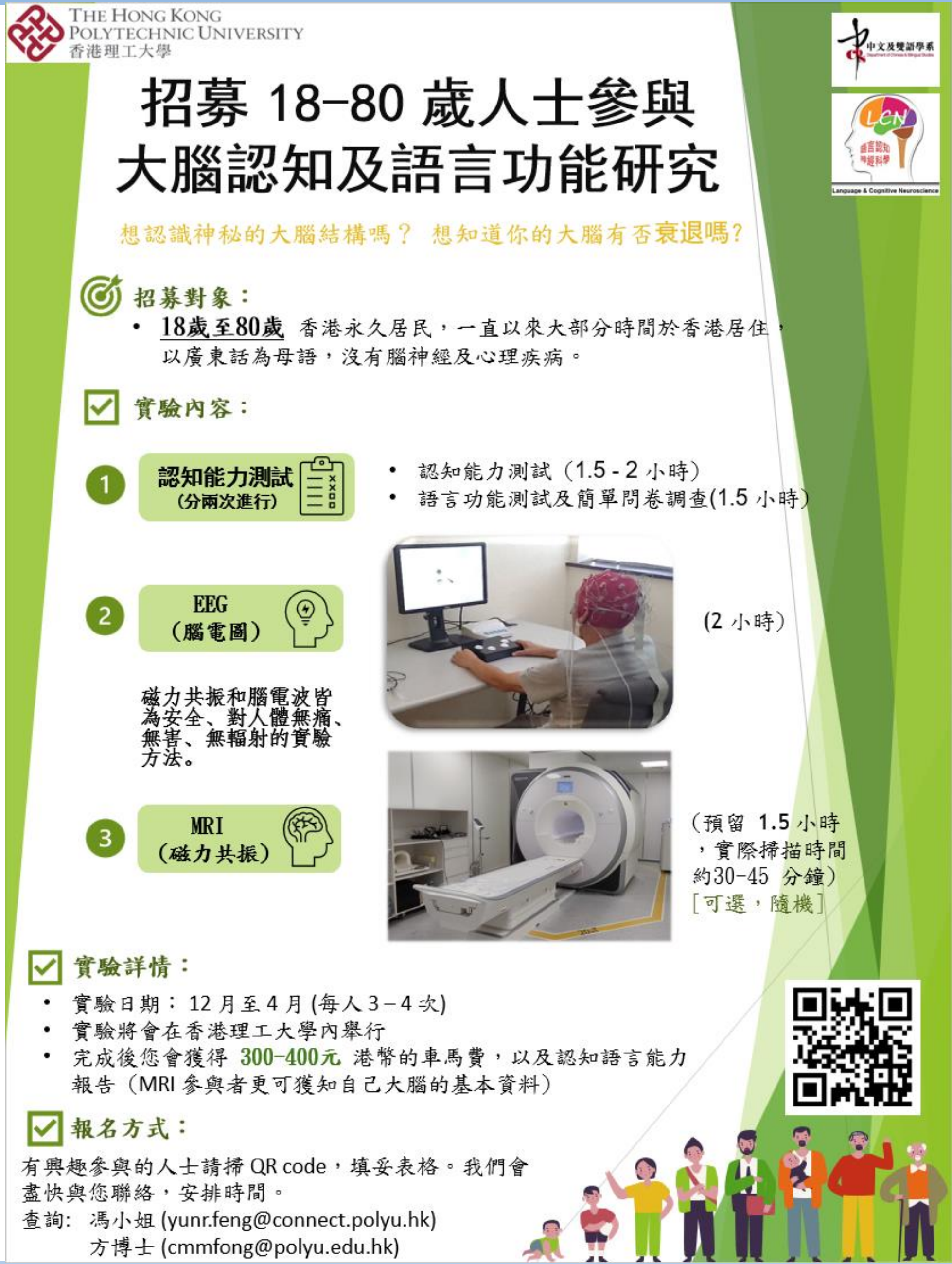
Within-network rsFC

Between-network rsFC

Network brain age

Ongoing experiments

Functional Connectome of Semantic Processing



THE HONG KONG
POLYTECHNIC UNIVERSITY
香港理工大學

招募 18–80 歲人士參與
大腦認知及語言功能研究

想認識神秘的大腦結構嗎？ 想知道你的大腦有否衰退嗎?

招募對象：

- **18歲至80歲** 香港永久居民，一直以來大部分時間於香港居住，以廣東話為母語，沒有腦神經及心理疾病。

實驗內容：

① **認知能力測試**
(分兩次進行)

- 認知能力測試（1.5 - 2 小時）
- 語言功能測試及簡單問卷調查(1.5 小時）

② **EEG**
（腦電圖）

(2 小時）

磁力共振和腦電波皆為安全、對人體無痛、無害、無輻射的實驗方法。

③ **MRI**
（磁力共振）

（預留 1.5 小時，實際掃描時間約30-45 分鐘）
［可選，隨機］

實驗詳情：

- 實驗日期：12 月至 4 月 (每人 3 – 4 次)
- 實驗將會在香港理工大學內舉行
- 完成後您會獲得 **300-400元** 港幣的車馬費，以及認知語言能力報告（MRI 參與者更可獲知自己大腦的基本資料）

報名方式：

有興趣參與的人士請掃 QR code，填妥表格。我們會盡快與您聯絡，安排時間。

查詢: 馮小姐 (yunr.feng@connect.polyu.hk)
方博士 (cmmfong@polyu.edu.hk)

Acknowledgment

- HKRGC-GRF 15601718 & 15606119 awarded to Prof. William SY Wang (CBS)
- Research Institute for Smart Aging (RISA)
- University facility for Big Data Analytics (UBDA)
- University facility for Behavioral and Systems Neuroscience (UBSN)
- Prof. William SY Wang & other team members

References

- Bajaj, S., Alkozei, A., Dailey, N. S., & Killgore, W. D. (2017). Brain aging: uncovering cortical characteristics of healthy aging in young adults. *Frontiers in Aging Neuroscience*, *9*, 412.
- Biswal, B., Zerrin Yetkin, F., Haughton, V. M., & Hyde, J. S. (1995). Functional connectivity in the motor cortex of resting human brain using echo‐planar MRI. *Magnetic Resonance in Medicine*, *34*(4), 537-541.
- Cole, J. H., Poudel, R. P., Tsagkrasoulis, D., Caan, M. W., Steves, C., Spector, T. D., & Montana, G. (2017). Predicting brain age with deep learning from raw imaging data results in a reliable and heritable biomarker. *NeuroImage, 163*, 115-124.
- Coupé, P., Catheline, G., Lanuza, E., Manjón, J. V., & Alzheimer's Disease Neuroimaging Initiative. (2017). Towards a unified analysis of brain maturation and aging across the entire lifespan: A MRI analysis. *Human Brain Mapping*, *38*(11), 5501-5518.
- Fong, M. C-M., …, Wang, W. S. (2020). Which cognitive functions subserve clustering and switching in category fluency? Generalisations from an extended set of semantic categories using linear mixed-effects modelling. *Quarterly Journal of Experimental Psychology, 73*(12), 2132-2147.

References

- Fong, M. C. M., Law, T. S. T., Ma, M. K. H., Hui, N. Y., & Wang, W. S. (2021). Can inhibition deficit hypothesis account for age-related differences in semantic fluency? Converging evidence from Stroop color and word test and an ERP flanker task. *Brain and Language*, *218*, 104952.
- Fong, Ma, Chui, Law, Hui, Au, & Wang. (Under review). Foreign language learning in older adults: anatomical and cognitive markers of vocabulary learning success.
- Fjell, A. M., McEvoy, L., Holland, D., Dale, A. M., Walhovd, K. B., & Alzheimer's Disease Neuroimaging Initiative. (2014). What is normal in normal aging? Effects of aging, amyloid and Alzheimer's disease on the cerebral cortex and the hippocampus. *Progress in Neurobiology*, *117*, 20-40.
- Ma, M. K. H., Fong, M. C. M., Xie, C., Lee, T., Chen, G., & Wang, W. S. (2021). Regularity and randomness in ageing: Differences in resting-state EEG complexity measured by largest Lyapunov exponent. *Neuroimage: Reports*, *1*(4), 100054.
- Walhovd, K. B., Wfoestlye, L. T., Amlien, I., Espeseth, T., Reinvang, I., Raz, N., ... & Dale, A. M. (2011). Consistent neuroanatomical age-related volume differences across multiple samples. *Neurobiology of Aging*, *32*(5), 916-932.

Happy Winter Solstice!
&
Merry Christmas!