

SUPPLEMENTARY METHODS

Efficiency

Given a network composed of a set of nodes and edges, shortest path length, d_{ij} , is the minimum number of edges between two nodes i and j , and the efficiency, e_{ij} , between them is defined as the inverse of shortest path length: $e_{ij} = 1/d_{ij}$, such that $0 \leq e_{ij} \leq 1$.

Average efficiency for a network component

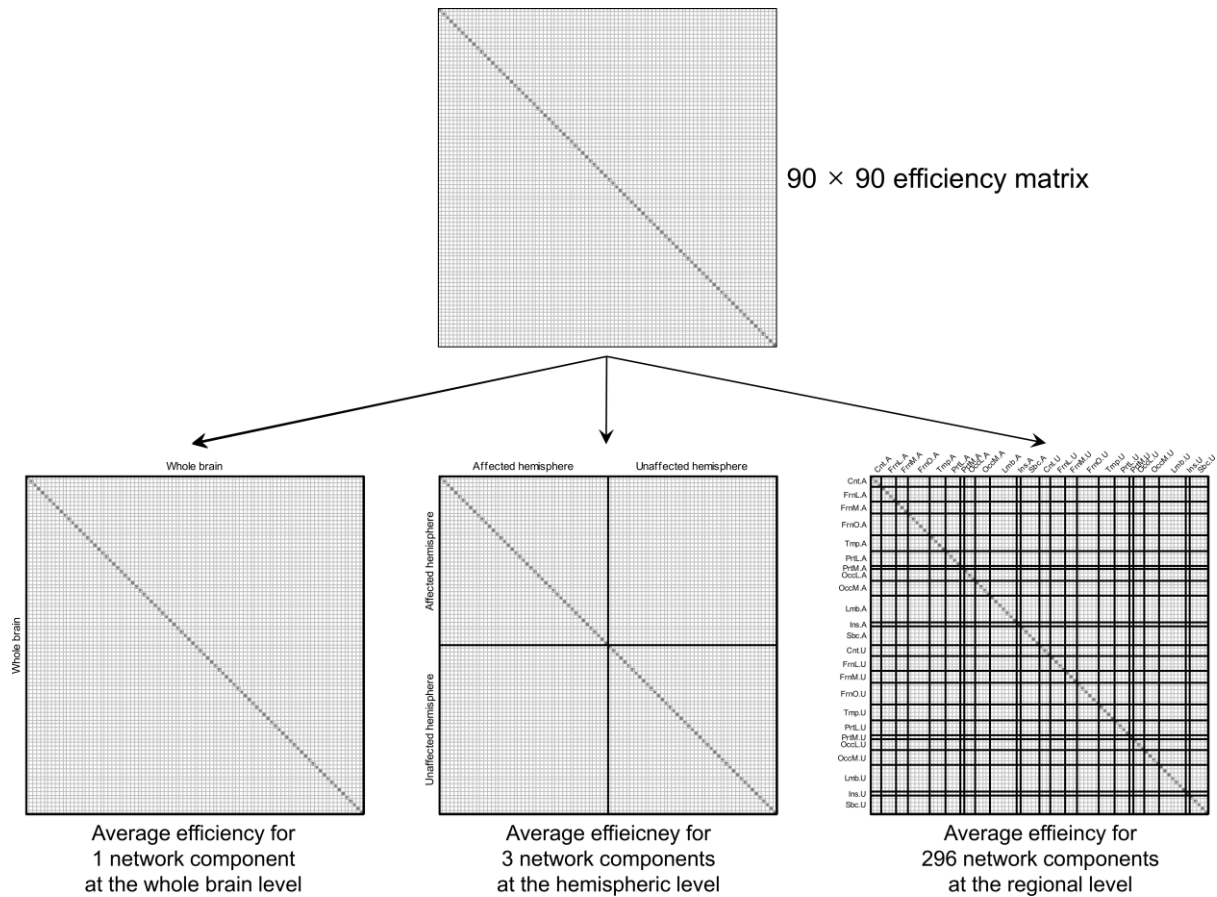
Network components were defined at different spatial levels from the whole brain level via the hemispheric level to the regional level (Supplementary Figure S1 and Supplementary Table S2): at the whole brain level, there was only one network component; at the hemispheric level, three network components, including within affected hemisphere, within unaffected hemisphere, and between hemispheres, were determined by dividing the whole brain into two hemispheres; and at the regional level, 296 network components were specified by dividing the whole brain into 12 regions in each hemisphere. The aim of considering the different spatial levels was to examine the hierarchical relationship of functional integration changes. We expected that contributions of each network component at the regional level to the whole brain changes would reveal the pattern of abnormalities.

For any network component composed of nodes, average efficiency is calculated as the average of efficiency for every pair of nodes in the network component. For instance, for the network component at the whole brain level, average efficiency can be calculated as the average of efficiency for every pair of 90 nodes in the network component.

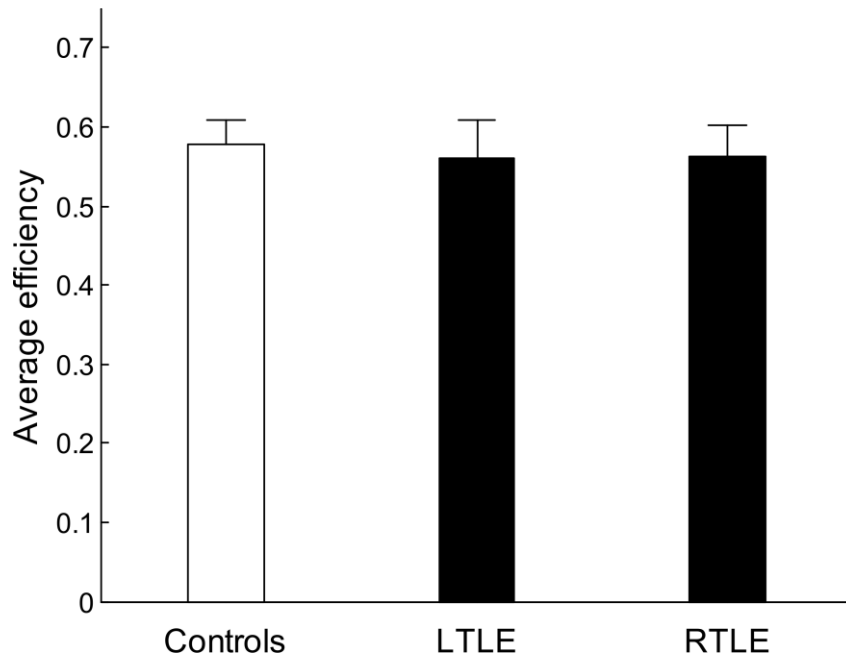
Cost-integrated measure of average efficiency

Since connection topology is inherently dependent on the sparsity or cost of a network which is defined as a proportion of the number of edges in a network {2}, a cost-integrated measure

of a network N may be computed by integrating cost-wise values over a cost domain {3}. A cost-integrated measure of average efficiency, $E(N)$, was acquired by integrating cost-wise average efficiency, $E(N, k)$ at cost k , according to a probability mass function of cost, $p(k)$, over a cost domain Ω : $E(N) = \sum_{k \in \Omega} E(N, k) p(k)$. For $p(k)$, we chose a uniform distribution over a favoured cost domain, so-called a small-world regime, across which brain networks satisfy the properties of small-world networks {4}.



SUPPLEMENTARY FIGURE S1. Calculation of the average efficiency for each subnetwork at three spatial levels. The efficiency calculated for each pair of nodes in a functional brain network yields a 90×90 efficiency matrix, and for any subnetwork composed of nodes, the average efficiency is calculated as the average of the efficiency for every pair of nodes in the subnetwork. Edges, and thus the efficiency, are not determined for diagonal elements (indicated in grey) as self-connections are not considered. The region labels are as given in Supplementary Table S1.



SUPPLEMENTARY FIGURE S2. Comparisons of the average efficiency between healthy controls and patients with left/right temporal lobe epilepsy (LTLE/RTLE) at the whole brain level. Error bars represent standard deviations.

SUPPLEMENTARY TABLE S1. Forty-five brain parcellations for each hemisphere corresponding to the nodes of functional brain networks. Each brain parcellation was assigned to one of 12 brain regions: central (Cnt), lateral frontal (FrnL), medial frontal (FrnM), orbital frontal (FrnO), temporal (Tmp), lateral parietal (PrtL), medial parietal (PrtM), lateral occipital (OccL), medial occipital (OccM), limbic (Lmb), insular (Ins), and subcortical (Sbc) regions.

| Parcellation | Region label |
|-----------------------------------------|---------------------|
| Precentral gyrus | |
| Rolandic operculum | Cnt |
| Postcentral gyrus | |
| Superior frontal gyrus, dorsolateral | |
| Middle frontal gyrus | FrnL |
| Inferior frontal gyrus, opercular part | |
| Inferior frontal gyrus, triangular part | |
| Superior frontal gyrus, medial | |
| Supplementary motor area | FrnM |
| Paracentral lobule | |
| Superior frontal gyrus, orbital part | |
| Superior frontal gyrus, medial orbital | |
| Middle frontal gyrus, orbital part | FrnO |
| Inferior frontal gyrus, orbital part | |
| Gyrus rectus | |
| Olfactory cortex | |
| Superior temporal gyrus | Tmp |

| | |
|----------------------------------------------------------|------|
| Heschl gyrus | |
| Middle temporal gyrus | |
| Inferior temporal gyrus | |
| Superior parietal gyrus | |
| Inferior parietal, but supramarginal and angular gyri | PrtL |
| Angular gyrus | |
| Supramarginal gyrus | |
| Precuneus | PrtM |
| Superior occipital gyrus | |
| Middle occipital gyrus | OccL |
| Inferior occipital gyrus | |
| Cuneus | |
| Calcarine fissure and surrounding cortex | OccM |
| Lingual gyrus | |
| Fusiform gyrus | |
| Temporal pole: superior temporal gyrus | |
| Temporal pole: middle temporal gyrus | |
| Anterior cingulate and paracingulate gyri | |
| Median cingulate and paracingulate gyri | Lmb |
| Posterior cingulate gyrus | |
| Hippocampus | |
| Parahippocampal gyrus | |
| Insula | Ins |

Amygdala

Caudate nucleus

Lenticular nucleus, putamen

Sbc

Lenticular nucleus, pallidum

Thalamus

SUPPLEMENTARY TABLE S2. Hierarchical spatial levels of functional brain networks. The number of subnetworks at each spatial level was counted for every possible subnetwork specified within and between whole brain divisions.

| Spatial level | Whole brain division | No. of subnetworks |
|----------------------|-----------------------------|---------------------------|
| Whole brain level | 1 whole brain | 1 |
| Hemispheric level | 2 hemispheres | 3 |
| Regional level | 24 regions | 296 |

SUPPLEMENTARY TABLE S3. Demographic characteristics of temporal lobe epilepsy (TLE) patients.

| No | Age (year) | Sex | Onset (year) | Duration (year) | Seizure | | CVLT | | | ROCFT | | |
|----|---------------|-----|-----------------|--------------------|------------------|------------|--------|--------|-------|--------|--------|-------|
| | | | | | control level | Laterality | IR (%) | DR (%) | R (%) | IR (%) | DR (%) | R (%) |
| 1 | 67 | M | 57 | 10 | GSC | RTLE | 50.00 | 16.00 | 50.00 | 49.17 | 56.87 | 66.54 |
| 2 | 51 | M | 21 | 30 | GSC | RTLE | 86.00 | 86.00 | 86.00 | 60.12 | 54.91 | 18.63 |
| 3 | 54 | F | 35 | 19 | GSC | RTLE | 50.00 | 16.00 | 50.00 | 76.85 | 83.39 | 80.96 |
| 4 | 45 | M | 19 | 26 | GSC | LTLE | 16.00 | 50.00 | 86.00 | 8.53 | 7.93 | 13.70 |
| 5 | 57 | M | 46 | 11 | GSC | RTLE | 50.00 | 50.00 | 86.00 | 52.06 | 52.68 | 11.43 |
| 6 | 40 | M | 20 | 20 | GSC | RTLE | 16.00 | 16.00 | 50.00 | 0.50 | 5.00 | 14.00 |
| 7 | 63 | F | 14 | 49 | GSC | LTLE | 50.00 | 50.00 | 50.00 | 29.38 | 0.54 | 28.39 |
| 8 | 42 | M | 35 | 7 | PSC | RTLE | 50.00 | 50.00 | 16.00 | 0.50 | 0.50 | 50.00 |
| 9 | 44 | F | 42 | 2 | PSC | LTLE | 86.00 | 86.00 | 50.00 | 7.00 | 5.00 | 73.00 |
| 10 | 22 | M | 17 | 5 | GSC | RTLE | 50.00 | 16.00 | 16.00 | 0.50 | 0.50 | 0.50 |
| 11 | 44 | F | 15 | 30 | PSC | RTLE | 2.00 | 2.00 | 50.00 | 54.00 | 46.00 | 5.00 |
| 12 | 43 | M | 17 | 26 | GSC | RTLE | 50.00 | 16.00 | 50.00 | 8.00 | 12.00 | 50.00 |

| | | | | | | | | | | | | |
|----|----|---|----|----|-----|------|-------|-------|-------|-------|-------|-------|
| 13 | 63 | F | 24 | 39 | GSC | RTLE | 16.00 | 16.00 | 16.00 | 1.70 | 2.00 | 0.01 |
| 14 | 24 | F | 22 | 2 | GSC | LTLE | 50.00 | 86.00 | 86.00 | 42.00 | 42.00 | 34.00 |
| 15 | 46 | F | 45 | 1 | GSC | RTLE | 50.00 | 16.00 | 16.00 | 65.45 | 60.87 | 36.62 |
| 16 | 37 | F | 34 | 3 | GSC | LTLE | 50.00 | 50.00 | 16.00 | 42.00 | 34.00 | 1.00 |
| 17 | 24 | F | 12 | 12 | PSC | RTLE | 50.00 | 50.00 | 86.00 | 62.00 | 58.00 | 4.00 |
| 18 | 43 | M | 29 | 14 | PSC | LTLE | 50.00 | 86.00 | 50.00 | 69.00 | 34.00 | 73.00 |
| 19 | 45 | F | 12 | 33 | GSC | LTLE | 50.00 | 86.00 | 50.00 | 34.00 | 69.00 | 1.00 |
| 20 | 21 | F | 17 | 4 | GSC | LTLE | 2.00 | 16.00 | 50.00 | 88.00 | 81.00 | 0.50 |
| 21 | 22 | M | 17 | 5 | GSC | LTLE | 50.00 | 86.00 | 50.00 | 76.00 | 76.00 | 96.00 |
| 22 | 52 | F | 35 | 17 | GSC | RTLE | 86.00 | 86.00 | 50.00 | 25.02 | 51.90 | 34.11 |
| 23 | 39 | F | 23 | 16 | PSC | RTLE | 50.00 | 16.00 | 16.00 | 3.00 | 2.00 | 1.00 |
| 24 | 68 | F | 52 | 16 | GSC | LTLE | 0.50 | 2.00 | 0.50 | 6.49 | 7.68 | 65.46 |
| 25 | 27 | F | 25 | 1 | PSC | RTLE | 50.00 | 50.00 | 86.00 | 50.00 | 16.00 | 62.00 |
| 26 | 45 | F | 17 | 29 | GSC | RTLE | 16.00 | 50.00 | 50.00 | 29.20 | 23.05 | 36.62 |
| 27 | 54 | M | 11 | 43 | GSC | LTLE | 0.50 | 0.50 | 50.00 | 6.44 | 4.22 | 1.55 |
| 28 | 38 | M | 37 | 1 | GSC | LTLE | 16.00 | 16.00 | 50.00 | 95.00 | 82.00 | 27.00 |

| | | | | | | | | | | | | |
|----|----|---|----|----|-----|------|-------|-------|-------|-------|-------|-------|
| 29 | 54 | F | 28 | 26 | PSC | LTLE | 2.00 | 0.50 | 2.00 | 2.43 | 2.82 | 0.50 |
| 30 | 26 | F | 12 | 24 | GSC | LTLE | 86.00 | 50.00 | 50.00 | 97.00 | 96.00 | 62.00 |
| 31 | 39 | F | 13 | 26 | PSC | RTLE | 16.00 | 50.00 | 50.00 | 10.00 | 27.00 | 12.00 |
| 32 | 26 | F | 4 | 22 | GSC | RTLE | 50.00 | 50.00 | 16.00 | 99.50 | 66.00 | 1.00 |
| 33 | 51 | F | 1 | 50 | PSC | LTLE | 16.00 | 16.00 | 16.00 | 2.04 | 2.07 | 9.62 |
| 34 | 44 | F | 28 | 16 | PSC | LTLE | 16.00 | 16.00 | 50.00 | 0.50 | 0.50 | 4.00 |
| 35 | 32 | M | 16 | 16 | GSC | RTLE | 16.00 | 16.00 | 50.00 | 27.00 | 50.00 | 42.00 |
| 36 | 30 | F | 22 | 8 | GSC | LTLE | 50.00 | 50.00 | 86.00 | 92.00 | 79.00 | 66.00 |
| 37 | 46 | F | 34 | 12 | GSC | RTLE | 16.00 | 16.00 | 16.00 | 1.13 | 2.74 | 17.02 |
| 38 | 43 | M | 24 | 19 | GSC | RTLE | 16.00 | 16.00 | 50.00 | 84.00 | 88.00 | 73.00 |
| 39 | 50 | M | 25 | 25 | GSC | RTLE | 50.00 | 50.00 | 86.00 | 2.04 | 1.10 | 15.11 |
| 40 | 33 | M | 20 | 13 | PSC | LTLE | 2.00 | 2.00 | 0.50 | 0.50 | 0.50 | 0.50 |
| 41 | 54 | F | 53 | 1 | GSC | RTLE | 98.00 | 86.00 | 86.00 | 9.09 | 26.52 | 8.33 |
| 42 | 44 | F | 12 | 32 | PSC | LTLE | 2.00 | 16.00 | 50.00 | 0.50 | 0.50 | 1.00 |
| 43 | 34 | F | 22 | 12 | GSC | LTLE | 0.50 | 16.00 | 86.00 | 0.50 | 0.50 | 0.50 |
| 44 | 36 | F | 26 | 8 | GSC | RTLE | 50.00 | 50.00 | 50.00 | 62.00 | 69.00 | 12.00 |

| | | | | | | | | | | | | |
|----|----|---|----|----|-----|------|-------|-------|-------|-------|-------|-------|
| 45 | 49 | F | 46 | 3 | GSC | LTLE | 50.00 | 50.00 | 50.00 | 37.09 | 44.86 | 57.82 |
| 46 | 28 | F | 20 | 8 | PSC | LTLE | 16.00 | 2.00 | 86.00 | 76.00 | 76.00 | 4.00 |
| 47 | 24 | M | 10 | 14 | PSC | LTLE | 86.00 | 50.00 | 50.00 | 0.50 | 0.50 | 0.50 |
| 48 | 23 | F | 13 | 10 | GSC | LTLE | 50.00 | 50.00 | 50.00 | 69.00 | 54.00 | 14.00 |

M, male; F, female; GSC, good seizure control; PSC, poor seizure control; LTLE, left TLE; RTLE, right TLE; CVLT, California Verbal Learning Test; ROCFT, Rey-Osterrieth Complex Figure Test; IR, immediate recall; DR, delayed recall; R, recognition.

SUPPLEMENTARY TABLE S4. Subnetworks showing alterations in the average efficiency at the regional level in (A) temporal lobe epilepsy patients with good seizure control (TLE_{GSC}) and (B) temporal lobe epilepsy patients with poor seizure control (TLE_{PSC}) relative to healthy controls. Positive and negative *t* values represent increases and decreases, respectively, in the average efficiency in the patient subgroups.

| Subnetwork | <i>t</i> value | <i>p</i> value |
|---------------------------------|-----------------------|-----------------------|
| (A) TLE _{GSC} patients | | |
| Between Sbc A and PrtM U | 2.7334 | 0.0078 |
| Between Sbc A and Lmb U | 2.6437 | 0.0100 |
| Within Sbc A | 2.5900 | 0.0115 |
| Between Sbc A and PrtM A | 2.5062 | 0.0143 |
| (B) TLE _{PSC} patients | | |
| Within Sbc A | 3.8244 | 0.0003 |
| Between Sbc A and Lmb U | 3.6943 | 0.0005 |
| Between Sbc A and FrnO U | 3.1422 | 0.0026 |
| Between Sbc A and PrtM A | 3.1234 | 0.0028 |
| Between Sbc U and Lmb U | 3.0143 | 0.0038 |
| Between Sbc A and FrnO A | 2.9288 | 0.0049 |
| Between Sbc A and Lmb A | 2.9133 | 0.0051 |
| Between Sbc A and OccM A | 2.8308 | 0.0064 |
| Between Sbc A and Sbc U | 2.8111 | 0.0067 |
| Within PrtL A | -2.7841 | 0.0072 |
| Between Sbc U and FrnO U | 2.6683 | 0.0099 |
| Between FrnL U and Cnt U | -2.6588 | 0.0101 |

| | | |
|---------------------------|--------|--------|
| Between Sbc U and FrnO A | 2.6369 | 0.0107 |
| Between Sbc A and Tmp U | 2.6218 | 0.0112 |
| Between Sbc A and OccM U | 2.5978 | 0.0119 |
| Between Sbc A and PrtM U | 2.5623 | 0.0130 |
| Between Lmb A and FrnO U | 2.5281 | 0.0142 |
| Between Sbc A and FrnM U | 2.5263 | 0.0143 |
| Between Sbc U and Lmb A | 2.4965 | 0.0154 |
| Between Sbc U and PrtM A | 2.4715 | 0.0164 |
| Between FrnO A and OccM A | 2.4041 | 0.0194 |
| Between Sbc A and OccL A | 2.3611 | 0.0216 |
| Between Sbc A and Tmp A | 2.3450 | 0.0225 |
| Between Lmb A and FrnO A | 2.3295 | 0.0233 |
| Between FrnO A and OccL A | 2.3117 | 0.0244 |
| Between Lmb U and Ins A | 2.3099 | 0.0245 |

The region labels are given in Supplementary Table S1. A, affected hemisphere; U, unaffected hemisphere.

SUPPLEMENTARY TABLE S5. Subnetworks showing correlations between the average efficiency and (A) immediate recall (IR), (B) delayed recall (DR), and (C) recognition (R) scores of the Rey-Osterrieth Complex Figure Test (ROCFT) at the regional level in temporal lobe epilepsy patients with poor seizure control (TLE_{PSC}). Positive ρ values represent positive relationships between the average efficiency and memory performance.

| Network component | ρ value | p value |
|--------------------------|--------------------------------|-----------------------------|
| (A) ROCFT-IR | | |
| Within Sbc A | 0.6692 | 0.0064 |
| Between Sbc A and FrnO U | 0.6656 | 0.0068 |
| Between Sbc A and Sbc U | 0.6510 | 0.0086 |
| Between Sbc A and Lmb A | 0.6183 | 0.0140 |
| Between Sbc U and Lmb A | 0.6183 | 0.0140 |
| Between Sbc U and FrnO U | 0.6146 | 0.0148 |
| Between Sbc A and Lmb U | 0.5965 | 0.0189 |
| Between Sbc U and FrnO A | 0.5746 | 0.0250 |
| (B) ROCFT-DR | | |
| Between Sbc A and FrnO U | 0.7165 | 0.0027 |
| Within Sbc A | 0.6510 | 0.0086 |
| Between Sbc U and FrnO U | 0.6474 | 0.0091 |
| Between Sbc A and Lmb A | 0.6365 | 0.0107 |
| Between Sbc A and Lmb U | 0.6219 | 0.0133 |
| Between Sbc A and FrnO A | 0.5892 | 0.0208 |
| Between Sbc A and Sbc U | 0.5892 | 0.0208 |
| Between Sbc U and Lim A | 0.5856 | 0.0218 |

| | | |
|--------------------------|--------|--------|
| Between Sbc A and Tmp A | 0.5783 | 0.0239 |
| Between Sbc A and OccM A | 0.5746 | 0.0250 |
| (C) ROCFT-R | | |
| Between Lmb A and FrnO U | 0.6018 | 0.0176 |

The region labels are as given in Supplementary Table S1. A, affected hemisphere; U, unaffected hemisphere.

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