

## Supplementary

**Table S1** Correlation between processing speed and ratios of metabolite concentration distribution in the PD group.

| Variables                     | ACC_NAA:Cr         | ACC_Cho:Cr | RPF_NAA:Cr | RPF_Cho:Cr | LPF_NAA:Cr | LPF_Cho:Cr         |
|-------------------------------|--------------------|------------|------------|------------|------------|--------------------|
| Stroop A completion times     |                    |            |            |            |            |                    |
| Rho                           | -0.253             | 0.072      | -0.154     | -0.055     | -0.083     | -0.067             |
| P                             | 0.055 <sup>a</sup> | 0.593      | 0.247      | 0.684      | 0.538      | 0.619              |
| WAIS-Digit symbol coding test |                    |            |            |            |            |                    |
| Rho                           | -0.029             | -0.067     | 0.342      | 0.112      | 0.110      | 0.236              |
| P                             | 0.827              | 0.615      | 0.009*     | 0.404      | 0.409      | 0.074 <sup>a</sup> |

<sup>a</sup>, trend-level, 0.05<P<0.1; \*, P<0.05. PD, Parkinson disease; ACC, anterior cingulate cortex; RPF, right prefrontal cortex; LPF, left prefrontal cortex; Cho, choline-containing compounds; Cr, creatine; NAA, N-acetyl-aspartate; WAIS, Wechsler Adult Intelligence Scale.

**Table S2** Correlation between processing speed and clinical characteristics in the PD group

| Variables                        | 1. Stroop A completion times | 2. WAIS-Digit symbol coding test | 3. Age | 4. Gender | 5. Education years | 6. MDS-UPDRS-III | 7. Modified Hoehn-Yahr scale |
|----------------------------------|------------------------------|----------------------------------|--------|-----------|--------------------|------------------|------------------------------|
| 1. Stroop A completion times     |                              |                                  |        |           |                    |                  |                              |
| Rho                              | 1                            |                                  |        |           |                    |                  |                              |
| P                                |                              |                                  |        |           |                    |                  |                              |
| 2. WAIS-Digit symbol coding test |                              |                                  |        |           |                    |                  |                              |
| Rho                              | -0.386                       | 1                                |        |           |                    |                  |                              |
| P                                | 0.003                        |                                  |        |           |                    |                  |                              |
| 3. Age                           |                              |                                  |        |           |                    |                  |                              |
| Rho                              | 0.094                        | -0.218                           | 1      |           |                    |                  |                              |
| P                                | 0.484                        | 0.100                            |        |           |                    |                  |                              |
| 4. Gender                        |                              |                                  |        |           |                    |                  |                              |
| Rho                              | -0.076                       | -0.004                           | 0.168  | 1         |                    |                  |                              |
| P                                | 0.568                        | 0.975                            | 0.209  |           |                    |                  |                              |
| 5. Education years               |                              |                                  |        |           |                    |                  |                              |
| Rho                              | -0.083                       | 0.123                            | 0.050  | -0.181    | 1                  |                  |                              |
| P                                | 0.536                        | 0.357                            | 0.712  | 0.174     |                    |                  |                              |
| 6. MDS-UPDRS-III                 |                              |                                  |        |           |                    |                  |                              |
| Rho                              | 0.220                        | -0.247                           | -0.136 | -0.023    | 0.099              | 1                |                              |
| P                                | 0.097 <sup>a</sup>           | 0.062 <sup>a</sup>               | 0.310  | 0.864     | 0.462              |                  |                              |
| 7. Modified Hoehn-Yahr scale     |                              |                                  |        |           |                    |                  |                              |
| Rho                              | 0.151                        | -0.190                           | 0.150  | 0.033     | -0.037             | 0.581            | 1                            |
| P                                | 0.259                        | 0.152                            | 0.260  | 0.808     | 0.780              | 0.000            |                              |
| 8. LEDD total                    |                              |                                  |        |           |                    |                  |                              |
| Rho                              | -0.099                       | -0.054                           | 0.070  | 0.014     | -0.039             | 0.159            | 0.273                        |
| P                                | 0.462                        | 0.685                            | 0.599  | 0.916     | 0.772              | 0.233            | 0.038*                       |

<sup>a</sup>, trend-level, 0.05<P<0.1; \*, P<0.05. PD, Parkinson disease; MDS-UPDRS-III, Movement Disorder Society-sponsored Revision of the Unified Parkinson Disease Rating Scale part III; LEDD, Levodopa equivalent daily dose; WAIS, Wechsler Adult Intelligence Scale.

**Table S3** Correlation between the metabolites in the PD group

| Variables     | 1. ACC_NAA:Cr      | 2. ACC_Cho:Cr | 3. RPF_NAA:Cr | 4. RPF_Cho:Cr      | 5. LPF_NAA:Cr |
|---------------|--------------------|---------------|---------------|--------------------|---------------|
| 1. ACC_NAA:Cr |                    |               |               |                    |               |
| Rho           |                    | 1             |               |                    |               |
| P             |                    |               |               |                    |               |
| 2. ACC_Cho:Cr |                    |               |               |                    |               |
| Rho           | 0.214              |               | 1             |                    |               |
| P             | 0.107              |               |               |                    |               |
| 3. RPF_NAA:Cr |                    |               |               |                    |               |
| Rho           | 0.218              | 0.126         |               | 1                  |               |
| P             | 0.100              | 0.347         |               |                    |               |
| 4. RPF_Cho:Cr |                    |               |               |                    |               |
| Rho           | 0.352              | 0.441         | 0.154         |                    | 1             |
| P             | 0.007*             | 0.001*        | 0.249         |                    |               |
| 5. LPF_NAA:Cr |                    |               |               |                    |               |
| Rho           | 0.164              | 0.006         | 0.485         | 0.234              |               |
| P             | 0.218              | 0.962         | 0.000*        | 0.077 <sup>a</sup> |               |
| 6. LPF_Cho:Cr |                    |               |               |                    |               |
| Rho           | 0.235              | 0.281         | 0.214         | 0.615              | 0.505         |
| P             | 0.076 <sup>a</sup> | 0.032*        | 0.106         | 0.000*             | 0.000*        |

<sup>a</sup>, trend-level, 0.05<P<0.1; \*, P<0.05. PD, Parkinson disease; ACC, anterior cingulate cortex; RPF, right prefrontal cortex; LPF, left prefrontal cortex; Cho, choline-containing compounds; Cr, creatine; NAA, N-acetyl-aspartate.

**Table S4** Multiple linear regression models testing the association between the ratios of metabolite concentrations and cognitive performance in the HC group

| Models         | $\beta$ | Std. Error | Standardized coefficient beta | t      | P value |
|----------------|---------|------------|-------------------------------|--------|---------|
| <b>Model 1</b> |         |            |                               |        |         |
| Age            | -0.077  | 0.194      | -0.082                        | -0.396 | 0.696   |
| ACC_NAA:Cr     | -0.574  | 9.016      | -0.013                        | -0.064 | 0.950   |
| ACC_Cho:Cr     | 5.265   | 8.682      | 0.123                         | 0.606  | 0.550   |
| <b>Model 2</b> |         |            |                               |        |         |
| Age            | 0.199   | 0.259      | 0.155                         | 0.769  | 0.449   |
| ACC_NAA:Cr     | -6.428  | 12.274     | -0.103                        | -0.524 | 0.605   |
| ACC_Cho:Cr     | -9.176  | 11.563     | -0.156                        | -0.794 | 0.435   |
| RPF_NAA:Cr     | 9.349   | 7.154      | 0.254                         | 1.307  | 0.203   |

In multiple linear regression model 1 and model 2, including age as covariates. Stroop A completion times as dependent variable in model 1. Digit symbol coding score as dependent variable in model 2. HC, healthy control; ACC, anterior cingulate cortex; RPF, right prefrontal cortex; LPF, left prefrontal cortex; Cho, choline-containing compounds; Cr, creatine; NAA, N-acetyl-aspartate.