Aberrant functional connectivity architecture in Alzheimer's disease and mild cognitive impairment: A whole-brain, data-driven analysis

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Table S1.

Table S1. Demographic, clinical and neuropsychological data in normal control (NC), mild cognitive impairment (MCI) and Alzheimer’s disease (AD) subjects.

|                          | NC(n=27) | MCI(n=27) | AD(n=35) | p value |
|--------------------------|----------|-----------|----------|---------|
| Gender (M/F)             | 16/11    | 13/14     | 12/23    | 0.143   |
| Age (year)               | 69.2±6.5 | 73.8±7.8  | 72.4±8.5 | 0.09    |
| MMSE                     | 28.9±1.0 | 26.8±1.8a | 19.7±4.1ab | <0.001 |
| CDR                      | 0        | 0.5       | 1.3±0.5ab | <0.001 |
| AVLT-Immediate Recall c  | 5.9±1.1  | 4.6±1.5   | 2.6±1.6ab | <0.001 |
| AVLT-Delay Recall c      | 5.8±2.0  | 3.1±2.0a  | 0.6±1.2ab | <0.001 |
| Head Motion              | 0.25±0.27| 0.16±0.10 | 0.30±0.27| 0.084   |

Chi-square was used for gender comparisons, One-way ANOVA with Bonferroni post hoc test was used for age, and neuropsychological tests comparisons.

aSignificant compared to NC. bSignificant compared to MCI. cThree AD subjects refuse to continue this test.

MMSE, mini-mental state examination; CDR, Clinical Dementia Rating; AVLT, auditory verbal learning test.

Note: For all the data was the same with our previous studies (Zhou et al., 2013, Zhang et al., 2014), hence the data information is the same with those papers.
Table S2.

Table S2. Cortical and subcortical regions defined in Automated Anatomical Labeling
template image in standard stereotaxic space

| Region Name                          | Abbreviation | MNI coordinates (L/R) |
|--------------------------------------|--------------|-----------------------|
| **Prefrontal Lobe**                  |              |                       |
| Superior frontal gyrus, dorsolateral | SFGdor       | (-17,47,13) / (18,48,14) |
| Superior frontal gyrus, orbital      | SFGorb       | (-5,49,31) / (9,51,30) |
| Superior frontal gyrus, medial       | SFGmed       | (-5,54,7) / (8,52,7)   |
| Superior frontal gyrus, medial orbital | SFGmorb     | (-33,33,35) / (38,33,34) |
| Middle frontal gyrus                 | MFG          | (-31,50,10) / (33,53,11) |
| Middle frontal gyrus, orbital        | MFGorb       | (-48,13,19) / (50,15,21) |
| Inferior frontal gyrus, opercular    | IFGoper      | (-46,30,14) / (50,30,14) |
| Inferior frontal gyrus, triangular   | IFGtri       | (-36,31,12) / (41,32,12) |
| Inferior frontal gyrus, orbital      | IFGorb       | (-5,37,18) / (8,36,18)  |
| Gyrus rectus                         | REG          | (-4,35,14) / (8,37,16)  |
| Anterior cingulate gyrus             | ACC          | (-8,15,11) / (10,16,11) |
| Olfactory cortex                     | OLF          | (-18,35,42) / (22,31,44) |
| **Other Prefrontal Lobe**            |              |                       |
| Precentral gyrus                     | PreCG        | (-39,-6,51) / (41,-8,52) |
| Supplementary motor area             | SMA          | (-5,5,61) / (9,6,62)    |
| Rolandic operculum                   | ROL          | (-47,-8,14) / (53,-6,15) |
| Median- and para-cingulate gyrus     | MCC          | (-5,-15,42) / (8,-9,40) |
| **Occipital Lobe**                   |              |                       |
| Calcarine fissure and surrounding cortex | CAL         | (-7,-79,6) / (16,-73,9) |
| Cuneus                               | CUN          | (-6,-80,27) / (14,-79,28) |
| Lingual gyrus                        | LING         | (-15,-68,5) / (16,-67,4) |
| Superior occipital gyrus             | SOG          | (-17,-84,28) / (24,-81,31) |
| Middle occipital gyrus               | MOG          | (-32,-81,16) / (37,-80,19) |
| Inferior occipital gyrus             | IOG          | (-36,-78,8) / (38,-82,8) |
| Fusiform gyrus                       | FG           | (-31,-40,20) / (34,-39,20) |
| **Parietal Lobe**                    |              |                       |
| Superior parietal gyrus              | SPG          | (-23,-60,59) / (26,-59,62) |
| Paracentral lobule                   | PCL          | (-7,-56,48) / (10,-56,44) |
| Postcentral gyrus                    | PoCG         | (-42,-23,49) / (41,-25,53) |
| Inferior parietal gyrus              | IPG          | (-43,-46,47) / (46,-46,50) |
| Supramarginal gyrus                  | SMG          | (-56,-34,30) / (58,-32,34) |
| Angular gyrus                        | ANG          | (-44,-61,36) / (46,-60,39) |
| Precuneus                            | PCNU         | (-8,-25,70) / (7,-32,68) |
| Posterior cingulate gyrus            | PCC          | (-5,-43,25) / (7,-42,22)  |
| **Insula**                           | INS          | (-35,7,3) / (39,6,2)    |
| Region                              | Abbreviation | Coordinates        |
|------------------------------------|--------------|--------------------|
| **Thalamus**                       | THA          | (-11,-18,8)/ (13,-18,8) |
| **Temporal Lobe**                  |              |                    |
| Superior temporal gyrus            | STG          | (-53,-21,7)/ (58,-22,7) |
| Superior temporal gyrus, temporal pole | STGp       | (-40,15,-20)/ (48,15,-17) |
| Middle temporal gyrus              | MTG          | (-56,-34,-2)/ (57,-37,-1) |
| Middle temporal gyrus, temporal pole | MTGp      | (-36,15,-34)/ (44,15,-32) |
| Inferior temporal gyrus            | ITG          | (-50,-28,-23)/ (54,-31,-22) |
| Heschl gyrus                       | HES          | (-42,-19,10)/ (46,-17,10) |
| Hippocampus                        | HIP          | (-25,-21,-10)/ (29,-20,-10) |
| Parahippocampal gyrus              | PHIP         | (-21,-16,-21)/ (25,-15,-20) |
| Amygdala                           | AMYG         | (-23,-1,-17)/ (27,1,-18)  |
| **Basal Ganglia**                  |              |                    |
| Caudate nucleus                    | CAU          | (-11,11,9)/ (15,12,9)  |
| Lenticular nucleus, putamen        | PUT          | (-24,4,2)/ (28,5,2)    |
| Lenticular nucleus, pallidum       | PAL          | (-18,0,0)/ (21,0,0)    |

Note: The abbreviations listed are those used in this paper, which differ slightly from the original abbreviations by Tzourio-Mazoyer et al. (2002). And the center of mass coordinates are the same with Liu et al. (2007).

MNI: Montreal Neurological Institute.
### Table S3

Table S3, The impaired connectivity AD, also the correlation between MMSE and strength of the functional connectivity.

| Node_1   | Node_2  | P       | NC_mea m | NC_sd  | MCI mean | MCI sd  | AD mean | AD sd  | MMSE MC_ZR | MMSE MC_P | MMSE AD_ZR | MMSE AD_P | MMSE MC_AD_ZR | MMSE MC_AD_P | Type   |
|----------|---------|---------|----------|--------|----------|---------|---------|--------|------------|-----------|------------|-----------|----------------|---------------|--------|
| SFGmed.R | PCC.R   | 0.00042 | 0.538    | 0.284  | 0.472    | 0.226   | 0.229   | 0.351  | 0.344       | 0.389     | 0.021      | 0.513     | 0.000          | PreF-P        |        |
| MCC.R    | MOG.R   | 0.00076 | 0.403    | 0.291  | 0.384    | 0.249   | 0.135   | 0.298  | 0.248       | 0.212     | 0.189      | 0.276     | 0.421          | OthF-O        |        |
| MCC.R    | CAL.R   | 0.0011  | 0.339    | 0.273  | 0.271    | 0.233   | 0.017   | 0.324  | 0.230       | 0.248     | 0.177      | 0.310     | 0.410          | OthF-O        |        |
| PCC.R    | MTG.R   | 0.0005  | 0.471    | 0.278  | 0.409    | 0.208   | 0.167   | 0.264  | 0.144       | 0.472     | 0.132      | 0.448     | 0.408          | P-T           |        |
| MCC.R    | CUN.R   | 0.0006  | 0.459    | 0.257  | 0.394    | 0.213   | 0.153   | 0.291  | 0.296       | 0.134     | 0.121      | 0.489     | 0.402          | OthF-O        |        |
| MCC.R    | MTG.L   | 0.0010  | 0.415    | 0.265  | 0.362    | 0.249   | 0.128   | 0.272  | 0.279       | 0.158     | 0.141      | 0.419     | 0.402          | P-T           |        |
| MCC.R    | CAL.L   | 0.00147 | 0.411    | 0.342  | 0.328    | 0.310   | 0.127   | 0.326  | 0.192       | 0.338     | 0.262      | 0.129     | 0.372          | OthF-O        |        |
| MCC.R    | PCUN.R  | 0.0021  | 0.734    | 0.276  | 0.684    | 0.237   | 0.462   | 0.263  | 0.296       | 0.134     | 0.072      | 0.681     | 0.370          | OthF-P        |        |
| ROL.R    | HES.L   | 0.0023  | 0.492    | 0.250  | 0.371    | 0.298   | 0.198   | 0.320  | 0.106       | 0.599     | 0.321      | 0.060     | 0.365          | OthF-T        |        |
| MCC.R    | PCUN.L  | 0.00174 | 0.665    | 0.289  | 0.593    | 0.246   | 0.419   | 0.295  | 0.306       | 0.120     | 0.206      | 0.236     | 0.364          | OthF-P        |        |
| CUN.L    | MTG.L   | 0.0030  | 0.338    | 0.307  | 0.251    | 0.267   | 0.051   | 0.281  | 0.082       | 0.218     | 0.218      | 0.080     | 0.364          | O-P           |        |
| MCC.R    | SOG.L   | 0.00091 | 0.332    | 0.320  | 0.222    | 0.219   | 0.067   | 0.276  | 0.252       | 0.206     | 0.226      | 0.191     | 0.362          | OthF-O        |        |
| IFGoper.L| SMG.R   | 0.00185 | 0.659    | 0.366  | 0.611    | 0.232   | 0.377   | 0.315  | 0.101       | 0.617     | 0.129      | 0.460     | 0.357          | PreF-P        |        |
| PCC.R    | PCUN.L  | 0.00043 | 0.560    | 0.253  | 0.441    | 0.260   | 0.310   | 0.268  | 0.386       | 0.047     | 0.239      | 0.166     | 0.349          | P-P           |        |
| SFGmed.R | ITG.L   | 0.00134 | 0.415    | 0.249  | 0.313    | 0.240   | 0.200   | 0.249  | 0.343       | 0.080     | 0.270      | 0.116     | 0.347          | PreF-T        |        |
| MCC.R    | HES.L   | 0.00048 | 0.345    | 0.308  | 0.242    | 0.292   | 0.075   | 0.268  | 0.110       | 0.587     | 0.240      | 0.165     | 0.335          | OthF-T        |        |
| MCC.L    | CUN.R   | 0.00109 | 0.438    | 0.255  | 0.364    | 0.226   | 0.185   | 0.310  | 0.360       | 0.065     | 0.124      | 0.478     | 0.334          | OthF-O        |        |
|        | PCUN.R | HES.L | STG.R | 0.00092 | 0.638 | 0.349 | 0.036 | 0.294 | 0.276 | 0.097 | 0.297 | 0.148 | 0.461 | 0.200 | 0.248 | 0.322 | 0.011 | OthF-O | 0.315 | 0.13 | PreF-T | 0.324 | 0.010 | T-T | 0.000 | 0.009 | P-P |
|--------|--------|-------|-------|---------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| MCC.L | CUN.L | 0.00049 | 0.376 | 0.294 | 0.267 | 0.286 | 0.097 | 0.297 | 0.148 | 0.461 | 0.200 | 0.248 | 0.322 | 0.011 | OthF-O | 0.315 | 0.13 | PreF-T | 0.324 | 0.010 | T-T | 0.000 | 0.009 | P-P |
| SFGmed.R | MTG.R | 0.00009 | 0.706 | 0.305 | 0.534 | 0.281 | 0.380 | 0.302 | -0.022 | 0.915 | 0.275 | 0.110 | 0.066 | 0.165 | 0.314 | 0.066 | 0.324 | 0.010 | T-T | 0.000 | 0.009 | P-P |
| CAL.R | MTG.L | 0.00174 | 0.461 | 0.299 | 0.344 | 0.311 | 0.191 | 0.339 | 0.101 | 0.615 | 0.269 | 0.118 | 0.031 | 0.133 | 0.013 | O-P | 0.307 | 0.015 | OthF-O | 0.300 | 0.018 | OthF-O | 0.000 | 0.009 | P-P |
| MCC.R | SOG.L | 0.00124 | 0.342 | 0.281 | 0.255 | 0.220 | 0.109 | 0.259 | -0.038 | 0.850 | 0.205 | 0.237 | 0.030 | 0.007 | 0.018 | OthF-O | 0.286 | 0.024 | O-P | 0.280 | 0.027 | OthF-T | 0.000 | 0.009 | P-P |
| CUN.L | SFG.L | 0.00095 | 0.304 | 0.287 | 0.225 | 0.312 | 0.049 | 0.285 | 0.188 | 0.349 | 0.066 | 0.707 | 0.133 | 0.036 | 0.036 | O-P | 0.267 | 0.036 | OthF-O | 0.274 | 0.031 | OthF-O | 0.000 | 0.009 | P-P |
| SFG.L | MFG.L | 0.0027 | 0.822 | 0.275 | 0.953 | 0.336 | 0.131 | 0.337 | 0.155 | 0.440 | -0.214 | 0.218 | -0.264 | 0.035 | PreF-PreF | 0.263 | 0.039 | OthF-O | 0.261 | 0.041 | T-O | 0.000 | 0.009 | P-P |
| SMA.R | SOG.L | 0.00039 | 0.346 | 0.219 | 0.228 | 0.208 | 0.115 | 0.256 | 0.214 | 0.283 | 0.124 | 0.477 | 0.278 | 0.029 | T-B | 0.278 | 0.029 | OthF-T | 0.277 | 0.029 | OthF-T | 0.000 | 0.009 | P-P |
| HIP.R | CAU.R | 0.00012 | 0.207 | 0.196 | 0.094 | 0.273 | -0.048 | 0.272 | 0.246 | 0.216 | 0.116 | 0.507 | 0.076 | 0.225 | 0.013 | PreF-T | 0.261 | 0.041 | OthF-O | 0.260 | 0.041 | OthF-O | 0.000 | 0.009 | P-P |
| MCC.R | STG.L | 0.00005 | 0.508 | 0.385 | 0.282 | 0.352 | 0.129 | 0.297 | 0.158 | 0.432 | 0.185 | 0.289 | 0.277 | 0.016 | 0.076 | T-O | 0.261 | 0.041 | OthF-O | 0.260 | 0.041 | OthF-O | 0.000 | 0.009 | P-P |
| MCC.R | LG.R | 0.00019 | 0.374 | 0.312 | 0.246 | 0.248 | 0.063 | 0.300 | 0.075 | 0.711 | 0.071 | 0.686 | 0.274 | 0.031 | 0.031 | OthF-O | 0.267 | 0.036 | OthF-O | 0.250 | 0.050 | OthF-OthF | 0.000 | 0.009 | P-P |
| LG.R | HES.L | 0.00156 | 0.323 | 0.259 | 0.207 | 0.248 | 0.084 | 0.297 | 0.208 | 0.299 | 0.144 | 0.409 | 0.260 | 0.041 | OthF-OthF | 0.250 | 0.050 | OthF-OthF | 0.244 | 0.056 | PreF-O | 0.000 | 0.009 | P-P |
| ROL.R | MCC.R | 0.00015 | 0.447 | 0.302 | 0.294 | 0.301 | 0.140 | 0.291 | 0.089 | 0.660 | 0.111 | 0.525 | 0.250 | 0.050 | 0.050 | OthF-OthF | 0.244 | 0.056 | PreF-O | 0.244 | 0.056 | OthF-OthF | 0.000 | 0.009 | P-P |
| SMA.R | CAL.R | 0.00127 | 0.400 | 0.221 | 0.244 | 0.266 | 0.177 | 0.282 | 0.059 | 0.771 | 0.297 | 0.083 | 0.244 | 0.056 | 0.056 | PreF-O | 0.244 | 0.056 | OthF-OthF | 0.244 | 0.056 | OthF-OthF | 0.000 | 0.009 | P-P |
| HIP.L | SOG.L | 0.00043 | 0.272 | 0.225 | 0.158 | 0.291 | 0.041 | 0.254 | 0.149 | 0.457 | 0.144 | 0.408 | 0.244 | 0.056 | 0.056 | PreF-O | 0.244 | 0.056 | OthF-OthF | 0.244 | 0.056 | OthF-OthF | 0.000 | 0.009 | P-P |
| MCC.R | STG.R | 0.00001 | 0.621 | 0.366 | 0.327 | 0.339 | 0.210 | 0.320 | 0.079 | 0.696 | 0.188 | 0.279 | 0.230 | 0.073 | 0.073 | OthF-T | 0.229 | 0.074 | OthF-O | 0.222 | 0.083 | OthF-T | 0.000 | 0.009 | P-P |
| SFGmed.R | PHIP.L | 0.00005 | 0.332 | 0.261 | 0.181 | 0.225 | 0.034 | 0.273 | 0.374 | 0.054 | -0.076 | 0.663 | 0.217 | 0.090 | 0.090 | PreF-T | 0.217 | 0.090 | PreF-T | 0.217 | 0.090 | PreF-T | 0.000 | 0.009 | P-P |
|            | CUN.R |     |     |     |     |     |     |     |     |     |     |     |     |     |
|------------|-------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| PHIP.L     | 0.000170 | 0.298 | 0.227 | 0.218 | 0.271 | 0.089 | 0.261 | 0.297 | 0.132 | -0.007 | 0.969 | 0.216 | 0.091 |
| HES.L      | 0.00055 | 0.815 | 0.311 | 0.643 | 0.388 | 0.501 | 0.354 | 0.230 | 0.248 | -0.076 | 0.665 | 0.211 | 0.100 |
| LG.R       | 0.00166 | 0.524 | 0.299 | 0.375 | 0.334 | 0.263 | 0.316 | 0.070 | 0.727 | 0.123 | 0.481 | 0.193 | 0.133 |
| PHIP.L     | 0.00105 | 0.310 | 0.242 | 0.226 | 0.314 | 0.094 | 0.246 | 0.251 | 0.207 | -0.052 | 0.766 | 0.191 | 0.136 |
| SFGmed.R   | 0.00008 | 0.278 | 0.213 | 0.126 | 0.202 | 0.018 | 0.258 | 0.293 | 0.138 | -0.024 | 0.892 | 0.191 | 0.137 |
| ROLL       | 0.00124 | 0.722 | 0.302 | 0.488 | 0.414 | 0.421 | 0.378 | 0.306 | 0.121 | 0.163 | 0.350 | 0.189 | 0.141 |
| PCC.L      | 0.00011 | 1.141 | 0.277 | 0.918 | 0.315 | 0.821 | 0.320 | 0.441 | 0.021 | 0.010 | 0.955 | 0.185 | 0.151 |
| INS.L      | 0.00088 | 1.075 | 0.341 | 0.845 | 0.258 | 0.776 | 0.329 | 0.198 | 0.322 | 0.114 | 0.513 | 0.172 | 0.182 |
| MCC.L      | 0.00066 | 0.603 | 0.440 | 0.331 | 0.320 | 0.238 | 0.361 | 0.187 | 0.350 | 0.084 | 0.629 | 0.168 | 0.192 |
| HES.L      | 0.00112 | 0.802 | 0.428 | 0.577 | 0.433 | 0.478 | 0.320 | 0.079 | 0.694 | 0.122 | 0.485 | 0.162 | 0.208 |
| HIP.L      | 0.00160 | 0.302 | 0.278 | 0.143 | 0.281 | 0.056 | 0.301 | -0.113 | 0.573 | 0.118 | 0.500 | 0.149 | 0.248 |
| SFGmed.R   | 0.00169 | 0.271 | 0.252 | 0.163 | 0.196 | 0.081 | 0.203 | -0.050 | 0.804 | 0.016 | 0.927 | 0.146 | 0.256 |
| FGL        | 0.00108 | 0.575 | 0.313 | 0.400 | 0.286 | 0.291 | 0.330 | 0.073 | 0.717 | -0.002 | 0.989 | 0.135 | 0.296 |
| IFGoper.L  | 0.00050 | 0.556 | 0.309 | 0.323 | 0.261 | 0.306 | 0.225 | 0.018 | 0.930 | 0.220 | 0.204 | 0.128 | 0.323 |
| ROLL       | 0.00042 | 0.709 | 0.331 | 0.494 | 0.417 | 0.386 | 0.344 | -0.045 | 0.824 | 0.058 | 0.741 | 0.122 | 0.346 |
| ROL.R      | 0.00094 | 0.813 | 0.325 | 0.556 | 0.346 | 0.530 | 0.311 | 0.273 | 0.168 | 0.097 | 0.580 | 0.120 | 0.353 |
| IFGoper.L  | 0.00128 | 0.569 | 0.293 | 0.349 | 0.227 | 0.311 | 0.302 | 0.146 | 0.466 | 0.058 | 0.741 | 0.102 | 0.431 |
| PHIP.R     | 0.00084 | 0.329 | 0.242 | 0.143 | 0.342 | 0.122 | 0.221 | 0.177 | 0.378 | -0.411 | 0.014 | -0.094 | 0.466 |
| PHIP.L     | 0.00007 | 0.301 | 0.230 | 0.088 | 0.240 | 0.018 | 0.278 | 0.120 | 0.550 | -0.057 | 0.744 | 0.085 | 0.512 |
| SMA.L      | 0.00010 | 0.425 | 0.237 | 0.164 | 0.301 | 0.172 | 0.237 | 0.129 | 0.523 | -0.226 | 0.192 | -0.084 | 0.518 |
| Rectus_L   | 0.00090 | 0.363 | 0.266 | 0.167 | 0.284 | 0.122 | 0.271 | 0.167 | 0.406 | -0.007 | 0.969 | 0.083 | 0.523 |
| PHIP.L     | 0.00087 | 0.513 | 0.281 | 0.316 | 0.231 | 0.253 | 0.297 | 0.297 | 0.133 | -0.095 | 0.587 | 0.075 | 0.560 |
| SFG.R      | 0.00083 | 0.264 | 0.227 | 0.111 | 0.309 | 0.039 | 0.265 | 0.188 | 0.348 | -0.111 | 0.525 | 0.074 | 0.566 |
| PHIP.L     | 0.00010 | 0.273 | 0.221 | 0.108 | 0.263 | 0.032 | 0.230 | 0.076 | 0.706 | -0.118 | 0.499 | 0.072 | 0.578 |
| SFGmed.R   | 0.00004 | 0.287 | 0.248 | 0.107 | 0.224 | 0.020 | 0.229 | 0.236 | 0.236 | -0.228 | 0.189 | 0.066 | 0.612 |
Note: The abbreviations are listed in Table S2.

Color Fonts mean the strength of the impaired functional connectivity significant correlated with MMSE.
Figure S1. Distributed of the impaired functional connectivity in AD. Each line indicates the mean strength of the functional connectivity between each pair of brain regions. Blue lines represent inter connectivity between lobs and grey lines mean intra connectivity within the defined lobes in Table S2. Detail for these connectivity and it’s related to MMSE can be found at Table S3 and Figure 3.
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