# 如何去除fcMRI头动噪声

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自从Power et al. (2012)等研究表明头动对于估计功能连接的负面影响后，关于头动噪声的处理可能是fMRI数据分析中审稿人最为关注的一部分，特别是在发展和临床研究中。这里分享一篇2018年发表在*Nature Protocols*上的文章，该文章（尝试）提出了一个去除functional connectivity MRI（fcMRI）中头动噪声的最佳方案。更多细节请参考原文：

Ciric, Rastko, et al. "Mitigating head motion artifact in functional connectivity MRI." *Nature protocols* 13.12 (2018): 2801.

这篇文章可以归纳为8种去除头动噪声的方法、3种头动噪声类型、18个质量控制指标以及1个最佳的去除头动的方案（包含35个步骤）。

## 一、8种去除头动噪声的方法

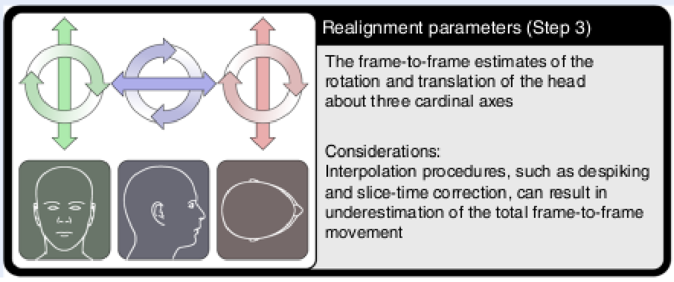
这8种方法可以统称为confound regression（亦称nuisance regression），相同之处在于均使用一般线性模型（GLM）回归掉与头动噪声有关的时间序列（confounds），不同之处在于不同方法获取头动噪声信号的方式不同。具体地：

1. 头动校正参数

头动校正得到6个头动参数，包括X/Y/Z三个方向的平移（translation）和X-Y/X-Z/Y-Z三个平面的转动（rotation）。

2. 白质/脑脊液平均信号

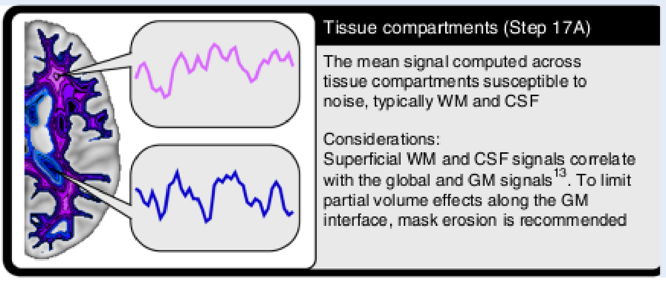
白质/脑脊液等组织的信号易受到噪声影响。



Realignment parameters (Step 3)

The frame-to-frame estimates of the rotation and translation of the head about three cardinal axes

Considerations:
Interpolation procedures, such as despiking and slice-time correction, can result in underestimation of the total frame-to-frame movement



Tissue compartments (Step 17A)

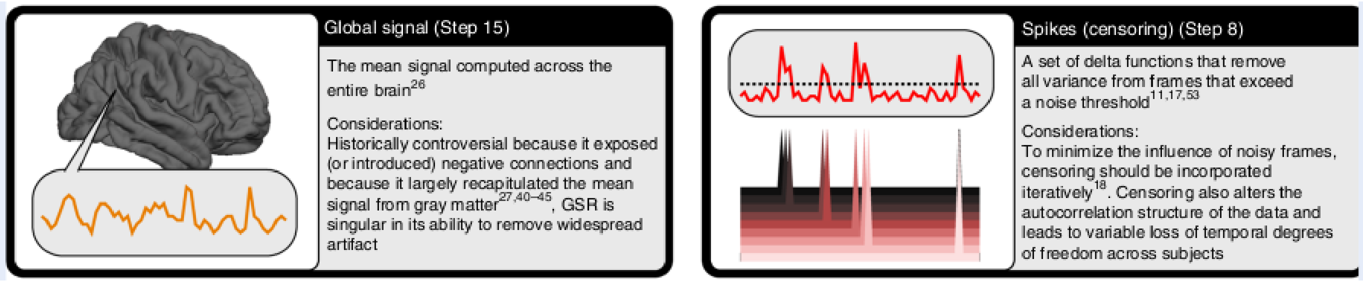
The mean signal computed across tissue compartments susceptible to noise, typically WM and CSF

Considerations:
Superficial WM and CSF signals correlate with the global and GM signals[13]. To limit partial volume effects along the GM interface, mask erosion is recommended

3. 全脑平均信号（GSR）

4. 离群信号（censoring）

超过某个头动阈值的时间点即为离群信号。



Global signal (Step 15)

The mean signal computed across the entire brain[26]

Considerations:
Historically controversial because it exposed (or introduced) negative connections and because it largely recapitulated the mean signal from gray matter[27,40–45]. GSR is singular in its ability to remove widespread artifact

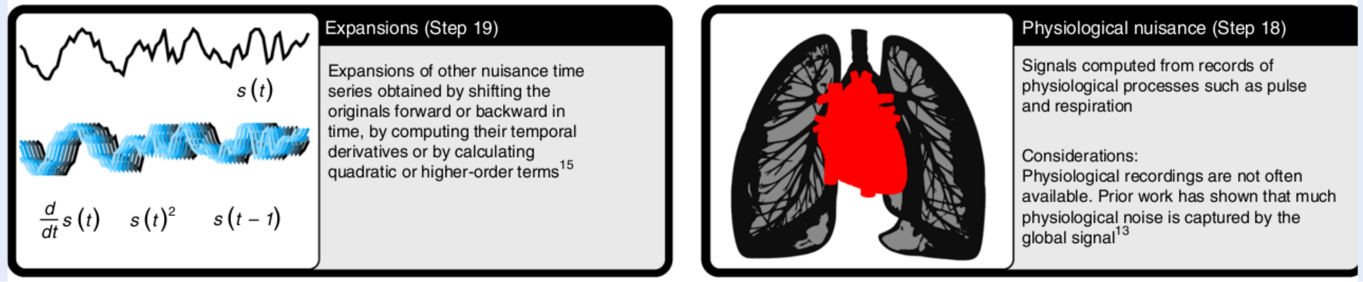
Spikes (censoring) (Step 8)

A set of delta functions that remove all variance from frames that exceed a noise threshold[11,17,53]

Considerations:
To minimize the influence of noisy frames, censoring should be incorporated iteratively[18]. Censoring also alters the autocorrelation structure of the data and leads to variable loss of temporal degrees of freedom across subjects

5. 噪声时间序列展开项

6. 生理信号



Expansions (Step 19)

Expansions of other nuisance time series obtained by shifting the originals forward or backward in time, by computing their temporal derivatives or by calculating quadratic or higher-order terms[15]

Physiological nuisance (Step 18)

Signals computed from records of physiological processes such as pulse and respiration

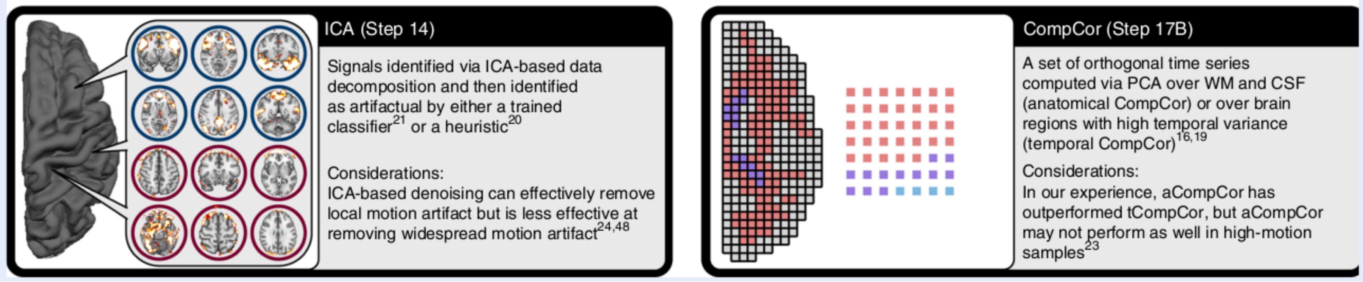
Considerations:
Physiological recordings are not often available. Prior work has shown that much physiological noise is captured by the global signal[13]

7. 独立成分分析（ICA）

使用ICA将数据分解为噪声和非噪声成分，去除噪声成分。

8. CompCor

对白质/脑脊液进行主成分分析（PCA），使用主成分作为噪声时间序列。



ICA (Step 14)

Signals identified via ICA-based data decomposition and then identified as artifactual by either a trained classifier[21] or a heuristic[20]

Considerations:
ICA-based denoising can effectively remove local motion artifact but is less effective at removing widespread motion artifact[24,48]

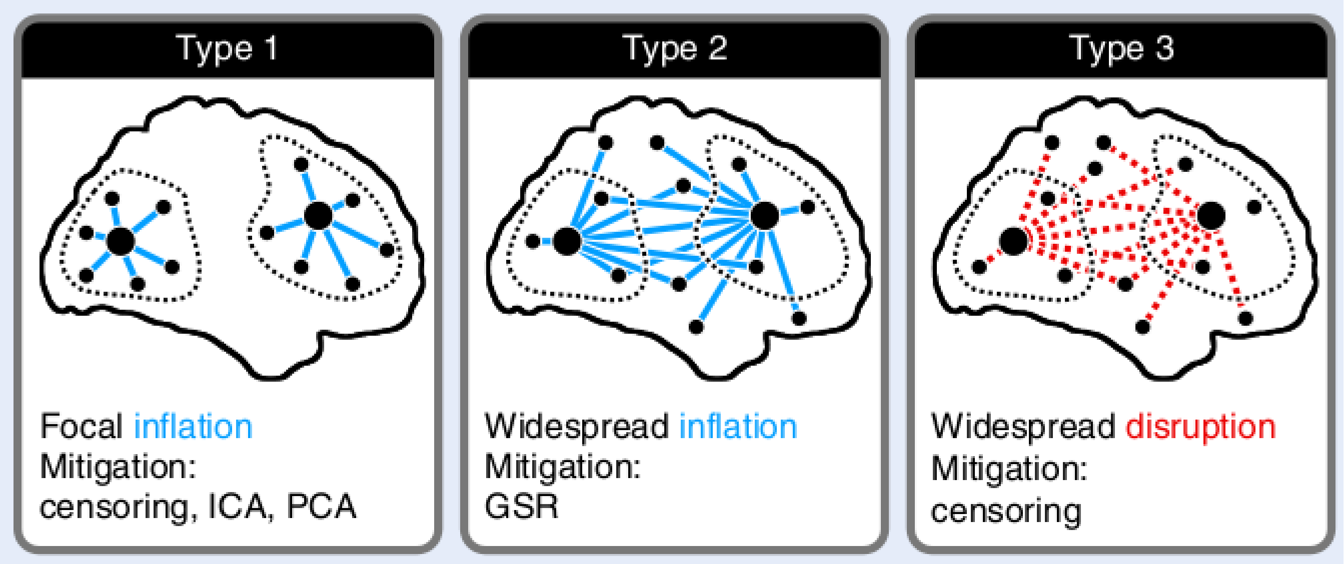
CompCor (Step 17B)

A set of orthogonal time series computed via PCA over WM and CSF (anatomical CompCor) or over brain regions with high temporal variance (temporal CompCor)[16,19]

Considerations:
In our experience, aCompCor has outperformed tCompCor, but aCompCor may not perform as well in high-motion samples[23]

## 二、3种头动噪声类型

根据头动引起的不同区域信号相关性增强还是减弱，将头动噪声分为3类：



1. 局部增强

相邻脑区信号受到头动相似的影响，表现出增强的局部相关性，可以使用censoring, ICA或PCA去除。

2. 全局增强

头动使得全脑相关性增强，这类头动噪声最明显，GSR适合于去除此类噪声。

3. 全局减弱

头动使全脑相关性减弱，这类头动噪声较少见。

## 三、18种质量控制指标

18个质量控制指标又分为12个被试水平指标（Subject level）和6个组水平指标（Sample level）。

被试水平指标：

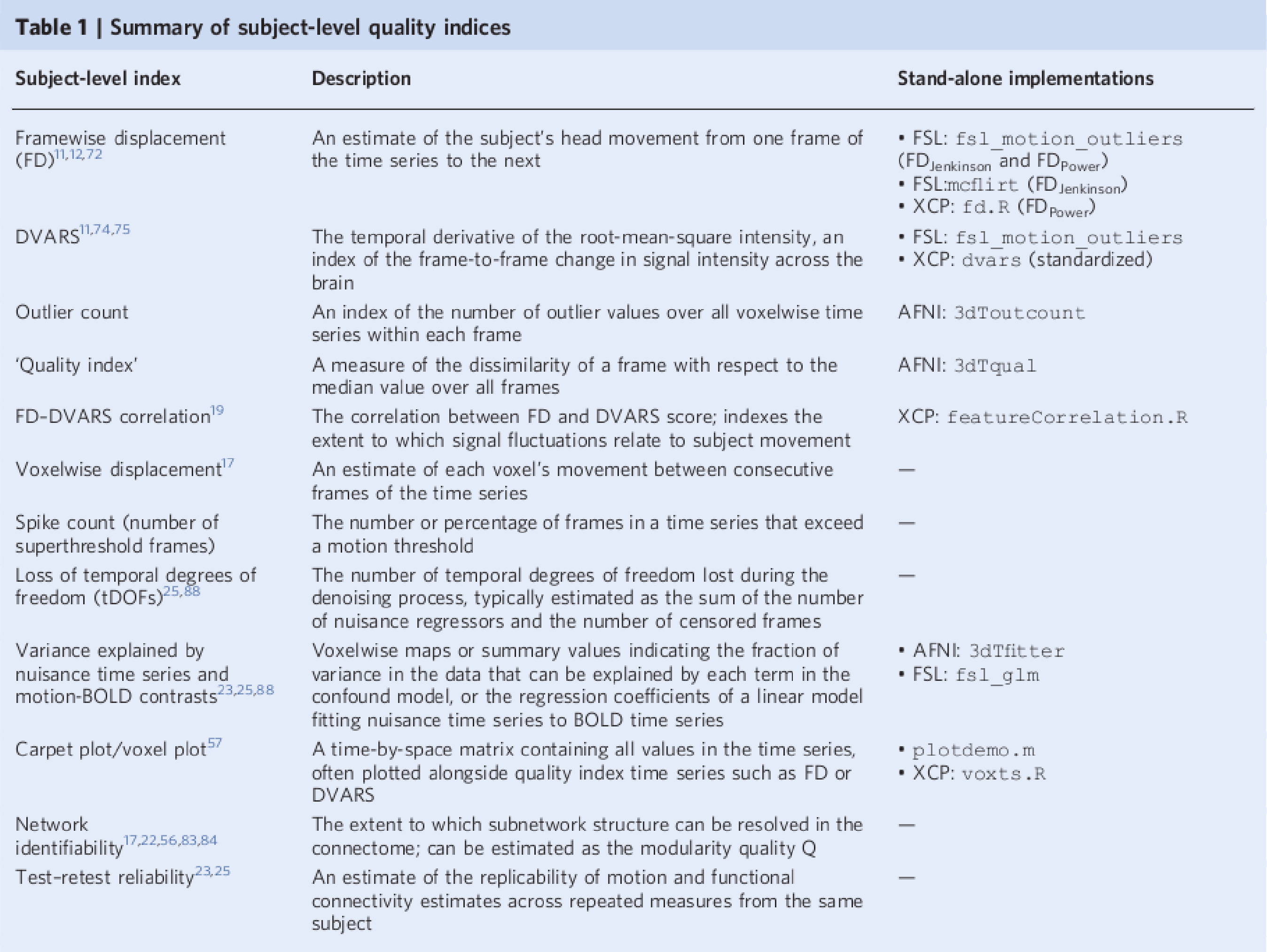


**Table 1 | Summary of subject-level quality indices**

| Subject-level index | Description | Stand-alone implementations |
|---|---|---|
| Framewise displacement (FD)[11,12,72] | An estimate of the subject's head movement from one frame of the time series to the next | • FSL: `fsl_motion_outliers` ($\text{FD}_{\text{Jenkinson}}$ and $\text{FD}_{\text{Power}}$)<br>• FSL:`mcflirt` ($\text{FD}_{\text{Jenkinson}}$)<br>• XCP: `fd.R` ($\text{FD}_{\text{Power}}$) |
| DVARS[11,74,75] | The temporal derivative of the root-mean-square intensity, an index of the frame-to-frame change in signal intensity across the brain | • FSL: `fsl_motion_outliers`<br>• XCP: `dvars` (standardized) |
| Outlier count | An index of the number of outlier values over all voxelwise time series within each frame | AFNI: `3dToutcount` |
| 'Quality index' | A measure of the dissimilarity of a frame with respect to the median value over all frames | AFNI: `3dTqual` |
| FD-DVARS correlation[19] | The correlation between FD and DVARS score; indexes the extent to which signal fluctuations relate to subject movement | XCP: `featureCorrelation.R` |
| Voxelwise displacement[17] | An estimate of each voxel's movement between consecutive frames of the time series | — |
| Spike count (number of superthreshold frames) | The number or percentage of frames in a time series that exceed a motion threshold | — |
| Loss of temporal degrees of freedom (tDOFs)[25,88] | The number of temporal degrees of freedom lost during the denoising process, typically estimated as the sum of the number of nuisance regressors and the number of censored frames | — |
| Variance explained by nuisance time series and motion-BOLD contrasts[23,25,88] | Voxelwise maps or summary values indicating the fraction of variance in the data that can be explained by each term in the confound model, or the regression coefficients of a linear model fitting nuisance time series to BOLD time series | • AFNI: `3dTfitter`<br>• FSL: `fsl_glm` |
| Carpet plot/voxel plot[57] | A time-by-space matrix containing all values in the time series, often plotted alongside quality index time series such as FD or DVARS | • `plotdemo.m`<br>• XCP: `voxts.R` |
| Network identifiability[17,22,56,83,84] | The extent to which subnetwork structure can be resolved in the connectome; can be estimated as the modularity quality Q | — |
| Test-retest reliability[23,25] | An estimate of the replicability of motion and functional connectivity estimates across repeated measures from the same subject | — |

1. 位移（Framewise displacement）

估计相邻时间点之间的位移。

2. 信号差（DVARS）

相邻时间点之间的信号差。

3. 离群体素个数（Outlier count）

每个时间点上包含离群值的体素个数。

4. 'Quality index'

每个时间点图像与中位数图像的相似性。

5. 位移与信号差相关性（FD-DVARS correlation）

FD与DVARS的相关系数，反映头动与信号变化的相似程度。

6. 体素位移（Voxelwise displacement）

估计每个体素在相邻时间点间的位移。

7. 离群时间点（Spike count）

超过某个头动阈值的时间点的个数。

8. 时间自由度的减少

9. 噪声时间序列解释的变异

10. 体素图（Carpet plot/voxel plot）

每个体素的信号随时间变化的矩阵图

11. 网络可辨别性（Network idenfiability）

12. 重测信度（test-retest reliability）

组水平指标：

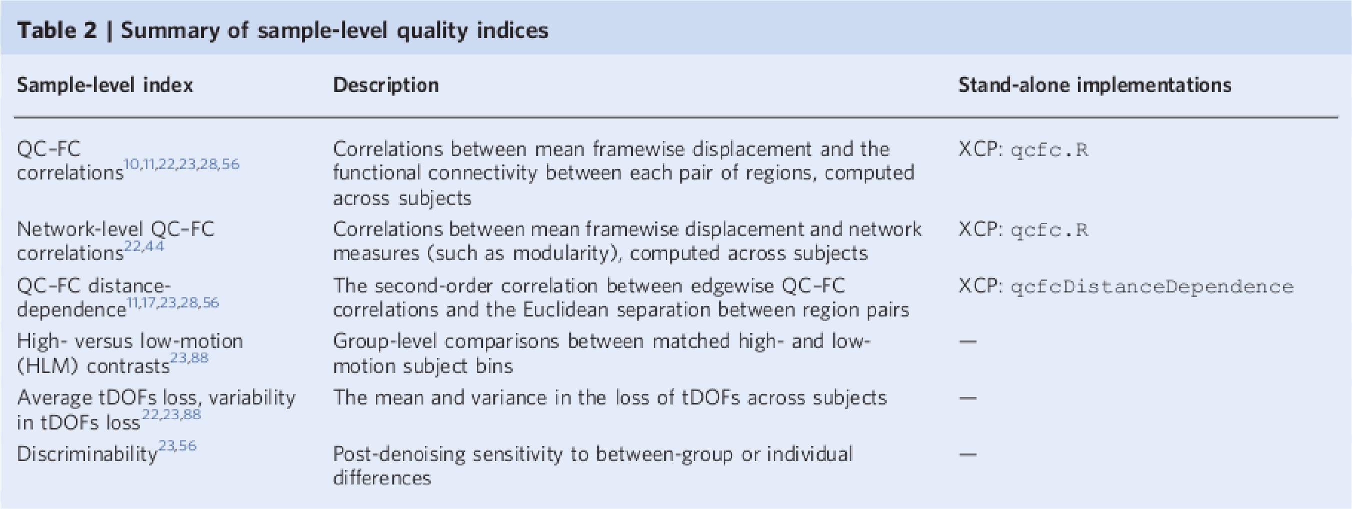


**Table 2 | Summary of sample-level quality indices**

| Sample-level index | Description | Stand-alone implementations |
|---|---|---|
| QC-FC correlations[10,11,22,23,28,56] | Correlations between mean framewise displacement and the functional connectivity between each pair of regions, computed across subjects | XCP: `qcfc.R` |
| Network-level QC-FC correlations[22,44] | Correlations between mean framewise displacement and network measures (such as modularity), computed across subjects | XCP: `qcfc.R` |
| QC-FC distance-dependence[11,17,23,28,56] | The second-order correlation between edgewise QC-FC correlations and the Euclidean separation between region pairs | XCP: `qcfcDistanceDependence` |
| High- versus low-motion (HLM) contrasts[23,88] | Group-level comparisons between matched high- and low-motion subject bins | — |
| Average tDOFs loss, variability in tDOFs loss[22,23,88] | The mean and variance in the loss of tDOFs across subjects | — |
| Discriminability[23,56] | Post-denoising sensitivity to between-group or individual differences | — |

1. 头动-功能连接相关性（QC-FC correlations）

平均头动位移（mean FD）与不同脑区间功能连接在被试间的相关系数。

2. 头动-网络指标相关性（Network-level QC-FC correlations）

平均头动位移（mean FD）与网络指标（比如模块化）在被试间的相关系数。

3. 头动-功能连接相关性与距离的依赖关系（QC-FC distance-dependence）

QC-FC相关系数与脑区之间欧式距离的相关系数。

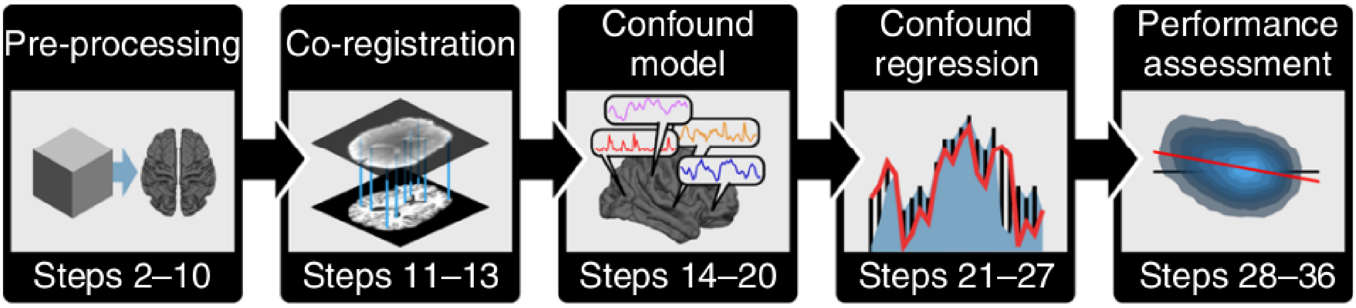
4. 高-低头动对比（High- versus low-motion contrasts）

5. 平均自由度减少
6. 可区分性（Discriminability）

区分不同组别或个体的敏感性。

## 四、1个最佳方案

该最佳方案可细分为4个部分，包括35个步骤：



基本处理：

1. 去除前几个时间点数据
2. 估计头动校正参数和FD
3. 时间层校正（可选）
4. 头动校正
5. 估计全脑边界
6. 估计DVARS
7. 估计离群时间点个数（如果不做censoring，可跳过此步骤）
8. 去除体素离群值（Despiking，可选）
9. 去除均值、线性和二次趋势

结构-功能像配准：

10. 根据结构像组织分割结果得到白质边界图像
11. 结构-功能像配准
12. 转换配准矩阵为ITK兼容格式（如果不使用ANTs配准，可跳过此步骤）

构建头动噪声模型：

13. 使用ICA-AROMA得到头动相关的独立成分，并去除相应的信号
14. 计算全脑平均信号
15. 获得白质/脑脊液mask图像，用于提取相应组织的噪声信号
16. 获得白质/脑脊液区域的噪声信号，可以计算平均信号或者使用PCA得到的主成分
17. 其他噪声信号（比如记录得到的生理信号，可选）
18. 计算噪声序列的展开项（可选）
19. 将第4步和第14-18步得到的噪声信号序列构成一个矩阵（头动噪声模型）

去除头动噪声：

20. 对离群时间点图像进行插值（如果不进行censoring，可跳过此步骤）
21. 时间滤波（0.01-0.08Hz），对头动噪声模型进行相同的滤波操作
22. 将离群时间点（spike regressors）加入头动造成模型
23. 使用GLM模型估计拟合参数，残差即为去除头动噪声后的信号
24. 去除离群时间点图像（censoring，可选）
25. 将在第9步中去掉的均值加回到残差中（可选）
26. 空间平滑（可选）

质量检查：

27. 根据某个大脑分区模板计算功能连接
28. 计算结构像不同组织的深度图谱，并转换到功能像空间
29. 计算经过基本处理和去除头动噪声后的体素信号图
30. 计算去除头动噪声后的DVARS
31. 计算FD-DVARS的相关系数（包括经过基本处理和去除头动噪声后的DVARS）
32. 估计减少的自由度
33. 将头动（mean FD）和功能连接指标汇总到一个矩阵中

34. 计算头动-功能连接相关性（QC-FC correlations）
35. 计算头动-功能连接相关性与距离的依赖关系