東北大学応用認知神経科学センター

fMRI解析の参考資料
(6) Resting-state fMRI原理とDPABI 解析: Functional Connectivity, FC

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Resting-state fMRIとは

- **Resting-State fMRI の定義**
- 被験者が特定の課題を行わず、安静にしている状態（閉眼または開眼安静）で fMRI データを取得する手法

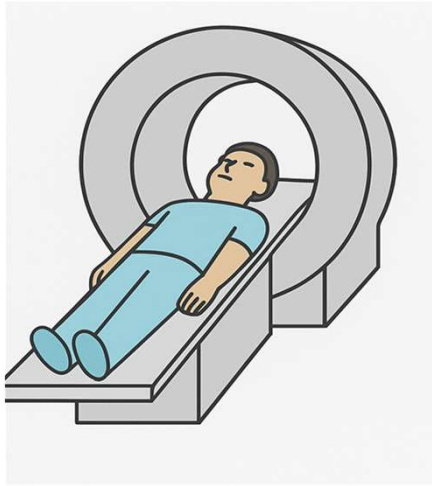
An fMRI technique where data are acquired while the subject is at rest (eyes open or closed), without performing any explicit task.

- BOLD信号の低周波変動（0.01–0.08 Hz）を解析し、脳領域間の**自発的な活動**同期性を評価

Analyzes low-frequency fluctuations (0.01–0.08 Hz) in the BOLD signal to assess spontaneous synchrony between brain regions.

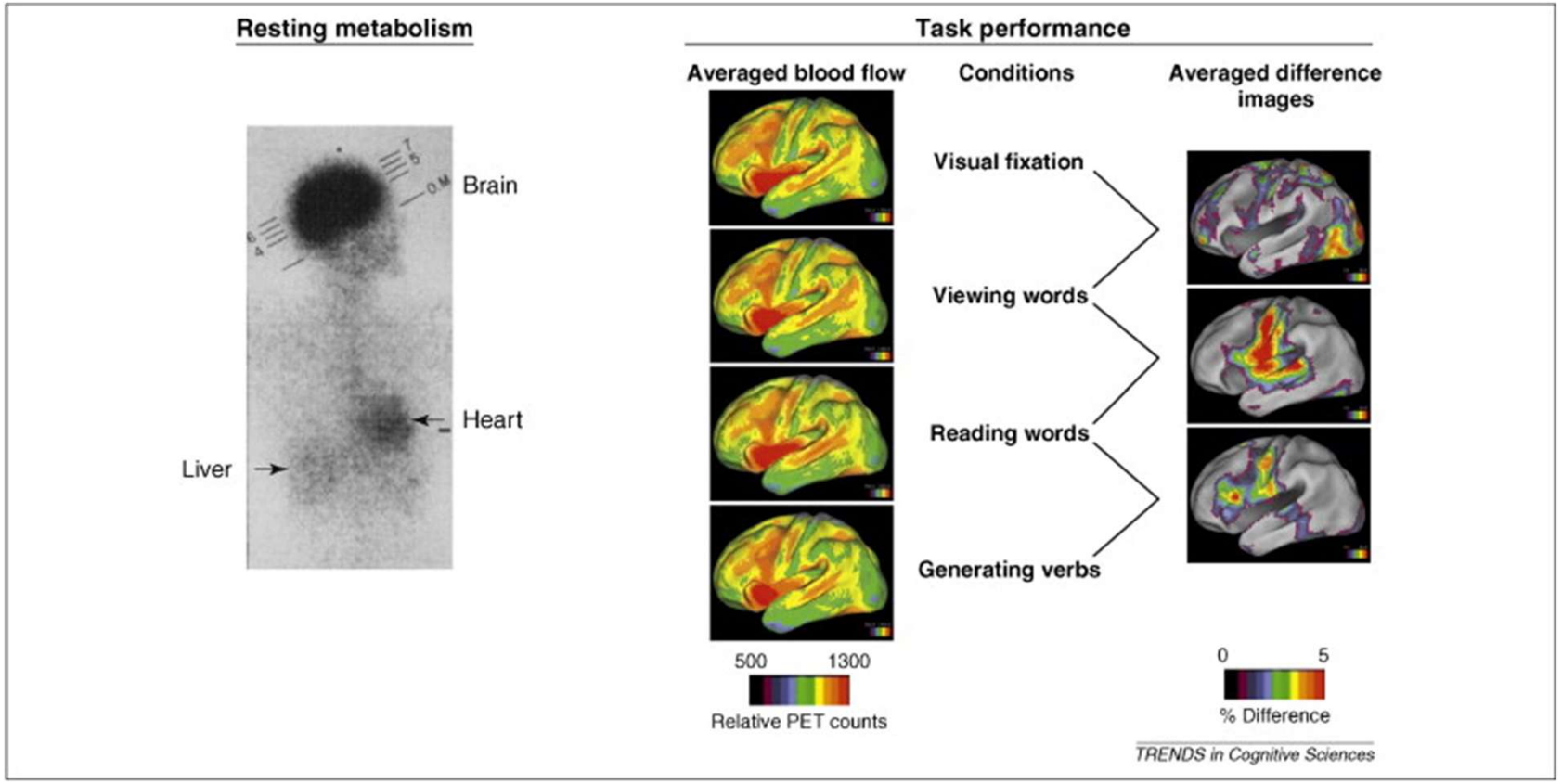
- 主に機能的結合（Functional Connectivity）の解析に用いられる

Primarily used for Functional Connectivity analysis.



Task-based fMRI との比較

The brain is not primarily reflexive



The blood flow changes during a task are usually less than 5% of the brain's resting blood flow.

課題を行っているときの脳血流の変化は、安静時の脳血流の5%未満であることが多い。

Raichle et al., 2010. Trends Cogn Sci

Task-based fMRI との比較

Resting-State fMRI

- 安静時（課題なし）
- 基盤的ネットワーク
- 簡便、臨床向き、大規模研究可
- 認知過程の特定が難しい
- Rest (no task)
- Intrinsic brain networks
- Simple, suitable for clinical use, and feasible for large-scale studies
- Difficult to identify specific cognitive processes

Task-based fMRI

- 課題遂行中（刺激提示あり）
- 特定機能に関連する脳活動
- 認知過程の特定が容易
- 課題設計が必要、負担大、臨床や大規模研究にはやや不向き
- Task performance (with stimuli)
- Brain activation related to specific functions
- Easy to identify specific cognitive processes
- Requires task design, higher participant burden, less suitable for clinical or large-scale studies

Resting-State fMRIという概念の誕生(1995)

■ **背景**：

当時のfMRI研究はほとんどが課題遂行時の脳活動に焦点

Most fMRI studies at the time focused on task-induced brain activity

しかし、安静時でも脳は自発的活動をしているのではないかと着目

■ **研究方法**：

EPI法を用い、安静状態での一次運動皮質のBOLD信号を計測

Measured BOLD signals in the primary motor cortex during rest using EPI

種領域（seed）を設定し、他領域とのBOLD信号の時間相関を解析

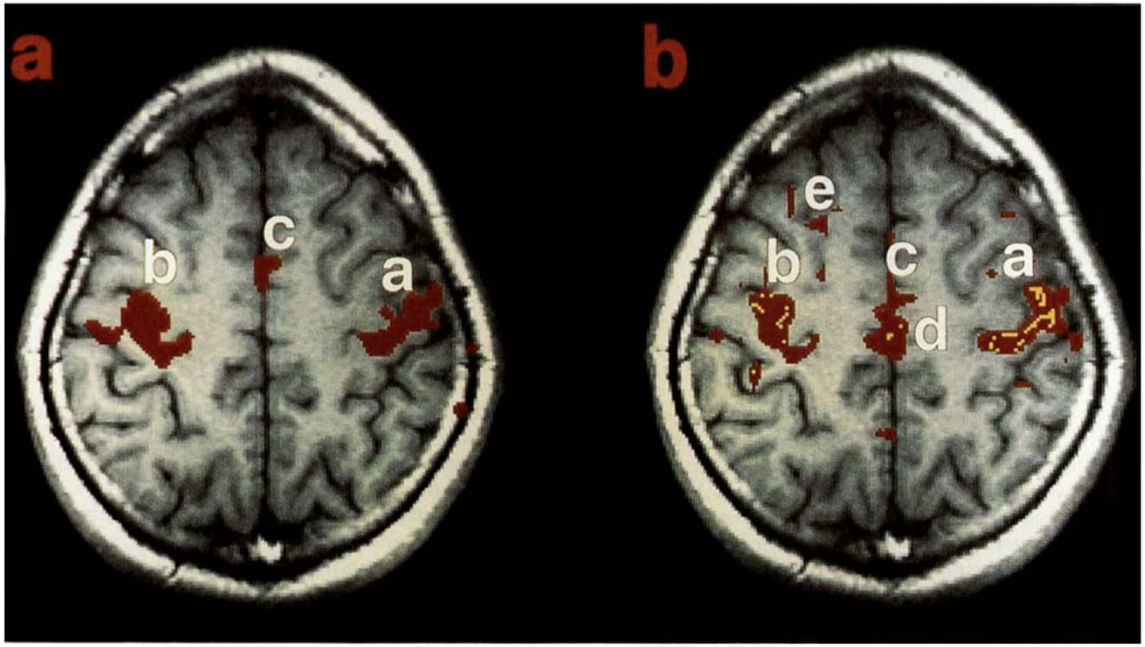


FIG. 3. (Left) FMRI task-activation response to bilateral left and right finger movement, superimposed on a GRASS anatomic image. (Right) Fluctuation response using the methods of this paper. See text for assignment of labeled regions. Red is positive correlation, and yellow is negative.

■ **主要発見**：

- **Significant temporal correlation between left and right motor cortices at rest**
- **Brain networks remain active without tasks**

- 安静時でも両側の運動皮質に有意な時間相関（機能的結合）が存在
- 脳は課題がなくてもネットワーク活動を維持している

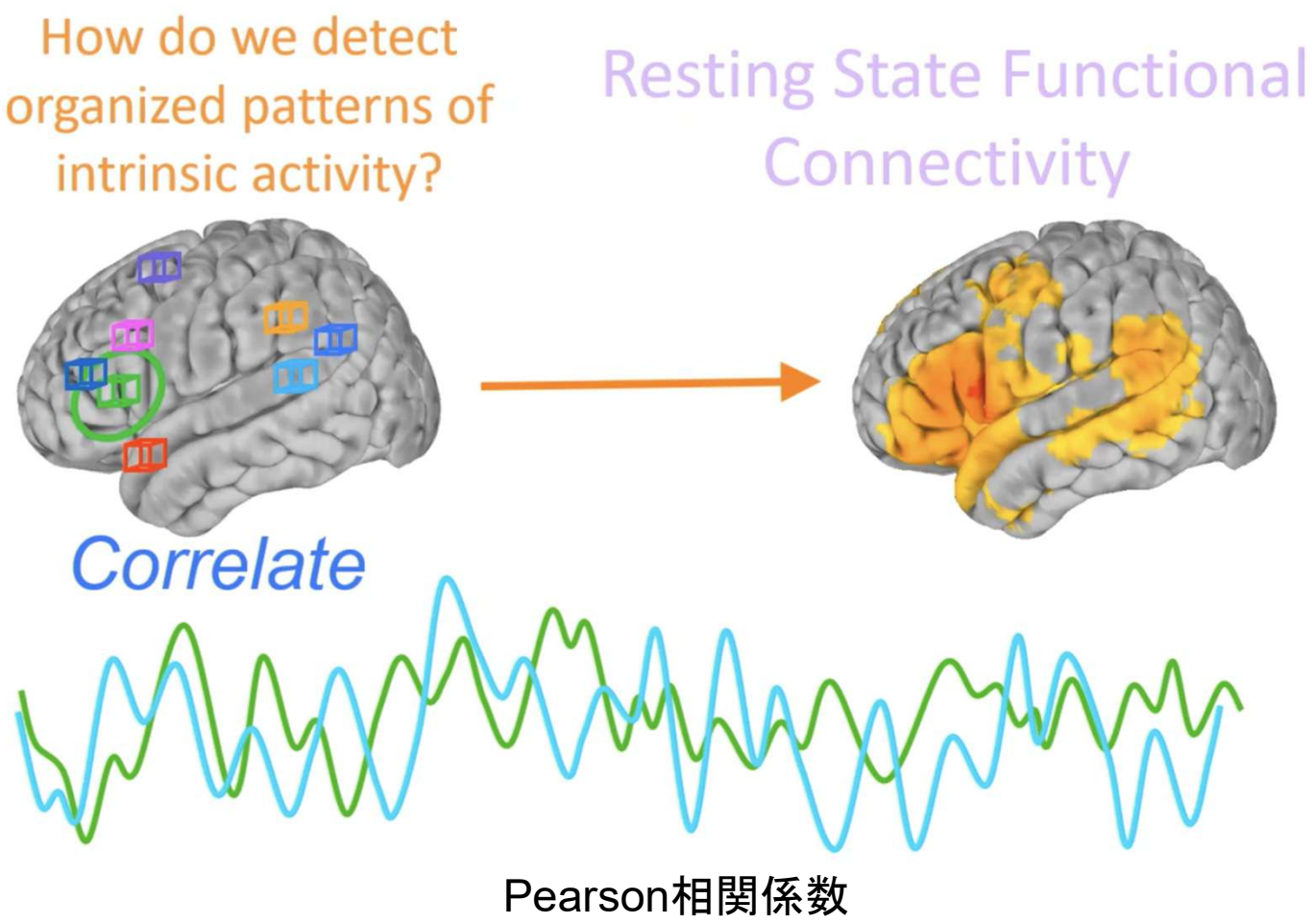
Biswal et. al., 1995. Magn Reson Med

Resting-state fMRI解析方法：機能的結合（Functional Connectivity）

- 定義:

異なる脳領域間のBOLD信号の時間的相関を測定し、脳内ネットワークの協調的活動を明らかにする手法。

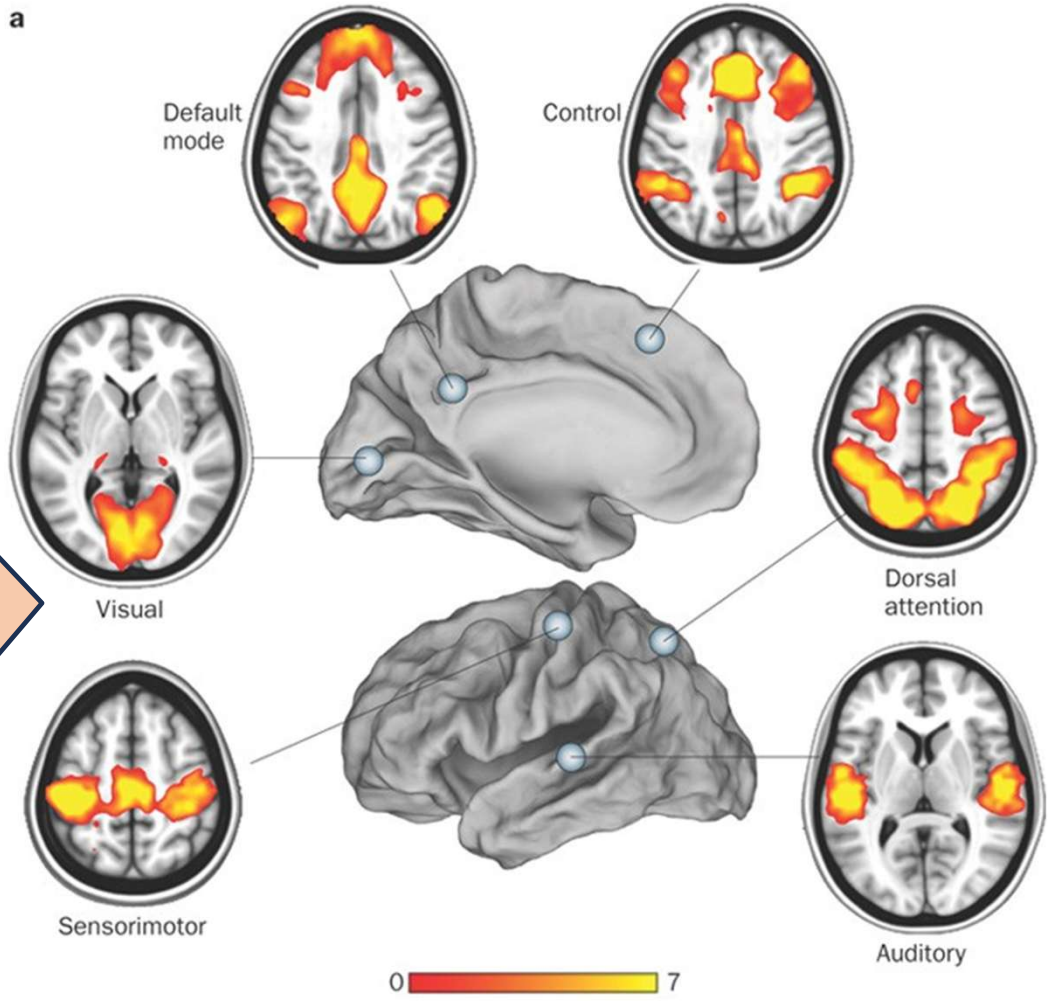
A measure of temporal correlation between BOLD signals in different brain regions, revealing coordinated activity within brain networks.



Seed-based Functional Connectivity（種領域解析）

- ROIを設定し、他領域とのBOLD信号相関を計算
- *Set a seed ROI, compute correlations with other brain regions*
- 主要な静止時脳ネットワーク
- Major Resting-State Brain Networks

- 種領域と脳全体の活動を比較して、類似した活動を持つ領域のマップを作成
- 視覚、感覚運動、聴覚、デフォルトモード、背側注意、実行制御
- Six major networks: visual, sensorimotor, auditory, default mode, dorsal attention, executive control.



Zhang and Raichle, 2010. Nat Rev Neurol

主な研究応用 / Main Applications

- 臨床研究 / Clinical research：うつ病における脳ネットワーク異常の検出

治療効果評価 / Treatment outcome assessment：抗うつ薬治療や心理療法（CBT等）前後のネットワーク変化を追跡

- 基礎神経科学 / Basic neuroscience

情動調節ネットワーク（DMN、Salience Network、ECN）の役割解明
Understanding the roles of emotional regulation networks (DMN, SN, ECN)

Question
脳画像学的バイオマーカーで診断や薬物選択を指導できるか？

Can neuroimaging biomarkers guide diagnosis and medication?

初診：うつ病
Initial diagnosis: Depression
↓
A薬を服用 → 自殺念慮出現
Took medication A → developed suicidal thoughts
↓
B薬に変更 → 躁転
Switched to medication B → switched to mania
↓
確定診断：双極性障害
Confirmed diagnosis: Bipolar disorder
↓
C薬に変更 → 病状悪化
Switched to medication C → condition worsened

抑うつ症におけるDMN機能的結合の大規模解析（REST-meta-MDD）

- 背景 / Background

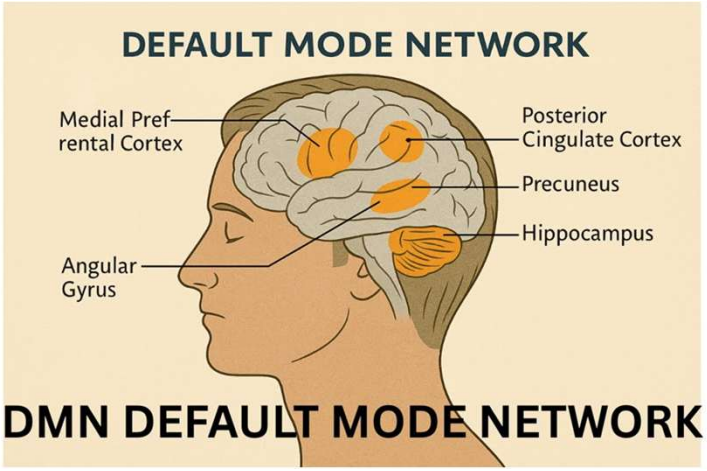
DMNの役割：自己関連思考、内省、記憶検索に関与

これまでのMDD研究ではDMN機能的結合（FC）が異常との報告多数も、小規模研究や解析手法の違いで結果が不一致

Role of DMN: Involved in self-referential thinking, introspection, and memory retrieval

Prior MDD studies reported abnormal DMN functional connectivity (FC), but results inconsistent due to small sample sizes and varied methodologies

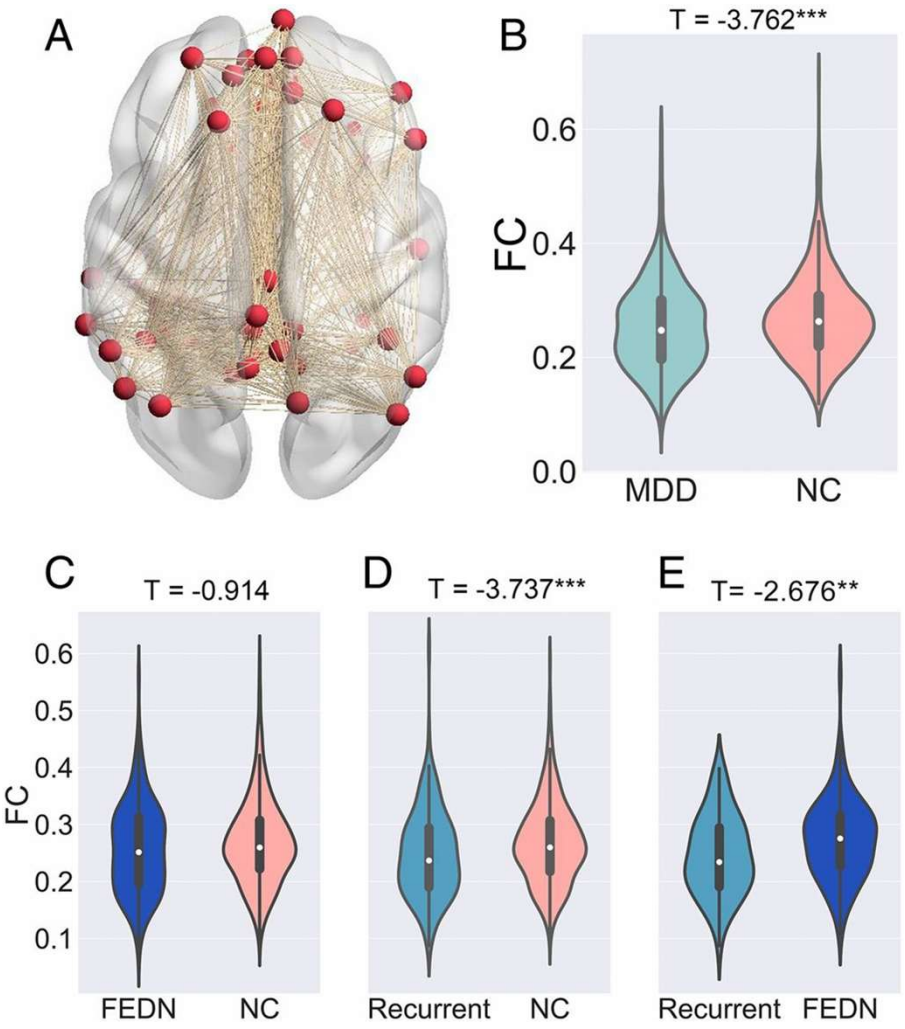
- 1,300 MDD patients / 患者
- 1,128 healthy controls / 健常対照



yan, et al., 2019. pnas

主な結果 / Key Findings

- MDD群でDMN内FCが低下
- 減少は再発性MDDのみで観察（初発・薬物未使用群では変化なし）
- FC減少は薬物使用と関連、罹病期間とは無関係
- 再発性MDDでは症状重症度と正の相関
- Decreased DMN FC in MDD compared to controls
- Reduction found only in recurrent MDD (no change in first-episode drug-naïve MDD)
- FC reduction associated with medication use, not illness duration
- In recurrent MDD, DMN FC positively correlated with symptom severity



yan, et al., 2019. pnas

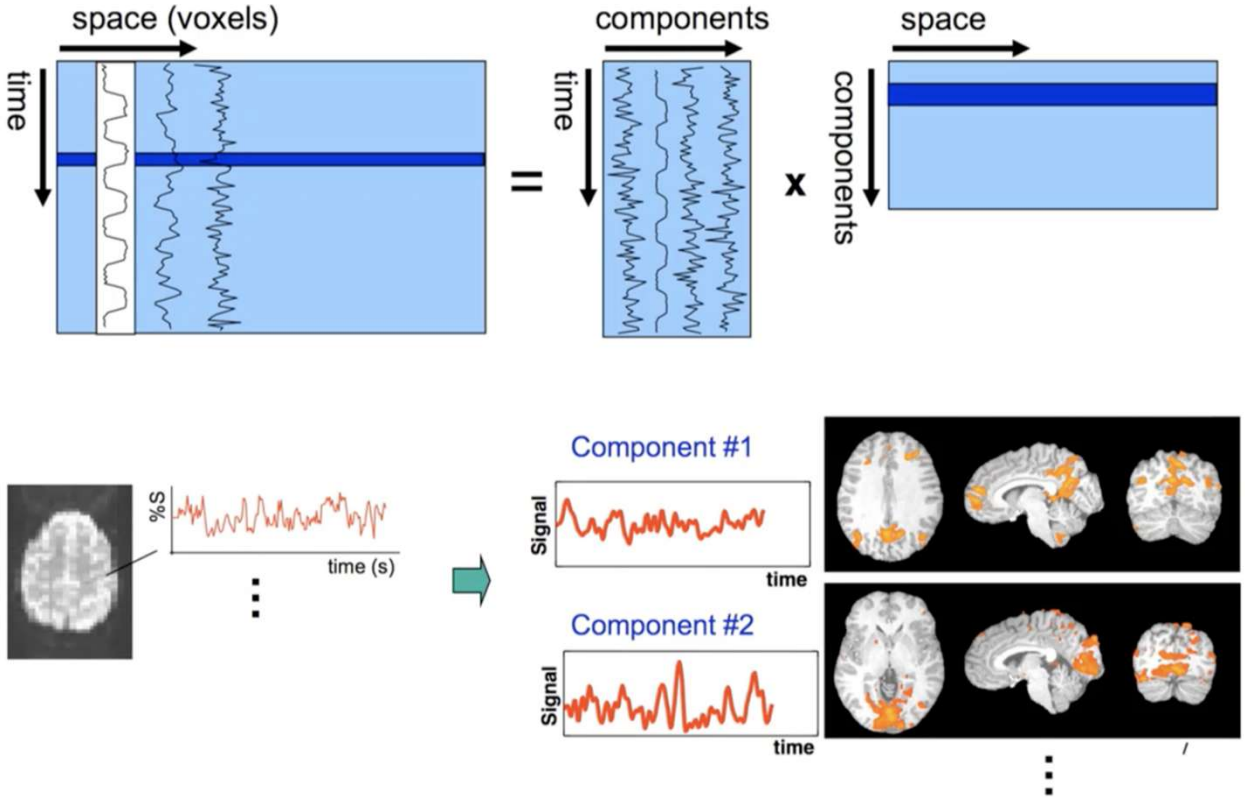
Resting-state fMRI解析方法：その他の解析方法

Independent Component Analysis (ICA)

脳全体の信号を統計的に分離し、独立した時空間パターン（成分）を抽出。

特徴：ROIを事前設定せず自動的にネットワークを抽出。

応用：DMNや感覚運動ネットワークの同定、疾患に伴うネットワーク変化評価。



Separates whole-brain signals into statistically independent spatiotemporal components.

Feature: Extracts networks automatically without predefined ROIs.

Application: Identify DMN, sensorimotor networks, and assess network changes in disorders.

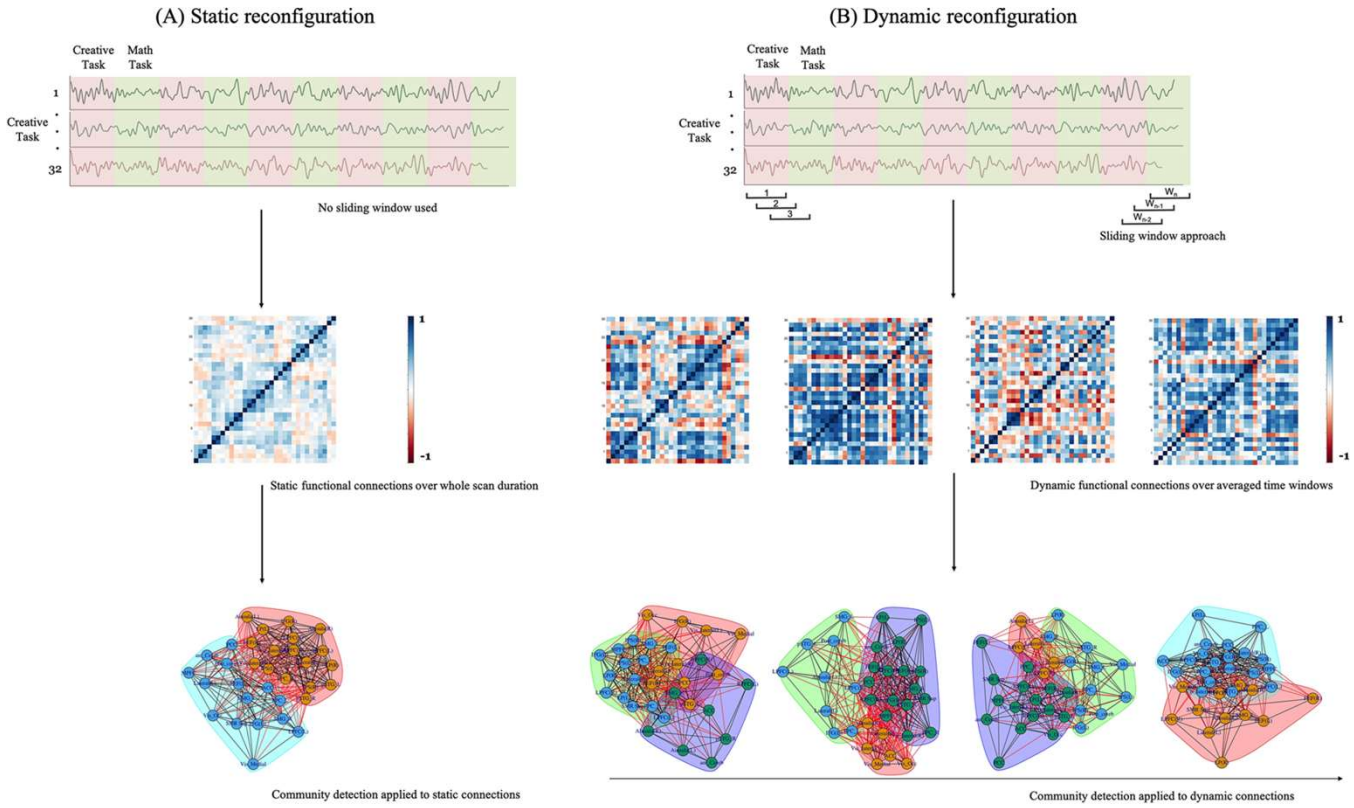
Resting-state fMRI解析方法：その他の解析方法

Dynamic Functional Connectivity (dFC)

スライディングウィンドウで時間を分割し、機能的結合の時間変動を解析。

特徴：ネットワークの動的変化を捉える。

研究例：統合失調症患者でDMNと前頭葉ネットワーク間の結合が時間的に不安定であることを発見（症状変動と関連）



Uses a sliding-window approach to analyze time-varying changes in functional connectivity.

Feature: Captures dynamic changes in networks.

Example: In schizophrenia, dFC analysis revealed unstable connectivity between the DMN and frontal networks, associated with symptom fluctuations.

Patil, A. U, et al., 2021. Scientific report

Resting-state fMRI 解析
DPABI 解析: **Functional Connectivity, FC**

DPABIとは

- 概要：MATLAB + SPM をベースにした GUI ツール
- 特徴：

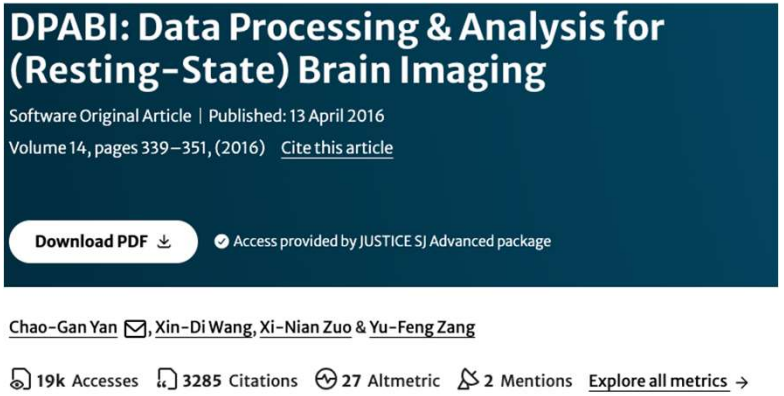
直感的なインターフェース

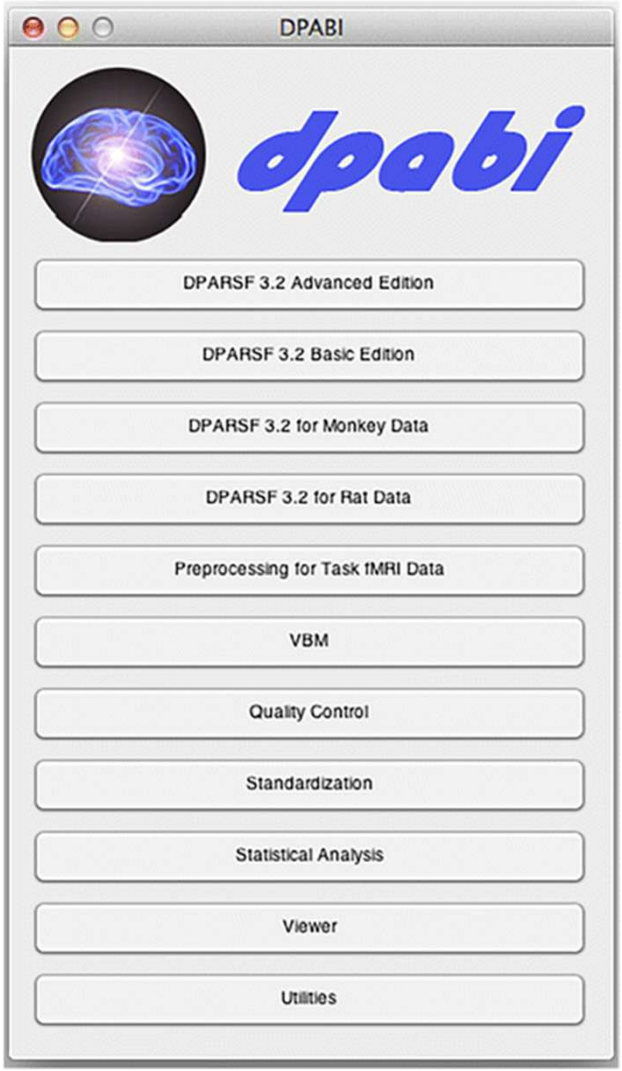
Resting-state fMRI解析に特化

大規模データのバッチ処理が可能

依存環境：MATLAB, SPM

主なモジュール：Processing, Viewer, Statistical Analysis





GUI-based toolbox built on MATLAB and SPM

Features:

Intuitive interface

Specialized for resting-state fMRI analysis

Supports batch processing for large datasets

Dependencies: MATLAB, SPM

Main modules: Processing, Viewer, Statistical Analysis

DPABI解析全体フロー / DPABI Analysis Overview

- データ準備（DICOMファイル → NIfTI形式に変換）
- 前処理（時系列補正、運動補正、正規化、平滑化など）
- 品質管理（QC）（頭動チェック、正規化確認）
- 統計解析（機能的結合、ALFF、ReHoなど指標計算）
- 多重比較補正（FDR、GRF、Permutation Test）
- 結果可視化（脳画像・ネットワーク表示）

- Data preparation (convert DICOM files to 4D NIfTI format)
- Preprocessing (slice timing, motion correction, normalization, smoothing, etc.)
- Quality control (QC) (check head motion, normalization quality)
- Statistical analysis (FC, ALFF, ReHo, etc.)
- Multiple comparison correction (FDR, GRF, permutation test)
- Result visualization

前処理の流れ / Preprocessing Workflow

Resting State fMRI Data Processing

Slice Timing

Realign

Nuisance Regression

Normalize

Smooth

ALFF/fALFF

→ Filter →

FC (SCA)

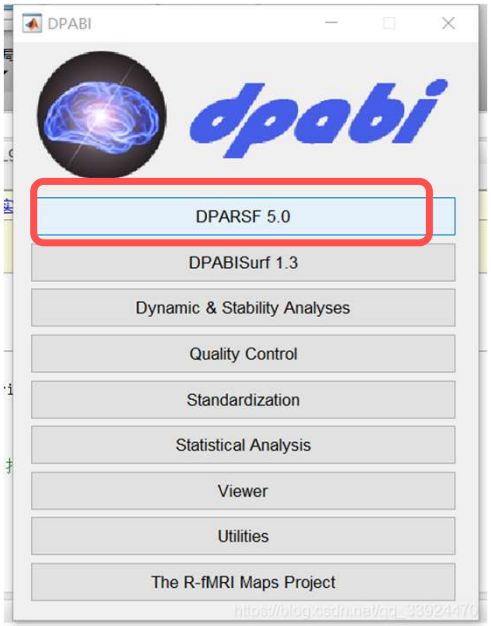
ReHo

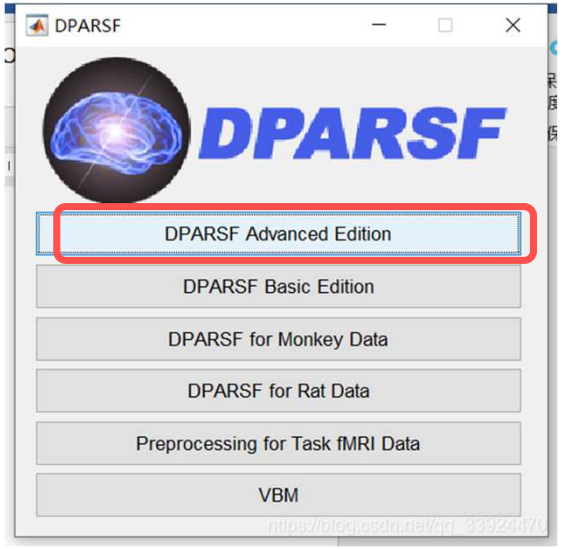
Degree

VMHC

...

Calculate in MNI Space: alternative order





データフォーマット整理/ Data Format Preparation

ProcessingDemoData.zip

FunImg

Sub_001
Sub_002
Sub_003

Functional NIfTI data (.nii.gz., .nii or .img)

T1Img

Sub_001
Sub_002
Sub_003

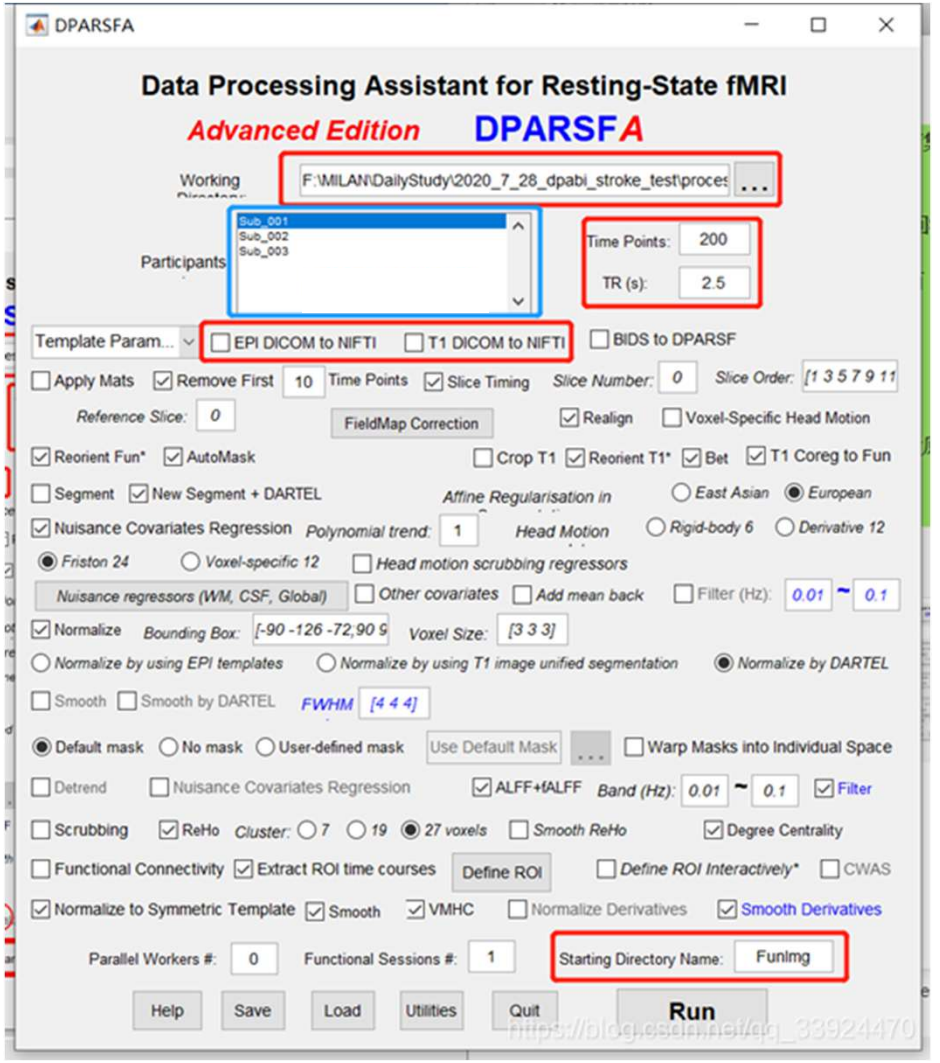
Structural NIfTI data (.nii.gz., .nii or .img)

Select Main Directory
Choose the folder that contains both **FunImg** (functional) and **T1Img** (structural) data.

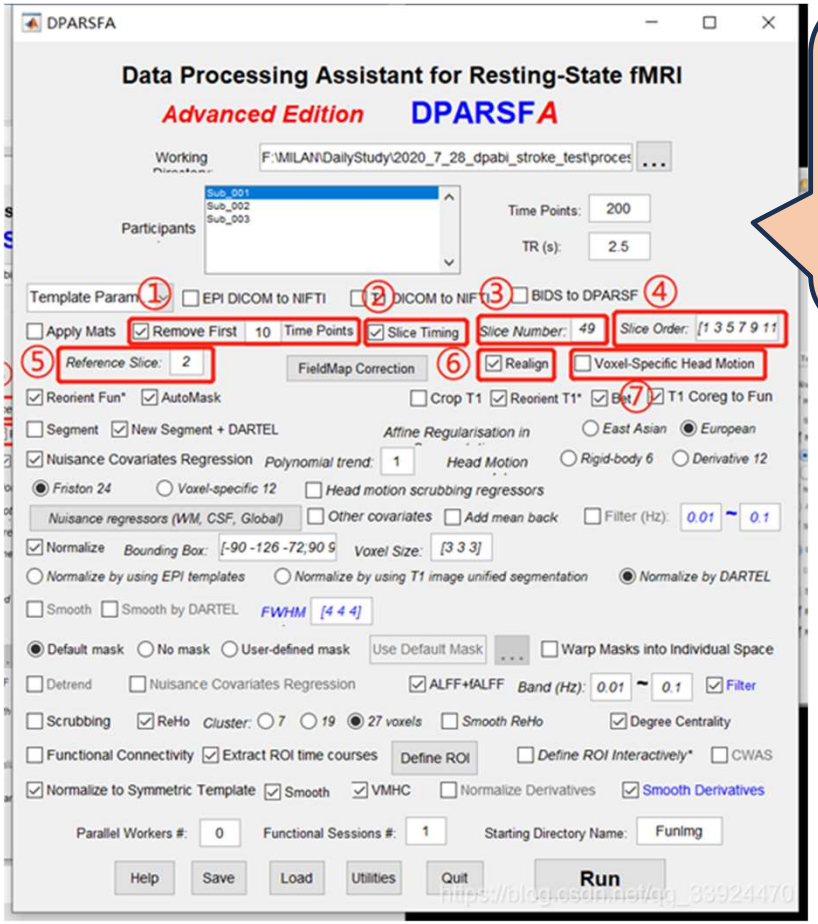
Enter Time Point and TR
Time Point: Number of fMRI volumes.
TR: Repetition time in seconds.

DICOM or NIfTI Selection
Check the box if input data are **DICOM**.
Uncheck if input data are **NIfTI (.nii)**.

Starting Directory Name
For **DICOM**: leave as default (**FunRaw**).
For **NIfTI**: change to **FunImg**, press Enter, skip any prompts that appear.

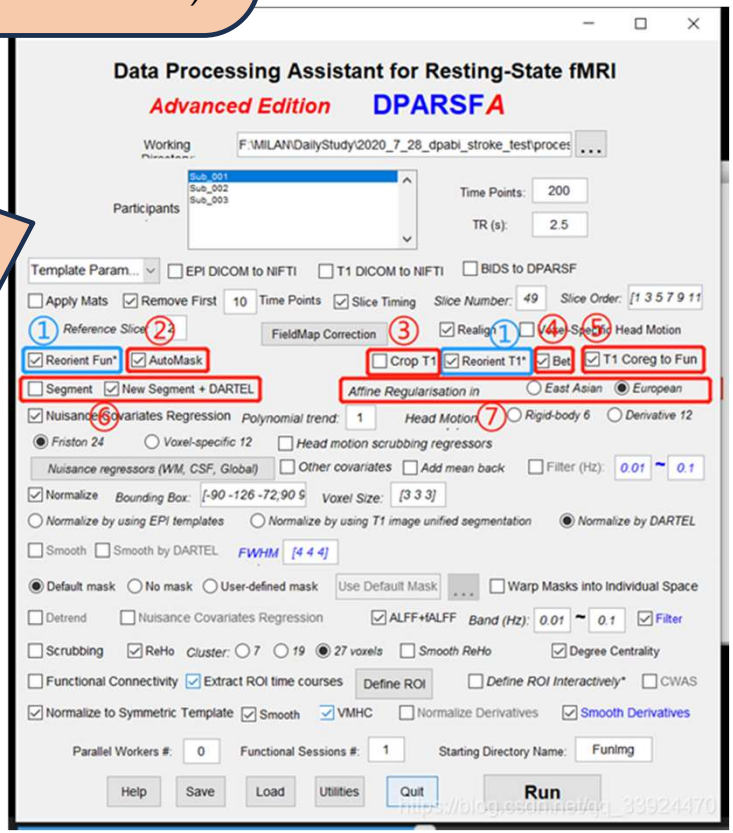


一括前処理（ワンクリック） / One-Click Preprocessing

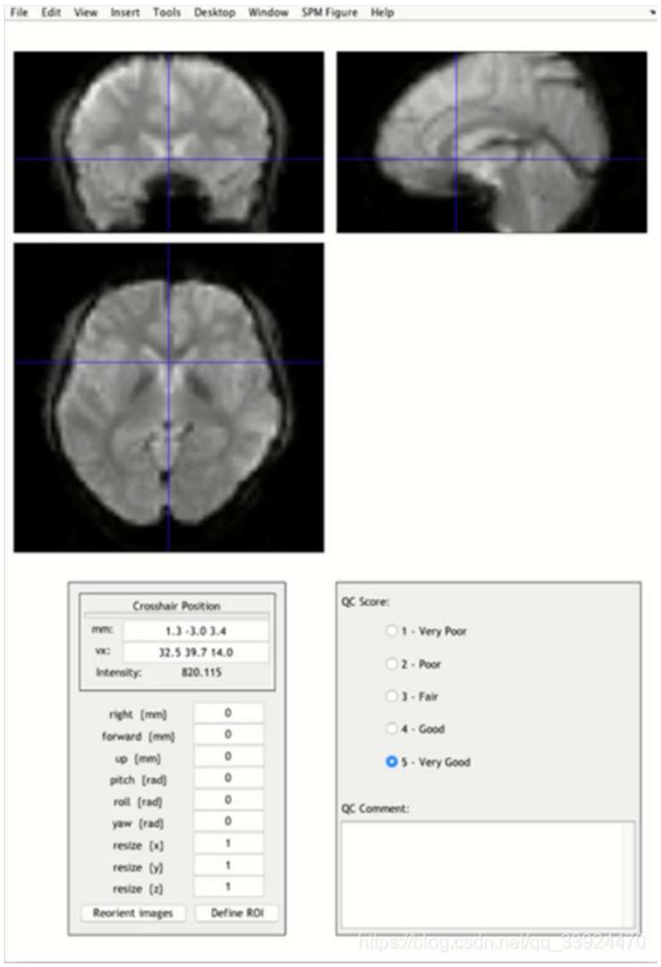


1. **Remove First 10 Time Points** *(Required)*
2. **Slice Timing Correction** *(Required)*
3. **Slice Number** *(Required)*
4. **Slice Order** *(Required)*
5. **Reference Slice** *(Required)*
6. **Realignment (Head Motion Correction)** *(Required)*
7. **Voxel-Specific Head Motion** *(Usually not selected)*

1. **Reorient Fun and T1** – Select if needed
2. **Auto Mask** – Recommended (for checking EPI coverage and generating group mask)
3. **Crop T1** – Usually not selected; depends on data format and neck removal status
4. **BET (Skullstrip)** – Required
5. **T1 Coreg to Fun** – Required
6. **Segment / New Segment + DARTEL** – Required
7. **Affine Regularization** – Select *European*

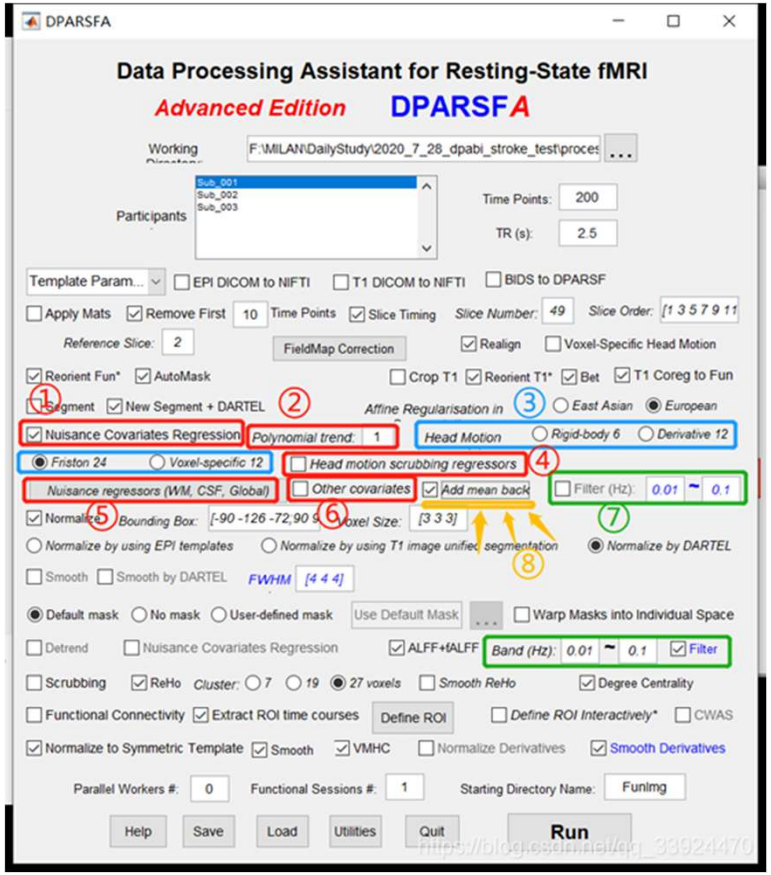


一括前処理（ワンクリック） / One-Click Preprocessing

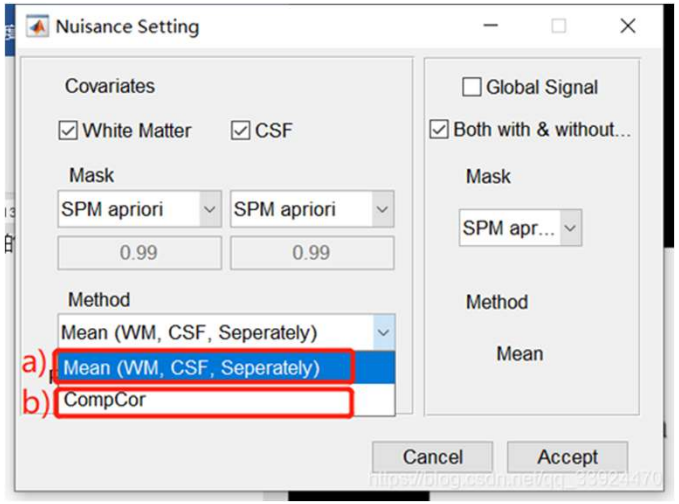


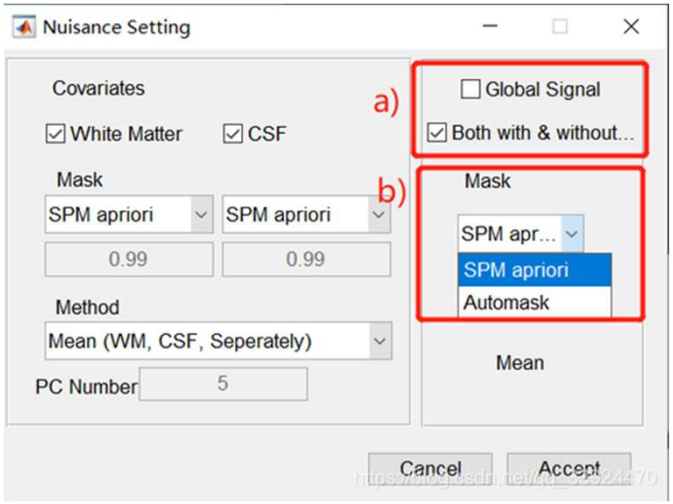
Reorient Fun and Automatic Quality Control Check – Review data for abnormalities and assign quality scores

一括前処理（ワンクリック） / One-Click Preprocessing

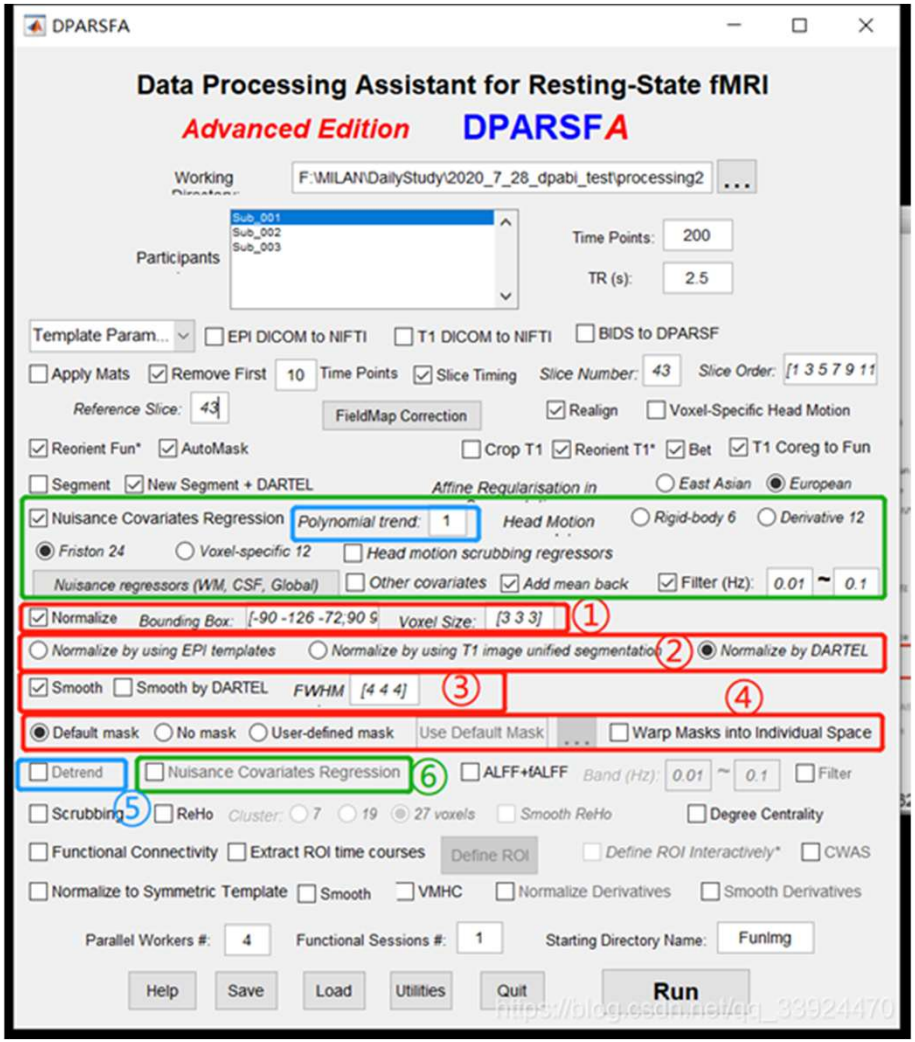


1. **Nuisance Covariates Regression** – Required
2. **Polynomial Trend** – Required (usually enter 1 to remove linear drift)
3. **Head Motion** – Required (use *Friston 24* parameter model)
4. **Head Motion Scrubbing Regression** – Optional
5. **Nuisance Regressors (WM, CSF, Global)** – Remove noise signals from white matter, CSF, and global signal
6. **Other Covariates** – Optional (select if you have additional covariates to remove)
7. **Filter (Hz)** – Required (commonly 0.01–0.1 Hz; adjust as needed; place after ALFF/fALFF if computing those metrics)
8. **Add Mean Back** – Optional



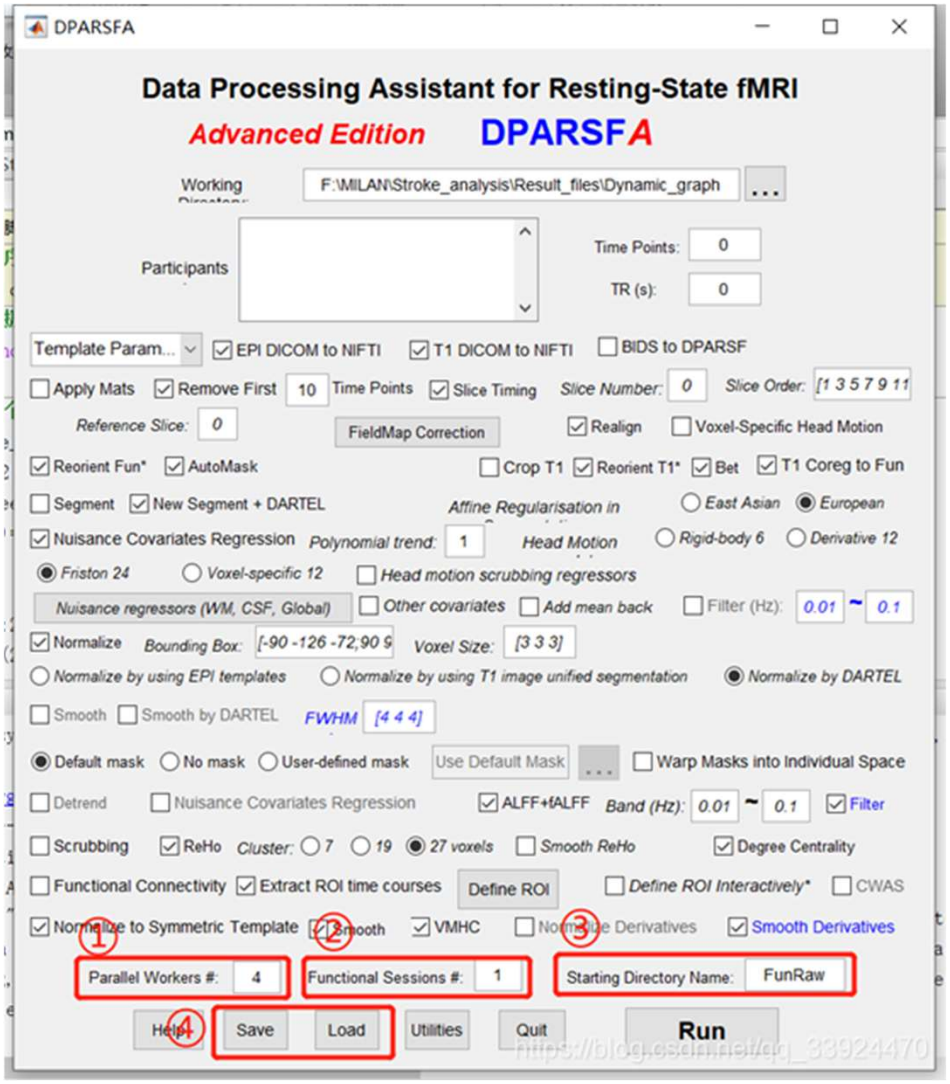


一括前処理（ワンクリック） / One-Click Preprocessing



1.Normalize – Adjust as needed
2.Normalization Method – EPI template / T1 unified segmentation / DARTEL
3.Smooth – Apply if needed (skip before ReHo or DC)
4.Default Mask – Required
5.Detrend – Not selected
6.Nuisance Covariates Regression – Optional

一括前処理（ワンクリック） / One-Click Preprocessing

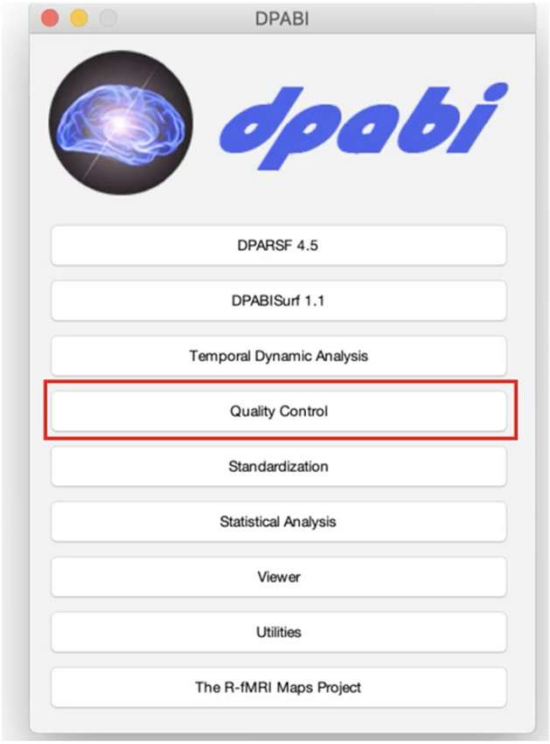


- **Parallel Workers #** – Set according to CPU cores (e.g., 4 cores → enter 4)
- **Functional Session #** – Select if multiple sessions; organize as FunRaw, S2_FunRaw, S3_FunRaw, etc.
- **Starting Directory Name** – Choose the step to start from (e.g., FunImgARWSD to start at filtering)
- **Save / Load** – Save current settings as .mat for reuse; load to avoid re-entering parameters
- **RUN** – Start processing

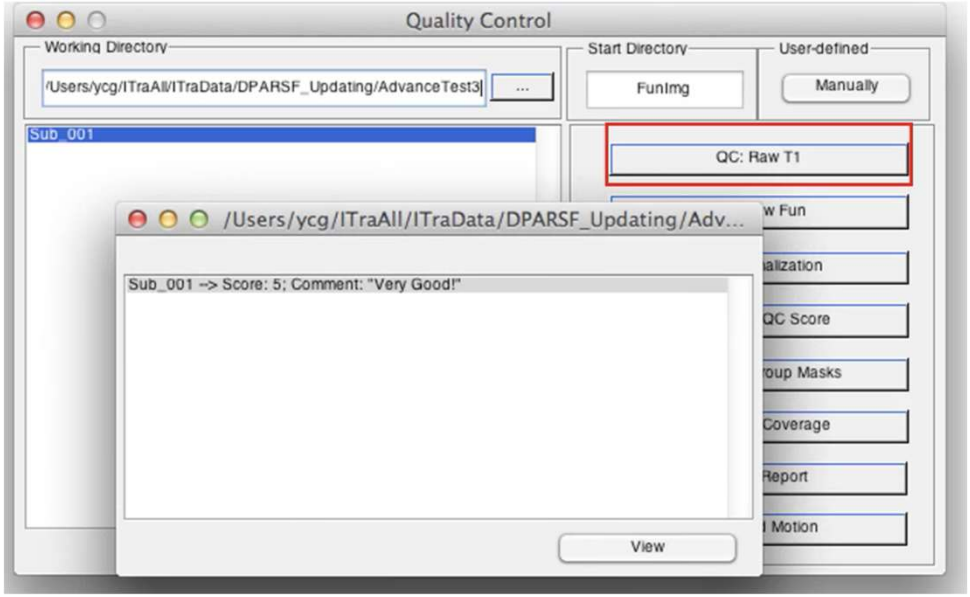
```
Congratulations, the running of DPARSFA is done!!! :)
```

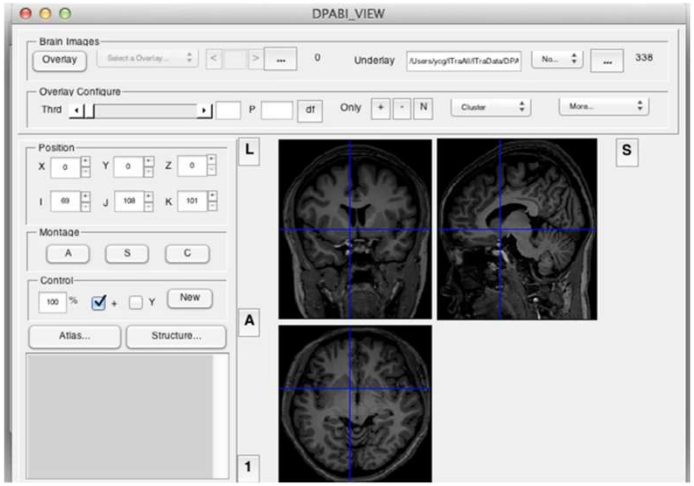
If the data are processed successfully, the following will appear.

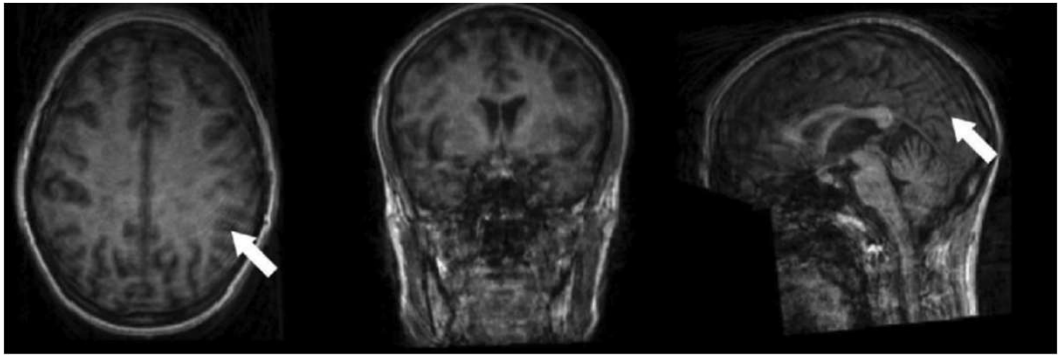
品質管理（QC） / Quality Control (QC)



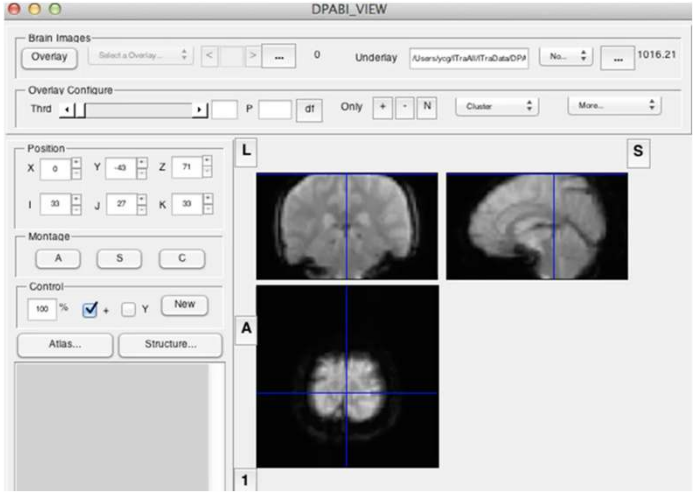
- Raw T1/ Fun check





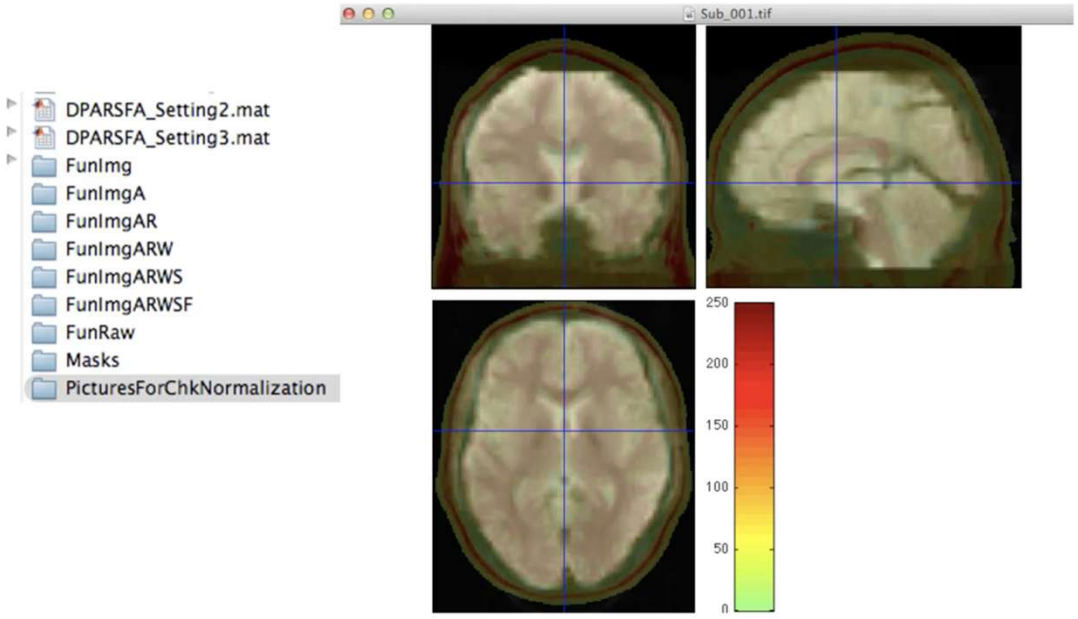


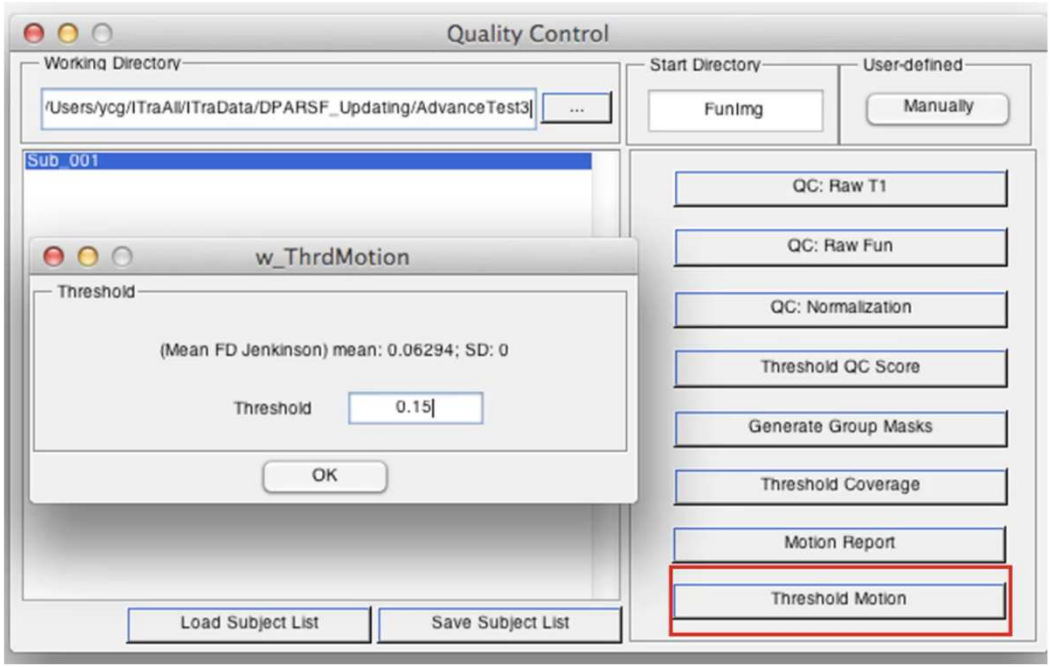
- Head motion related artifacts



品質管理（QC） / Quality Control (QC)

- Normalization check → verify alignment in MNI space
- Head motion check → FD < 0.2 mm





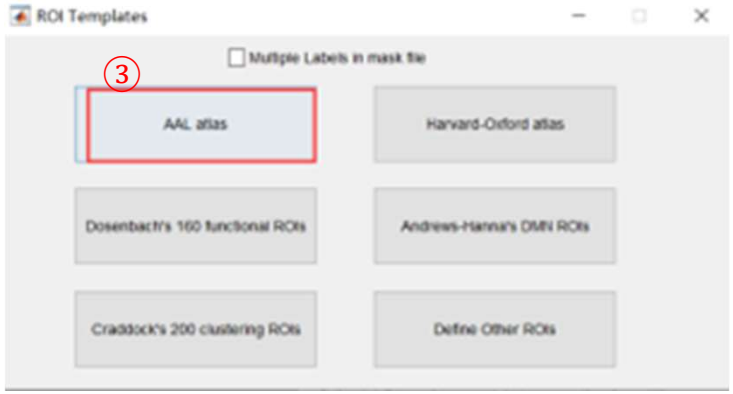
種子点機能的結合解析（DPABI） / Seed-based Functional Connectivity (DPABI)

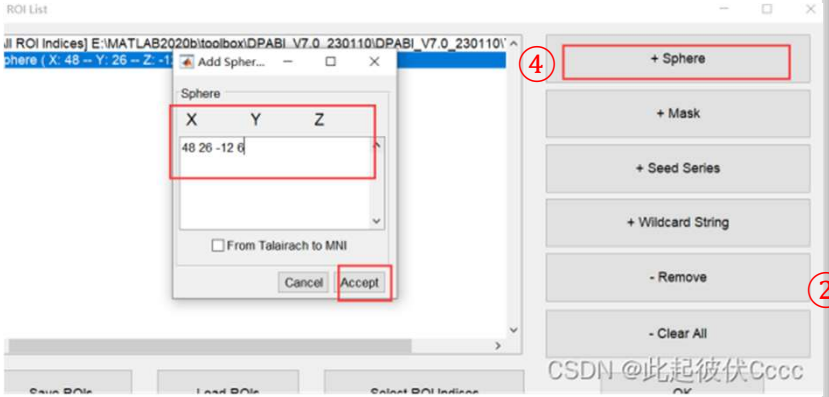
- Select a seed ROI
- Compute correlation between seed BOLD time series and all voxels/ROIs
- Correlation coefficient **-1 ≤ r ≤ 1**
  - **Positive (r > 0)**: same trend
  - **Negative (r < 0)**: opposite trend
  - **r ≈ 0**: no relation
- Output: **Z-map (correlation map)**
  - **z** Fisher's Z-transformed (correlation values converted for statistical analysis).
  - **ROI1** → Refers to Region of Interest 1 (the first seed/ROI you defined).

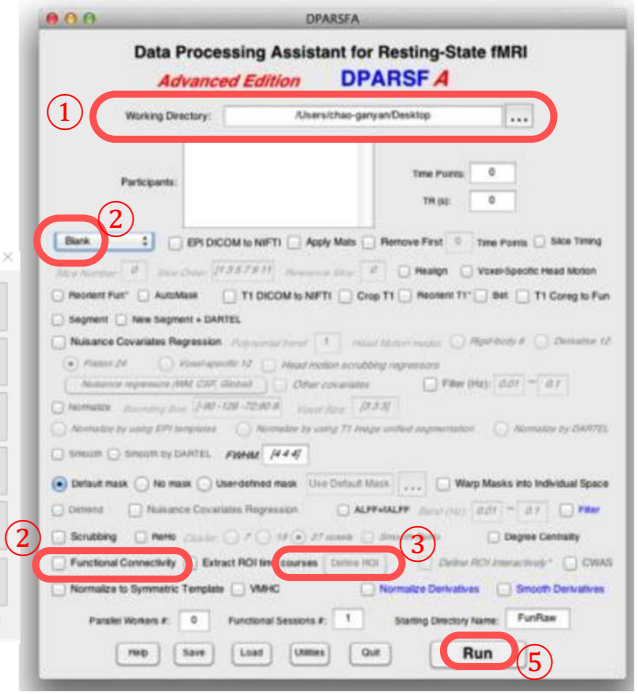
1. In **the Starting directory name**, select the preprocessed fMRI folder
2. Choose **Blank** and check **Functional Connectivity** tab
3. Click **Define ROI** → select the seed voxel/ROI
4. Click **Sphere**, enter X, Y, Z coordinates and radius of seed
5. Click **Run** → results saved in **Results folder**

FC_FunImg

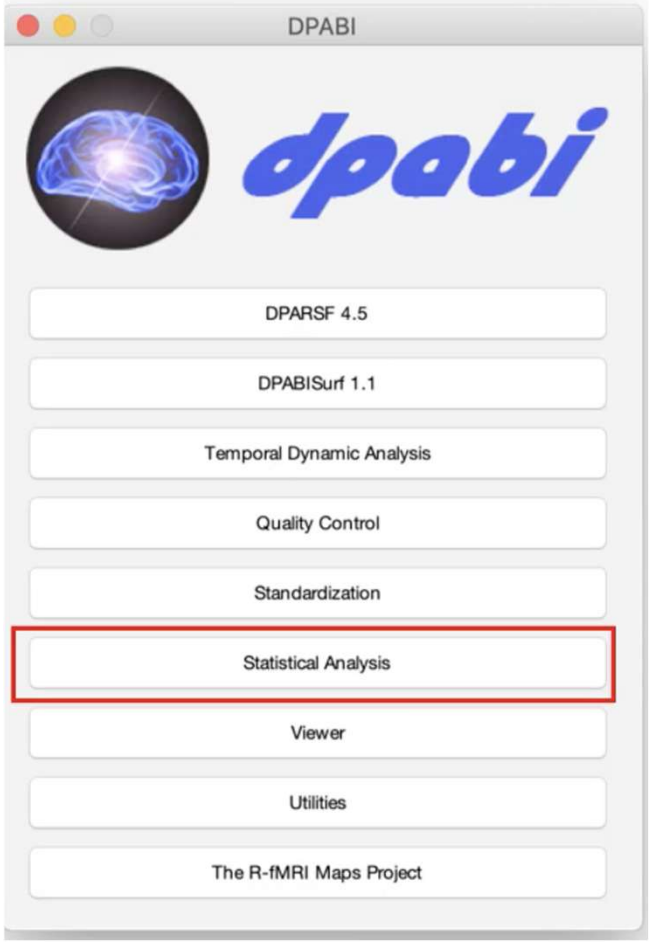
File name: zROI1FCMap_sub_001.nii

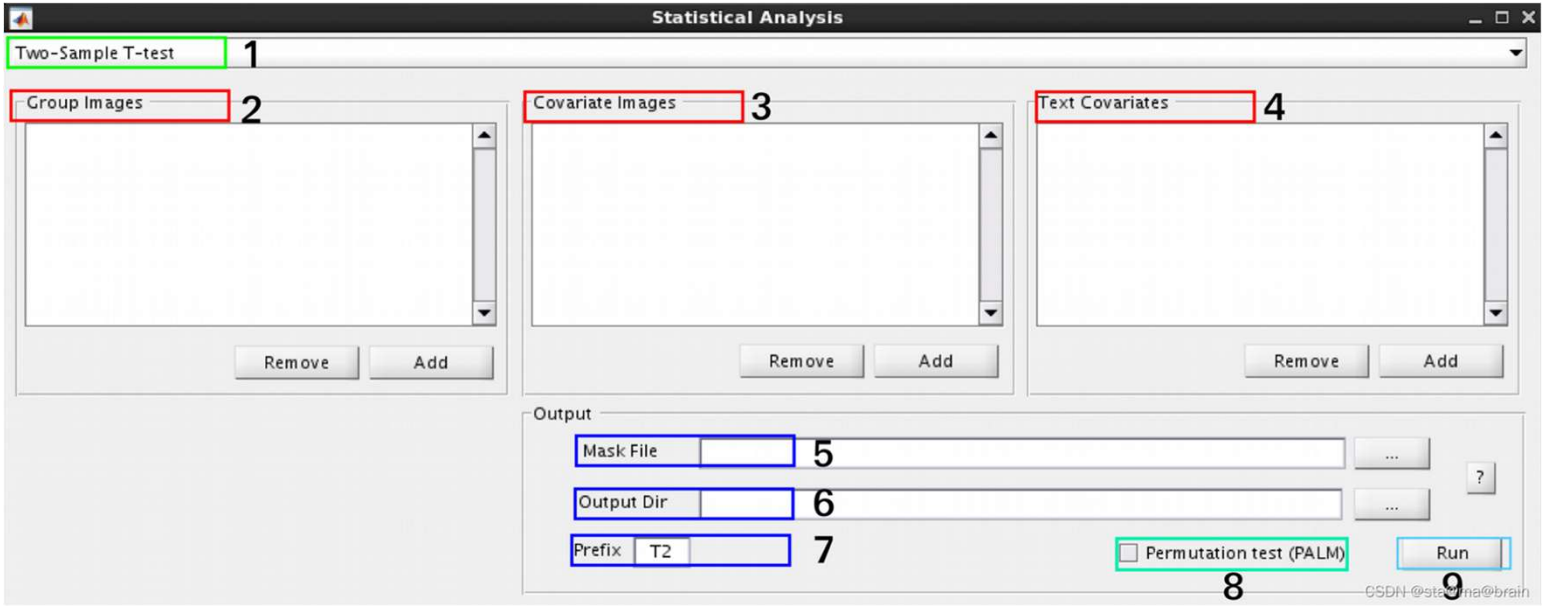


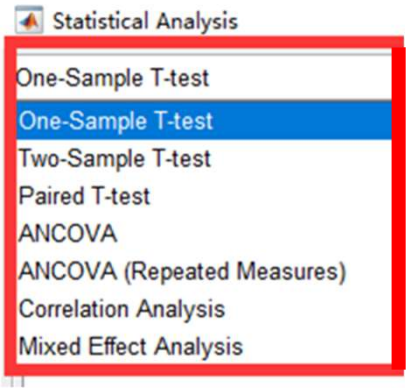




統計解析と多重比較補正 / Statistical Analysis & Multiple Comparison Correction

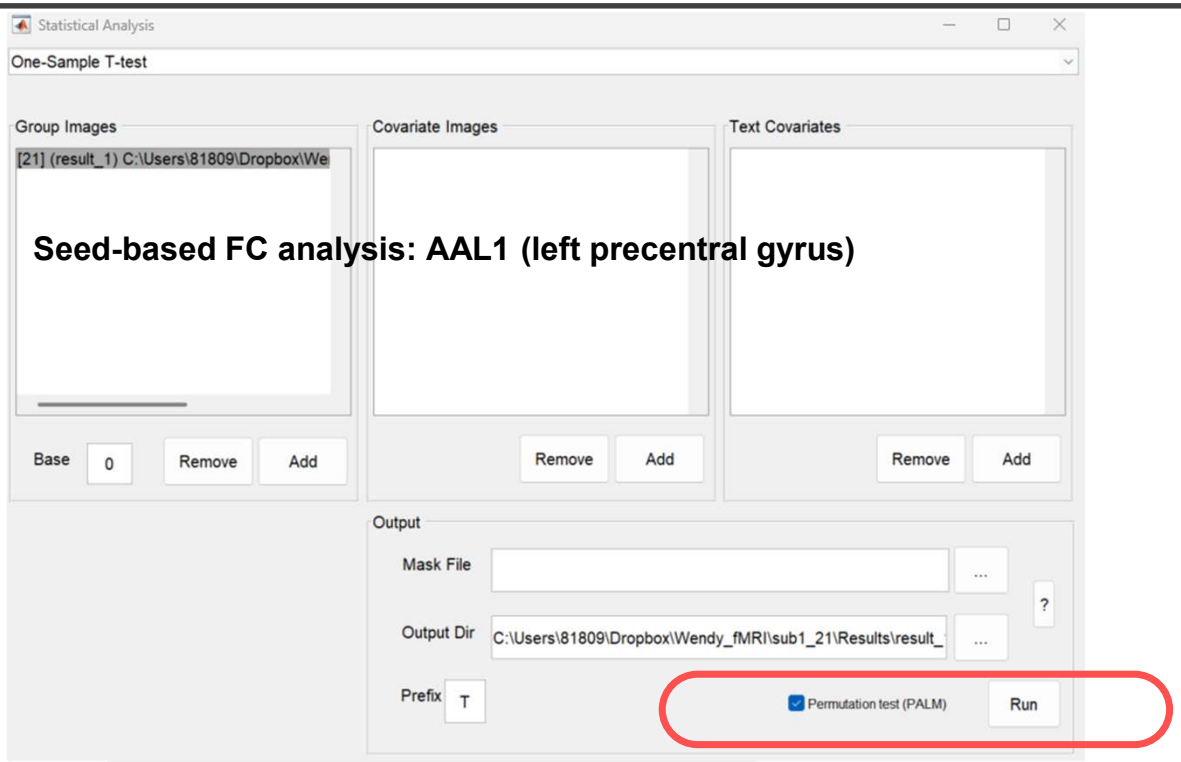


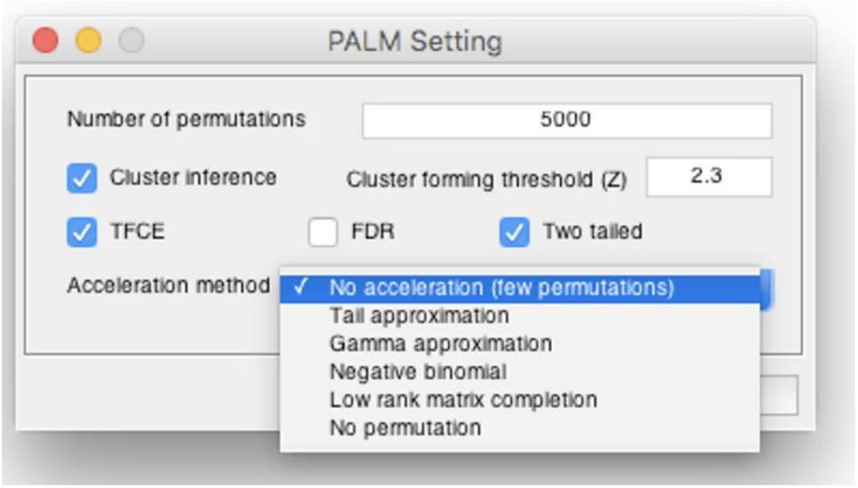


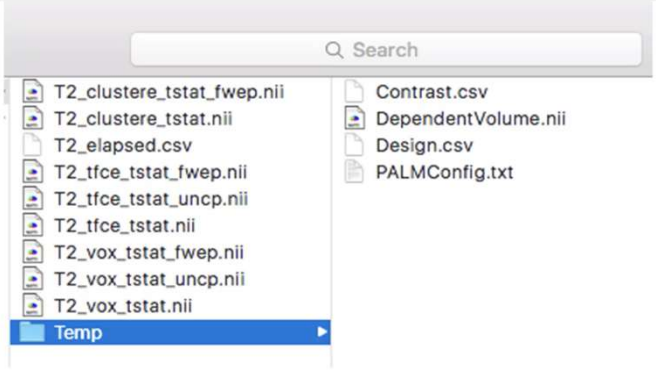


1. **Select statistical model**
2. **Select image files for analysis**：e.g., ReHo files
3. **Select covariate image files**：e.g., gray matter volume
4. **Select non-image covariates**：e.g., age
5. **Select group-level mask file**：e.g., DPABI BrainMask_05_61x73x61
6. **Set output directory**：e.g., /home/Alex/Data/Output
7. **Set output file prefix** (default = T2)
8. **Choose whether to perform permutation test** (via PALM)
9. **Click Run to start analysis**

多重比較補正 / Multiple Comparison Correction： Permutation Test







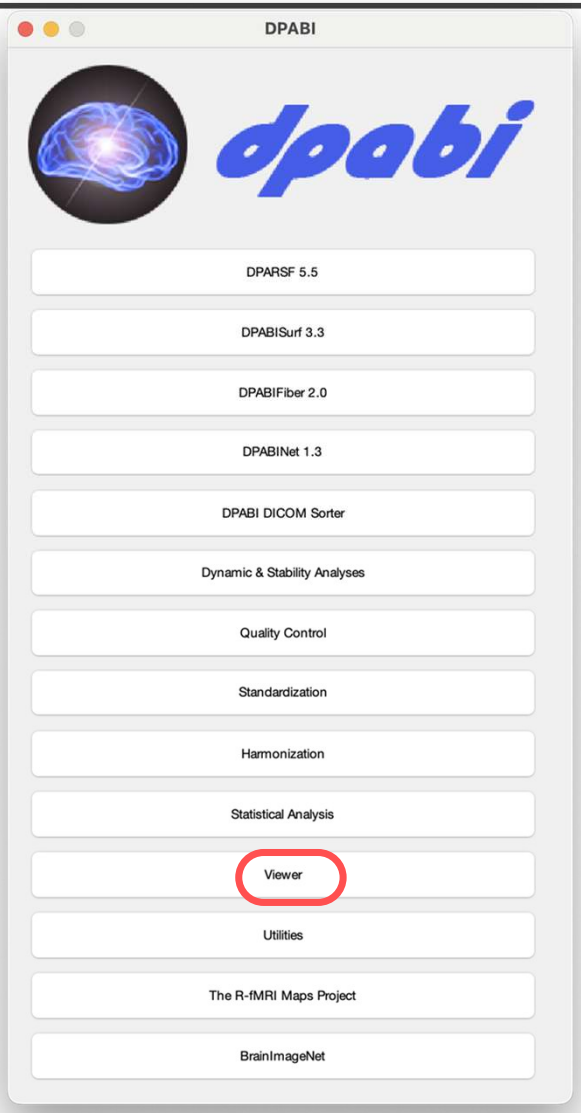
Output files:

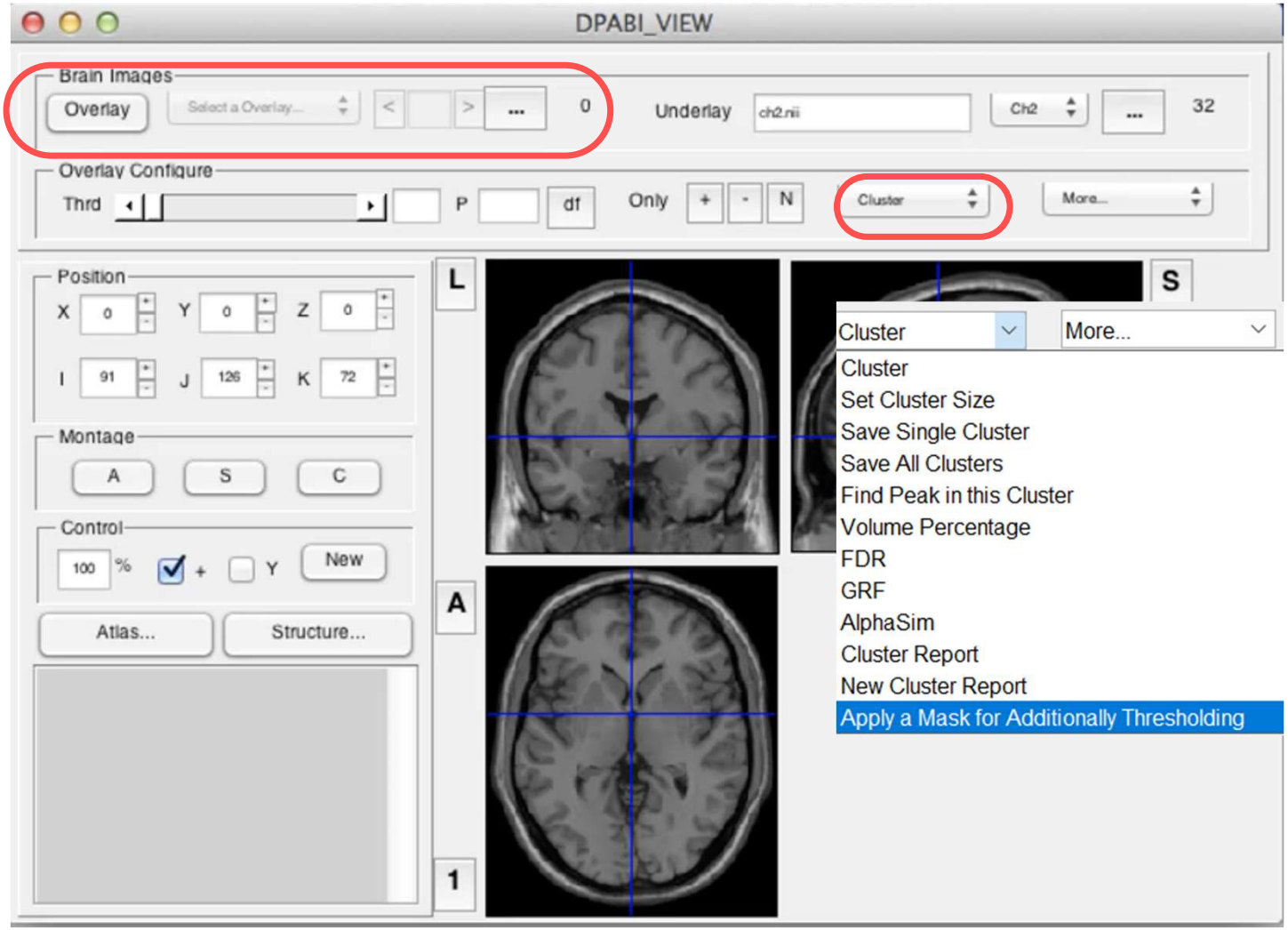
T_tfce_tstat.nii → T-value map

T_tfce_tstat_uncp.nii → uncorrected p-value map

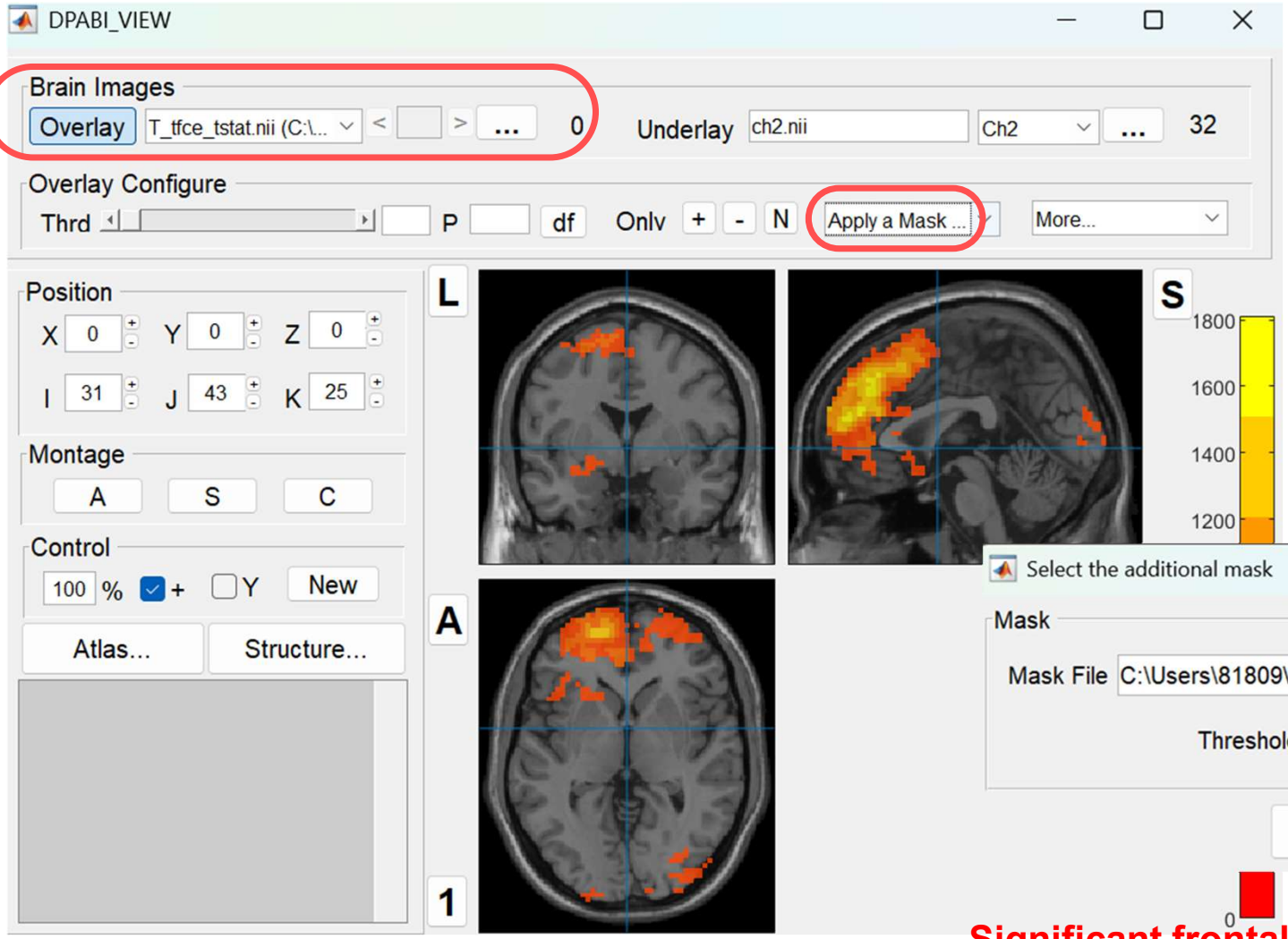
T_tfce_tstat_fwep.nii → FWE-corrected p-value map

結果の可視化 / Result Visualization DPAB- Viewer





Permutation Testの出力と可視化 / Outputs & Visualization of Permutation Test



Visualization steps (DPABI Viewer):

Load T2_tfce_tstat.nii in Overlay

In Cluster, choose **Apply a Mask for Additionally Thresholding**

Select T2_tfce_tstat_fwep.nii as mask

Set threshold < 0.05 (TFCE-based FWE correction)

Significant frontal association cortex connectivity was observed from the left precentral gyrus seed.