Supplementary Materials

Details of CFS Baseline Analysis combined with MVPA

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Contents

1. Supplementary information about the pre-process

The fMRI data were acquired from Dongzhimen Hospital affiliated to Beijing University of Chinese Medicine, though an MRI scanner of Siemens Novus 3.0 T produced by Germany.

The parameters are followings:

Structural sequence TR = 1900 ms, TE = 2.53 ms, flip angle = 9°, coverage = whole brain including cerebellum, Fov read = 250 mm, echo spacing = 7.6 ms slice thickness = 1.0 mm, volumes = 176.

The fMRI data were pre-processed via DPABISurf 1.6 [1], an ensemble fMRI analysis tool based on the fMRIPrep, Freesurfer, ANTs and others.

fMRIPrep steps:

Results included in this manuscript come from preprocessing performed using *fMRIPrep* 20.2.1 [2,3], which is based on *Nipype* 1.5.1 [4,5].

Anatomical data preprocessing: A total of 1 T1-weighted (T1w) images were found within the input BIDS dataset. The T1-weighted (T1w) image was corrected for intensity non-uniformity (INU) with `N4BiasFieldCorrection` [6], distributed with ANTs 2.3.3 [7], and used as T1w-reference throughout the workflow. The T1w-reference was then skull-stripped with a *Nipype* implementation of the `antsBrainExtraction.sh` workflow (from ANTs), using OASIS30ANTs as target template. Brain tissue segmentation of cerebrospinal fluid (CSF), white-matter (WM) and gray-matter (GM) was performed on the brain-extracted T1w using `fast` (FSL 5.0.9 [8]). Brain surfaces were reconstructed using `recon-all` (FreeSurfer 6.0.1 [9]), and the brain mask estimated previously was refined with a custom variation of the method to reconcile ANTs-derived and FreeSurfer-derived segmentations of the cortical gray-matter of Mindboggle [10]. Volume-based spatial normalization to two standard spaces (MNI152NLin2009cAsym, MNI152NLin6Asym) was performed through nonlinear registration with `antsRegistration` (ANTs 2.3.3), using brain-extracted versions of both T1w reference and the T1w template. The following templates were selected for spatial normalization: *ICBM 152 Nonlinear Asymmetrical template version 2009c* [11] (TemplateFlow ID: MNI152NLin2009cAsym), *FSL's MNI ICBM 152 non-linear 6th Generation Asymmetric Average Brain Stereotaxic Registration Model* [12] (TemplateFlow ID: MNI152NLin6Asym).

For more details of the pipeline, see the section corresponding to workflows in *fMRIPrep*'s documentation.

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DPABISurf steps:

under the DPABISurf 1.6, the voxel size of gray matter on standard volume space was resampled to 2 ×2 ×2 mm^3 and smoothed with Gaussian kernel of 6 ×6 ×6 mm^3. Thus, we got the prepared gray matter data of voxel-based morphometry (VBM) for further VBM analysis.

Besides, when the surface reconstruction finished, each subject would obtain their surface thicknesses of left and right hemispheres in fsaverage surface space. Then, DPABISurf 1.6 was used to smooth those thicknesses with Gaussian kernel of 6 mm^3. Hence, we got the prepared surface thicknesses data for further comparison.

2. Supplementary results

2.1 Supplementary tables

Table 1: Importance ranks of cortices

Left Hemisphere			Right Hemisphere		
Cortex.name	Importance.value	Absolute.value	Cortex.name	Importance.value	Absolute.value
Unknown	**0.162**	**0.162**	**G_front_sup**	**-0.110**	**0.110**
G_front_sup	**-0.120**	**0.120**	**Unknown**	**0.101**	**0.101**
S_central	**-0.100**	**0.100**	**S_intrapariet_and_P_trans**	**-0.057**	**0.057**
S_temporal_sup	**-0.068**	**0.068**	**G_pariet_inf-Supramar**	**-0.056**	**0.056**
G_and_S_paracentral	**-0.060**	**0.060**	**G_orbital**	**-0.055**	**0.055**
G_precentral	**-0.057**	**0.057**	**S_temporal_sup**	**-0.052**	**0.052**
G_postcentral	**-0.052**	**0.052**	**G_and_S_paracentral**	**-0.051**	**0.051**
S_circular_insula_inf	0.052	0.052	G_oc-temp_med-Parahip	0.049	0.049
G_precuneus	0.052	0.052	G_precentral	-0.046	0.046
S_pericallosal	0.046	0.046	S_front_inf	-0.044	0.044
G_and_S_subcentral	-0.043	0.043	G_temp_sup-Lateral	-0.041	0.041
G_parietal_sup	-0.041	0.041	S_central	-0.038	0.038
Lat_Fis-post	-0.040	0.040	G_precuneus	-0.034	0.034
G_temp_sup-Lateral	-0.040	0.040	Pole_occipital	-0.029	0.029
Pole_occipital	-0.039	0.039	S_orbital_med-olfact	-0.029	0.029
G_temp_sup-Plan_tempo	-0.039	0.039	S_postcentral	-0.028	0.028
S_subparietal	0.039	0.039	S_subparietal	0.027	0.027
G_front_inf-Triangul	-0.035	0.035	G_and_S_cingul-Mid-Post	-0.027	0.027
S_oc-temp_med_and_Lingual	-0.034	0.034	G_parietal_sup	0.024	0.024
G_pariet_inf-Supramar	-0.033	0.033	G_temp_sup-Plan_tempo	-0.023	0.023
G_front_inf-Opercular	-0.031	0.031	S_cingul-Marginalis	-0.019	0.019
G_and_S_cingul-Ant	0.027	0.027	G_and_S_transv_frontopol	-0.019	0.019
S_front_inf	-0.027	0.027	S_circular_insula_sup	0.019	0.019
S_cingul-Marginalis	0.026	0.026	G_cuneus	-0.018	0.018
S_calcarine	-0.024	0.024	G_temporal_inf	0.018	0.018
G_pariet_inf-Angular	-0.023	0.023	G_and_S_subcentral	-0.018	0.018
S_postcentral	0.022	0.022	S_oc-temp_med_and_Lingual	-0.017	0.017
G_cingul-Post-ventral	0.021	0.021	G_occipital_middle	-0.017	0.017
Pole_temporal	0.021	0.021	G_front_inf-Triangul	-0.017	0.017
S_orbital-H_Shaped	0.020	0.020	G_pariet_inf-Angular	-0.017	0.017
S_intrapariet_and_P_trans	-0.020	0.020	G_temporal_middle	-0.017	0.017
G_cingul-Post-dorsal	0.019	0.019	G_insular_short	0.017	0.017
S_temporal_transverse	-0.019	0.019	G_rectus	-0.017	0.017
S_occipital_ant	-0.018	0.018	G_cingul-Post-dorsal	0.016	0.016
S_circular_insula_ant	-0.017	0.017	G_cingul-Post-ventral	0.016	0.016
S_temporal_inf	-0.017	0.017	S_precentral-inf-part	0.015	0.015
G_rectus	-0.017	0.017	G_Ins_lg_and_S_cent_ins	0.014	0.014
G_temp_sup-Plan_polar	0.016	0.016	G_postcentral	0.014	0.014
S_orbital_lateral	-0.015	0.015	S_circular_insula_ant	0.014	0.014
G_insular_short	0.014	0.014	S_orbital-H_Shaped	-0.014	0.014
S_circular_insula_sup	0.014	0.014	S_calcarine	-0.012	0.012
S_front_middle	0.014	0.014	Pole_temporal	0.012	0.012
G_oc-temp_med-Lingual	-0.013	0.013	S_pericallosal	-0.011	0.011
G_oc-temp_med-Parahip	0.013	0.013	G_and_S_occipital_inf	-0.011	0.011
S_precentral-sup-part	0.012	0.012	S_circular_insula_inf	-0.011	0.011
S_interm_prim-Jensen	-0.012	0.012	S_collat_transv_ant	0.011	0.011
G_Ins_lg_and_S_cent_ins	0.012	0.012	G_and_S_frontomargin	-0.010	0.010
G_cuneus	-0.012	0.012	S_occipital_ant	0.010	0.010
G_and_S_cingul-Mid-Ant	0.011	0.011	G_front_middle	-0.009	0.009

Table 1: Importance ranks of cortices *(continued)*

Left Hemisphere			Right Hemisphere		
Cortex.name	Importance.value	Absolute.value	Cortex.name	Importance.value	Absolute.value
Lat_Fis-ant-Vertical	0.011	0.011	G_front_inf-Orbital	-0.009	0.009
S_front_sup	-0.011	0.011	S_oc-temp_lat	-0.008	0.008
Lat_Fis-ant-Horizont	-0.011	0.011	G_and_S_cingul-Mid-Ant	0.008	0.008
S_collat_transv_ant	0.010	0.010	S_front_middle	-0.008	0.008
G_oc-temp_lat-fusifor	-0.009	0.009	S_oc_sup_and_transversal	0.007	0.007
S_precentral-inf-part	-0.008	0.008	G_occipital_sup	-0.007	0.007
G_temp_sup-G_T_transv	-0.008	0.008	G_and_S_cingul-Ant	0.007	0.007
S_oc_sup_and_transversal	0.008	0.008	S_orbital_lateral	-0.007	0.007
G_and_S_occipital_inf	-0.007	0.007	S_interm_prim-Jensen	-0.007	0.007
G_front_middle	-0.007	0.007	S_parieto_occipital	0.006	0.006
S_collat_transv_post	-0.007	0.007	S_precentral-sup-part	0.006	0.006
S_parieto_occipital	0.007	0.007	G_oc-temp_med-Lingual	-0.006	0.006
G_and_S_frontomargin	0.007	0.007	Lat_Fis-ant-Vertical	0.005	0.005
G_orbital	0.007	0.007	G_temp_sup-Plan_polar	0.005	0.005
G_and_S_transv_frontopol	-0.007	0.007	S_front_sup	0.005	0.005
G_and_S_cingul-Mid-Post	-0.007	0.007	S_suborbital	-0.005	0.005
G_occipital_sup	0.005	0.005	G_oc-temp_lat-fusifor	-0.005	0.005
G_front_inf-Orbital	-0.005	0.005	S_temporal_inf	-0.003	0.003
G_occipital_middle	-0.005	0.005	Lat_Fis-post	0.003	0.003
G_temporal_inf	0.004	0.004	S_temporal_transverse	0.003	0.003
G_subcallosal	0.002	0.002	G_subcallosal	-0.002	0.002
S_oc-temp_lat	0.001	0.001	Lat_Fis-ant-Horizont	-0.002	0.002
S_suborbital	-0.001	0.001	G_temp_sup-G_T_transv	0.001	0.001
S_oc_middle_and_Lunatus	-0.001	0.001	G_front_inf-Opercular	-0.001	0.001
S_orbital_med-olfact	-0.001	0.001	S_oc_middle_and_Lunatus	0.000	0.000
G_temporal_middle	0.000	0.000	S_collat_transv_post	0.000	0.000

2.2. Supplementary analyses

2.2.1 Analysis 1 - GLM analysis for 12-cortical network

General linear model analysis was used. We took the base information into analysis, including age, gender and BMI.

```
summary(aov(Twelve_cortical_network$mean ~ information$group + information$age +
              information$gender + information$BMI))
```

```
##                      Df Sum Sq Mean Sq F value  Pr(>F)
## information$group     1 0.0333 0.03331   4.648 0.03474 *
## information$age       1 0.0518 0.05177   7.224 0.00909 **
## information$gender    1 0.0011 0.00106   0.148 0.70123
## information$BMI       1 0.0027 0.00274   0.383 0.53814
## Residuals            66 0.4729 0.00717
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

The result showed that after eliminating influences of age, gender and BMI, the mean thickness of 12-cortical network was significant between groups (P = 0.035).

Further, we took the base information and clinical evaluations into analysis, including age, gender, BMI, SF-36, PRI and FS-14.

```
summary(aov(Twelve_cortical_network$mean ~ information$group + information$age +
              information$gender + information$BMI + information$`SF-36` +
              information$PRI + information$`FS-14`))
```

```
##                       Df Sum Sq Mean Sq F value Pr(>F)
## information$group      1 0.0333 0.03331   4.520 0.0374 *
## information$age        1 0.0518 0.05177   7.024 0.0102 *
## information$gender     1 0.0011 0.00106   0.144 0.7052
## information$BMI        1 0.0027 0.00274   0.372 0.5439
## information$`SF-36`    1 0.0069 0.00690   0.936 0.3371
## information$PRI        1 0.0012 0.00117   0.159 0.6913
## information$`FS-14`    1 0.0006 0.00058   0.079 0.7799
## Residuals             63 0.4643 0.00737
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

The result showed that after eliminating influences of age, gender, BMI, SF-36, PRI and FS-14, the mean thickness of 12-cortical network was significant between groups (P = 0.037).

2.2.2 Analysis 2 - GLM analysis for 5-cortical network

General linear model analysis was used. We took the base information into analysis, including age, gender and BMI.

```
summary(aov(Five_cortical_network$mean ~ information$group + information$age +
              information$gender + information$BMI))
```

```
##                     Df Sum Sq Mean Sq F value Pr(>F)
## information$group    1 0.0368 0.03679   4.516 0.0373 *
## information$age      1 0.0497 0.04971   6.102 0.0161 *
## information$gender   1 0.0017 0.00165   0.203 0.6538
## information$BMI      1 0.0000 0.00000   0.000 0.9961
## Residuals           66 0.5376 0.00815
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

The result showed that after eliminating influences of age, gender and BMI, the mean thickness of 5-cortical network was significant between groups (P = 0.037).

Further, we took the base information and clinical evaluations into analysis, including age, gender, BMI, SF-36, PRI and FS-14.

```
summary(aov(Five_cortical_network$mean ~ information$group + information$age +
              information$gender + information$BMI + information$`SF-36` +
              information$PRI + information$`FS-14`))
```

```
##                       Df Sum Sq Mean Sq F value Pr(>F)
## information$group      1 0.0368 0.03679   4.376 0.0405 *
## information$age        1 0.0497 0.04971   5.913 0.0179 *
## information$gender     1 0.0017 0.00165   0.197 0.6589
## information$BMI        1 0.0000 0.00000   0.000 0.9961
## information$`SF-36`    1 0.0049 0.00494   0.588 0.4460
## information$PRI        1 0.0026 0.00263   0.313 0.5776
## information$`FS-14`    1 0.0004 0.00043   0.051 0.8221
## Residuals             63 0.5296 0.00841
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

The result showed that after eliminating influences of age, gender, BMI, SF-36, PRI and FS-14, the mean thickness of 5-cortical network was significant between groups (P = 0.041).

3. References

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