**SUPPLEMENTARY METHODS**

**Description of Network Metrics**

*Degree, strength, density and hubs*

The degree of a node (Deg) is the number of edges connected to it. The global degree of the network is the average degree over all nodes. The density (Dens) indicates the proportion of existing connections over the total possible connections. Similarly, the strength of a node (Sw) is given by the column sum of W.

*Clustering coefficient*

The clustering coefficient of a node (CC) is given by the proportion of edges connecting its neighbors over the total possible number between them. It is computed as:

where *degi* indicates the degree of node i [1]. For weighted graphs, the clustering coefficient (CCw) is computed simply by using W instead of A [2]. The global clustering coefficient is given by the average CC over all nodes.

*Distance measures and characteristic path length*

The length of every edge in a network is given by the inverse of its weight. In binary networks each edge has length 1. The distance function of a network gives the length of the shortest path between any two nodes. The average shortest path length (L) over all pairs of nodes is called characteristic path length [1].

*Efficiency*

The global efficiency (Eff) is a measure of the functional integration in the network, which is the ability of fast communication also between distributed regions. Global efficiency is the average node efficiency computed as

where *distij* is the length of the shortest path between i and j (computed for A or W) and N is the total number of nodes [3].

**REFERENCES**

[1] Watts DJ, Strogatz SH (1998) Collective dynamics of 'small-world' networks. *Nature* **393**, 440-442.

[2] Onnela JP, Saramaki J, Kertesz J, Kaski K (2005) Intensity and coherence of motifs in weighted complex networks. *Phys Rev E Stat Nonlin Soft Matter Phys* **71**, 065103.

[3] Latora V, Marchiori M (2001) Efficient behavior of small-world networks. *Phys Rev Lett* **87**, 198701.

Supplementary Table 1: Region of interest names and associated labels of the Destrieux atlas of Freesurfer.

|  |  |  |  |
| --- | --- | --- | --- |
| **LABEL** | **Region of interest name** | **LABEL** | **Region of interest name** |
| FT | G\_and\_S\_frontomargin | Tm | G\_temporal\_middle |
| oi | G\_and\_S\_occipital\_inf | Lh | Lat\_Fis-ant-Horizont |
| PC | G\_and\_S\_paracentral | Lv | Lat\_Fis-ant-Vertical |
| SC | G\_and\_S\_subcentral | Lp | Lat\_Fis-post |
| tF | G\_and\_S\_transv\_frontopol | PO | Pole\_occipital |
| CA | G\_and\_S\_cingul-Ant | PTp | Pole\_temporal |
| Ca | G\_and\_S\_cingul-Mid-Ant | CL | S\_calcarine |
| Cp | G\_and\_S\_cingul-Mid-Post | CE | S\_central |
| Cd | G\_cingul-Post-dorsal | CM | S\_cingul-Marginalis |
| Cv | G\_cingul-Post-ventral | ia | S\_circular\_insula\_ant |
| CN | G\_cuneus | ii | S\_circular\_insula\_inf |
| OP | G\_front\_inf-Opercular | Is | S\_circular\_insula\_sup |
| IO | G\_front\_inf-Orbital | tva | S\_collat\_transv\_ant |
| TR | G\_front\_inf-Triangul | tvp | S\_collat\_transv\_post |
| Fm | G\_front\_middle | Fi | S\_front\_inf |
| Fs | G\_front\_sup | fm | S\_front\_middle |
| in | G\_Ins\_lg\_and\_S\_cent\_ins | fs | S\_front\_sup |
| is | G\_insular\_short | PJ | S\_interm\_prim-Jensen |
| om | G\_occipital\_middle | IP | S\_intrapariet\_and\_P\_trans |
| os | G\_occipital\_sup | OL | S\_oc\_middle\_and\_Lunatus |
| TF | G\_oc-temp\_lat-fusifor | ST | S\_oc\_sup\_and\_transversal |
| TL | G\_oc-temp\_med-Lingual | oa | S\_occipital\_ant |
| TmP | G\_oc-temp\_med-Parahip | Cl | S\_oc-temp\_lat |
| OB | G\_orbital | tl | S\_oc-temp\_med\_and\_Lingual |
| Pa | G\_pariet\_inf-Angular | Ol | S\_orbital\_lateral |
| PS | G\_pariet\_inf-Supramar | OF | S\_orbital\_med-olfact |
| Ps | G\_parietal\_sup | HS | S\_orbital-H\_Shaped |
| Pp | G\_postcentral | PO | S\_parieto\_occipital |
| Pc | G\_precentral | PE | S\_pericallosal |
| Pu | G\_precuneus | pC | S\_postcentral |
| RT | G\_rectus | ci | S\_precentral-inf-part |
| sC | G\_subcallosal | Cs | S\_precentral-sup-part |
| TT | G\_temp\_sup-G\_T\_transv | sO | S\_suborbital |
| Tl | G\_temp\_sup-Lateral | sP | S\_subparietal |
| TP | G\_temp\_sup-Plan\_polar | ti | S\_temporal\_inf |
| Tt | G\_temp\_sup-Plan\_tempo | Ts | S\_temporal\_sup |
| Tinf | G\_temporal\_inf | tt | S\_temporal\_transverse |

Supplementary Table 2: Overview of the grey matter atrophy of the Alzheimer’s disease and semantic dementia groups. The number of voxels with significantly reduced volume per region as well as the percentage of coverage of that region are listed. The regions of interest match those of the Destrieux atlas used in this study and reported regions showed significant differences in at least 50 voxels and >1% of the region.

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **HC - AD** | | | | **HC - SD** | | | | **AD - SD** | | | |
|  | **LH** | | **RH** | | **LH** | | **RH** | | **LH** | | **RH** | |
| **Region of interest name** | **# of voxels** | **% coverage** | **# of voxels** | **% coverage** | **# of voxels** | **% coverage** | **# of voxels** | **% coverage** | **# of voxels** | **% coverage** | **# of voxels** | **% coverage** |
| **Frontal lobe** |  |  |  |  |  |  |  |  |  |  |  |  |
| Superior frontal sulcus |  |  | 109 | 2.9 |  |  |  |  |  |  |  |  |
| Inferior precentral sulcus |  |  | 103 | 4.6 |  |  |  |  |  |  |  |  |
| Orbital gyrus |  |  |  |  | 167 | 3.5 | 185 | 3.6 | 189 | 4.0 |  |  |
| Medial orbital olfactory sulcus |  |  |  |  | 155 | 18.6 |  |  |  |  |  |  |
| Rectus gyrus |  |  |  |  |  |  | 190 | 15.1 |  |  |  |  |
| Subcallosal gyrus |  |  |  |  |  |  | 74 | 21.9 |  |  |  |  |
| **Temporal lobe (including occipital lobe)** |  |  |  |  |  |  |  |  |  |  |  |  |
| Temporal pole |  |  | 78 | 1.8 | 2998 | 65.4 | 2362 | 53.5 | 3022 | 65.9 | 314 | 7.1 |
| Superior temporal gyrus / polar planum | 82 | 8.7 | 55 | 4.7 | 702 | 74.5 | 862 | 73.4 | 784 | 82.2 | 380 | 32.4 |
| Lateral superior temporal gyrus |  |  |  |  | 1242 | 28.1 | 953 | 23.4 | 1105 | 25.2 | 167 | 4.1 |
| Superior temporal sulcus |  |  | 146 | 1.9 | 142 | 2.1 | 948 | 12.2 | 164 | 2.4 |  |  |
| Middle temporal gyrus |  |  |  |  | 1055 | 20.3 | 747 | 12.4 | 576 | 11.1 |  |  |
| Inferior temporal gyrus |  |  |  |  | 880 | 16.9 | 520 | 9.8 | 763 | 14.7 |  |  |
| Inferior temporal sulcus |  |  |  |  | 273 | 27.3 | 162 | 13.8 | 157 | 14.1 |  |  |
| Hippocampus | 397 | 34.5 | 91 | 9.7 | 611 | 53.1 | 417 | 44.4 |  |  |  |  |
| Medial occipital-temporal parahippocampal gyrus | 111 | 4.6 | 232 | 8.5 | 768 | 31.9 | 858 | 31.6 | 604 | 25.1 |  |  |
| Medial occipital-temporal lingual sulcus |  |  |  |  |  |  |  |  | 102 | 4.9 |  |  |
| Lateral occipital-temporal fusiform gyrus |  |  |  |  | 79 | 2.5 | 50 | 1.8 | 108 | 3.6 |  |  |
| Lateral occipital-temporal sulcus |  |  |  |  |  |  | 81 | 8.6 |  |  |  |  |
| Anterior transverse collateral sulcus |  |  |  |  | 867 | 69.4 | 875 | 67.7 | 768 | 61.4 | 247 | 19.1 |
| Amygdala | 308 | 90.9 | 202 | 69.9 | 339 | 100 | 286 | 99.0 | 120 | 35.4 |  |  |
| Putamen |  |  |  |  |  |  |  |  |  |  |  |  |
| **Parietal lobe** |  |  |  |  |  |  |  |  |  |  |  |  |
| Inferior parietal supramar gyrus |  |  |  |  | 72 | 1.4 |  |  |  |  |  |  |
| **Insular cortex** |  |  |  |  |  |  |  |  |  |  |  |  |
| Short insular gyrus |  |  |  |  | 665 | 48.4 |  |  | 150 | 10.9 |  |  |
| Long insular gyrus / central insular sulcus |  |  |  |  | 385 | 47.7 | 279 | 36.5 | 172 | 21.3 |  |  |
| Superior circular insular sulcus |  |  |  |  | 62 | 3.4 |  |  |  |  |  |  |
| Inferior circular insular sulcus |  |  |  |  | 813 | 45.7 | 483 | 31.7 | 791 | 44.5 | 75 | 4.9 |

AD, Alzheimer’s disease; SD, semantic dementia; HC, healthy controls; LH, left hemisphere; RH, right hemisphere.

Supplementary Table 3: Comparison of global network metrics between the groups (ACN 2000).

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **HC** | **AD** | **SD** | **p-val**  **HC/AD** | **p-val**  **HC/SD** |  | **p-val**  **HC/AD** | **p-val**  **HC/SD** |
| **Dens** | 0.15±0.02 | 0.13±0.01 | 0.12±0.01 | 0.0005\* | 0.0020\* |  | 0.0002\* | 0.0056\* |
| **Eff** | 0.52±0.02 | 0.49±0.02 | 0.48±0.02 | 0.0001\* | 0.0004\* |  | <0.0001\* | 0.0020\* |
| **CC** | 0.63±0.02 | 0.62±0.02 | 0.61±0.01 | 0.14 | 0.09 |  | NS | 0.023\* |
| **L** | 2.22±0.09 | 2.38±0.12 | 2.39±0.08 | 0.0001\* | 0.0005\* |  | <0.0001\* | 0.0016\* |
| **Sw** | (1.4±0.3) x 106 | (1.1±0.2) x 106 | (1.1±0.2) x 106 | 0.0006\* | 0.0205\* |  | 0.0008\* | 0.0112\* |
| **Effw** | (5.9±1.0) x 104 | (4.3±0.8) x 104 | (4.6±0.7) x 104 | 0.0001\* | 0.0137\* |  | <0.0001\* | 0.0036\* |
| **CCw** | 0.015±0.003 | 0.017±0.003 | 0.019±0.003 | 0.0915 | 0.0398\* |  | NS | NS |
| **Lw** | (0.26±0.05) x 10-4 | (0.37±0.08) x 10-4 | (0.34±0.06) x 10-4 | <0.0001\* | 0.0019\* |  | 0.0001\* | 0.0002\* |

Mean values and standard deviation of the global network metrics for the groups healthy controls, Alzheimer’s disease, and semantic dementia, respectively, and output of the group comparisons corrected for multiple testing (columns 4 and 5) and additionally corrected for age and sex (columns 6 and 7). Networks were constructed with the anatomical connectivity number weighting scheme and a connectivity threshold of 2000. HC, healthy controls; AD, Alzheimer’s disease; SD, semantic dementia; Dens, density; Eff, efficiency; CC, clustering coefficient; L, characteristic path length; S, strength; w, weighted; NS, not significant

Supplementary Table 4: Comparison of global network metrics between the groups (ACN 3000).

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **HC** | **AD** | **SD** | **p-val**  **HC/AD** | **p-val**  **HC/SD** | **p-val**  **HC/AD** | **p-val**  **HC/SD** |
| **Dens** | 0.13±0.02 | 0.11±0.02 | 0.11±0.01 | <0.001 | <0.01 | <0.001 | <0.01 |
| **Eff** | 0.49±0.02 | 0.46±0.02 | 0.46±0.01 | <0.001 | <0.001 | <0.001 | <0.01 |
| **CC** | 0.63±0.02 | 0.62±0.02 | 0.61±0.01 | n.s. | n.s. | n.s. | n.s. |
| **L** | 2.34±0.10 | 2.53±0.13 | 2.53±0.08 | <0.001 | <0.001 | <0.001 | <0.01 |
| **Sw** | (1.4±0.3) x 106 | (1.1±0.2) x 106 | (1.1±0.2) x 106 | <0.001 | <0.05 | <0.001 | <0.05 |
| **Effw** | (5.83±1.0) x 104 | (4.37±0.9) x104 | (4.60±0.8) x104 | <0.001 | <0.05 | <0.0001 | <0.05 |
| **CCw** | 0.018±0.004 | 0.020±0.004 | 0.022±0.003 | n.s. | <0.05 | <0.05 | <0.05 |
| **Lw** | (0.26±0.05) x 10-4 | (0.37±0.08) x 10^-4 | (0.34±0.06) x 10-4 | <0.0001 | <0.01 | <0.0001 | <0.01 |

Mean values and standard deviation of the global network metrics for the groups healthy controls, Alzheimer’s disease, and semantic dementia, respectively, and output of the group comparisons corrected for multiple testing (columns 4 and 5) and additionally corrected for age and sex (columns 6 and 7). Networks were constructed with the anatomical connectivity number weighting scheme and connectivity threshold = 3000. HC, healthy controls; AD, Alzheimer’s disease; SD, semantic dementia; Dens, density; Eff, efficiency; CC, clustering coefficient; L, characteristic path length; S, strength; w, weighted; n.s., not significant.

Supplementary Table 5: Comparison of global network metrics between the groups (ACD 0.001).

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **HC** | **AD** | **SD** | **p-val**  **HC/AD** | **p-val**  **HC/SD** | **p-val**  **HC/AD** | **p-val**  **HC/SD** |
| **Dens** | 0.15±0.01 | 0.13±0.02 | 0.13±0.01 | <0.01 | <0.01 | <0.01 | <0.05 |
| **Eff** | 0.51±0.02 | 0.48±0.03 | 0.48±0.02 | <0.01 | <0.01 | <0.01 | <0.01 |
| **CC** | 0.61±0.02 | 0.60±0.01 | 0.60±0.02 | n.s. | n.s. | n.s. | n.s. |
| **L** | 2.26±0.10 | 2.41±0.15 | 2.43±0.09 | <0.01 | <0.01 | <0.01 | <0.01 |
| **Sw** | 0.63±0.07 | 0.56±0.10 | 0.58±0.09 | <0.05 | n.s. | <0.05 | n.s. |
| **Effw** | 0.023±0.002 | 0.020±0.003 | 0.021±0.003 | <0.01 | n.s. | <0.01 | n.s. |
| **CCw** | 0.020±0.004 | 0.022±0.006 | 0.021±0.002 | n.s. | n.s. | n.s. | n.s. |
| **Lw** | 64.2±8.3 | 78.5±16.6 | 74.0±12.0 | <0.01 | <0.05 | <0.01 | n.s. |

Mean values and standard deviation of the global network metrics for the groups healthy controls, Alzheimer’s disease, and semantic dementia, respectively, and output of the group comparisons corrected for multiple testing (columns 4 and 5) and additionally corrected for age and sex (columns 6 and 7). Networks were constructed with the anatomical connectivity density weighting scheme and connectivity threshold = 0.001. HC, healthy controls; AD, Alzheimer’s disease; SD, semantic dementia; Dens, density; Eff, efficiency; CC, clustering coefficient; L, characteristic path length; S, strength; w, weighted; n.s., not significant.

Supplementary Table 6: Overview of *P* values of the significant differences in local network strength for healthy controls versus Alzheimer’s disease and healthy controls versus semantic dementia, corrected for multiple testing. Networks were constructed with the ACN weighting scheme and a connectivity threshold of 2000.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **AD versus HC** | | **SD versus HC** | | **AD versus SD** | |
|  | **LH** | **RH** | **LH** | **RH** | **LH** | **RH** |
| **Frontal regions** |  |  |  |  |  |  |
| Transverse frontopolar gyrus and sulcus |  | <0.05 |  |  |  |  |
| Opercular inferior frontal gyrus | <0.0001 |  |  |  |  |  |
| Triangular inferior frontal gyrus | <0.0001 | <0.05 |  |  |  |  |
| Middle frontal gyrus |  | <0.01 |  |  |  |  |
| Superior frontal gyrus | <0.05 | <0.0001 |  |  |  |  |
| Inferior frontal sulcus | <0.05 | <0.05 |  |  |  |  |
| Middle frontal sulcus | <0.05 | <0.05 |  |  |  |  |
| Superior frontal sulcus | <0.05 | <0.05 |  |  |  |  |
| Lateral orbital sulcus |  | <0.05 |  |  |  |  |
| Medial orbital olfactory sulcus |  |  | <0.05 |  |  |  |
| Suborbital sulcus |  |  | <0.05 | <0.05 |  |  |
| **Occipital Regions** |  |  |  |  |  |  |
| Inferior occipital gyrus and sulcus |  | <0.0001 |  |  |  |  |
| Middle occipital gyrus |  | <0.05 |  |  |  |  |
| Superior occipital gyrus | <0.05 |  |  |  |  |  |
| Medial occipital temporal parahippocampal gyrus |  |  | <0.0001 |  | <0.0001 |  |
| Superior and transverse occipital sulcus |  | <0.05 |  |  |  |  |
| Anterior occipital sulcus |  | <0.05 |  |  |  |  |
| Lateral occipital-temporal sulcus |  |  |  | <0.05 |  |  |
| **Parietal Regions** |  |  |  |  |  |  |
| Inferior parietal angular gyrus | <0.05 | <0.0001 |  |  |  |  |
| Inferior supramarginal parietal gyrus | <0.05 | <0.05 |  |  |  |  |
| Superior parietal gyrus | <0.05 |  |  |  |  |  |
| Precuneus | <0.05 | <0.01 |  |  |  |  |
| Intraparietal sulcus |  | <0.05 |  |  |  |  |
| Subparietal sulcus | <0.05 |  |  |  |  |  |
| **Temporal Regions** |  |  |  |  |  |  |
| Lateral superior temporal gyrus | <0.05 |  | <0.0001 | <0.05 | <0.05 |  |
| Superior temporal gyrus / polar planum |  |  | <0.0001 | <0.05 | <0.0001 |  |
| Superior temporal gyrus / temporal planum | <0.05 |  | <0.05 |  |  |  |
| Inferior temporal gyrus | <0.05 | <0.05 | <0.0001 | <0.05 |  |  |
| Middle temporal gyrus | <0.05 | <0.05 | <0.01 |  |  |  |
| Temporal pole |  |  | <0.0001 | <0.01 | <0.0001 |  |
| Superior temporal sulcus | <0.05 | <0.05 | <0.01 |  |  |  |
| **Other regions** |  |  |  |  |  |  |
| Subcentral gyrus and sulcus | <0.05 |  |  |  |  |  |
| Dorsal posterior cingulate gyrus | <0.05 | <0.0001 |  |  |  |  |
| Lateral vertical anterior fissure | <0.05 |  |  |  |  |  |
| Lateral posterior fissure | <0.05 |  |  |  |  |  |
| Inferior circular insular sulcus |  |  | <0.05 | <0.05 |  |  |
| Anterior transverse collateral sulcus |  |  |  | <0.05 |  | <0.05 |
| Pericallosal sulcus |  |  | <0.01 |  |  |  |

AD, Alzheimer’s disease; SD, semantic dementia; HC, healthy controls; LH, left hemisphere; RH, right hemisphere.

Supplementary Table 7: Overview of differences in local network strength.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **AD versus HC** | | **SD versus HC** | | **AD versus SD** | |
|  | **LH** | **RH** | **LH** | **RH** | **LH** | **RH** |
| **Frontal regions** |  |  |  |  |  |  |
| Triangular inferior frontal gyrus | <0.05 |  |  |  |  |  |
| Superior frontal gyrus | <0.05 |  |  |  |  |  |
| Inferior frontal sulcus |  | <0.05 |  |  |  |  |
| **Occipital regions** |  |  |  |  |  |  |
| Inferior occipital gyrus and sulcus |  | <0.05 |  |  |  |  |
| Middle occipital gyrus |  | <0.05 |  |  |  |  |
| **Parietal regions** |  |  |  |  |  |  |
| Inferior parietal angular gyrus |  | <0.05 |  |  |  |  |
| Inferior supramarginal parietal gyrus | <0.05 |  |  |  |  |  |
| Precuneus | <0.05 | <0.05 |  |  |  |  |
| **Temporal regions** |  |  |  |  |  |  |
| Lateral superior temporal gyrus |  |  | <0.05 |  |  |  |
| Superior temporal gyrus / polar plane |  |  | <0.05 |  | <0.05 |  |
| Superior temporal gyrus / temporal plane | <0.05 |  |  |  |  |  |
| Middle temporal gyrus |  |  | <0.0001 |  |  |  |
| Temporal pole |  |  | <0.05 |  |  |  |
| **Other regions** |  |  |  |  |  |  |
| Dorsal posterior cingulate gyrus |  | <0.05 |  |  |  |  |
| Pericallosal sulcus |  |  | <0.05 |  |  |  |

p-values of the significant differences in local network strength (Sw) between the groups, corrected for multiple testing. The list of all the regions tested is given in Table 3. Networks were constructed with the anatomical connectivity density weighting scheme and a connectivity threshold of 0.001. HC, healthy controls; AD, Alzheimer’s disease; SD, semantic dementia; RH, right hemisphere; LH, left hemisphere.