Supplementary Materials

Choice of threshold for network generation

For a very low threshold, a graph is fully connected, and in this case, the clustering coefficient is one (the global maximum). If the threshold increases, edges are removed, and the clustering coefficient decreases. For very high thresholds, the graph is very sparse and the clustering coefficient goes to zero.

The clustering coefficient is defined as the probability that neighbors of a node are also connected. Now, we assume a strongly clustered structure and consider what happens if we add or remove links randomly (because the data set is noisy). If links are removed randomly, then it is likely that links between neighbors of a node are removed, and thus the clustering coefficient decreases. If we add new links randomly, then we generate new neighbors. These might have neighbors that are not connected among each other, and the clustering coefficient decreases as well.

Following the argumentation of K. Zweig (personal communication): if a system of interest (in this case functional connectivity networks) exhibits a large level of clustering, which is given for functional connectivity networks, then a local maximum in the clustering coefficient indicates that the threshold is chosen optimally to capture the underlying structure of the system. For thresholds around 0.85, we found almost for every subject a local maximum in the clustering coefficient (see Supplementary Fig. S1), and therefore consider this value an optimal threshold for our application.

Results

The relative hubness, degree, and betweenness for the gyri and Brodmann area level are shown as bar plots in Supplementary Figures S2 and S3. The solid line shows the expected value if the hubness were distributed entirely randomly and its sum therefore only determined by the size of the region.

Network structure for the Brodmann areas

Supplementary Figure S4 shows the connectivity structure on the level of the Brodmann areas, analog to the network for the gyri structures shown in Figure 4. Also, here a stronger connectivity of frontal areas for seniors was evident. Furthermore, stronger connectivity of the hippocampus in young individuals can be seen.



SUPPLEMENTARY FIG. S1. Dependence of the clustering coefficient on the threshold for six exemplary data sets. If local maxima exist (arrows), then in the range of θ =0.85–0.9.

Blood oxygenation level-dependent signal intensity analysis

As the connections between different regions were not symmetric, it seemed necessary to check the underlying neural activation evoked by the different tasks. To describe the blood oxygenation level-dependent (BOLD) response for the age groups, one-sample t-tests were conducted for the 10 young and the 10 senior subjects. The chosen threshold was very liberal (p=0.001, uncorrected for multiple comparison) and differences between the age groups are only descriptive. Supplementary Figure S5A shows the main effect within the frontal cortex. Young subjects (green) showed a symmetric activation of frontal areas. Activation in senior subjects (red) seems slightly asymmetric with reduced activation in the left hemisphere (yellow circles mark frontal areas with significant activation), but harmonizes with the activation in young subjects if a higher threshold (p = 0.005) was used. Supplementary Figure S5B shows the activation within the parietal cortex. Both age groups showed an elevated BOLD response bilateral in the superior parietal gyrus. In the right hemisphere, activation overlaps to a certain extent, which was not the case in the left hemisphere (yellow circles mark parietal areas with significant activation).



SUPPLEMENTARY FIG. S2. Barplots showing the distribution of the hubness (left), degree (middle), and betweenness (right) across the smaller structures.



SUPPLEMENTARY FIG. S3. Barplots showing the distribution of the hubness (left), degree (middle), and betweenness (right) across the Brodmann areas.



SUPPLEMENTARY FIG. S4. Connectivity network analog to Figure 4 for the level of Brodmann areas.



SUPPLEMENTARY FIG. S5. Blood oxygenation level-dependent response of senior (red) and young (green) subjects during working memory (main effect) in frontal (A) and parietal (B) cortex at threshold $p_{\text{voxel level}} = 0.001$ uncorrected and a minimal cluster size of 10 voxels. Circles mark areas of significant activation in the given regions.