**Supplementary Methods**

**Diffusion tensor image processing**

A custom script was used to process the DTI data by wrapping previously published algorithms as described below (script available upon request). DTI data were visually controlled for artifacts. If repeated sequences were not possible for images with low quality, the data were discarded and excluded (**Supplementary Figure 1**). Brain masks were created using the *BET* command in FSL and then revised with morphological operations, as well as manual corrections.

A separate step using *topup* to correct susceptibility induced distortions was skipped in our study as all B0 images and diffusion-weighted frames were acquired using identical antero-posterior phase encoding directions. Spurious image distortions that originated from a combination of eddy currents and real head movement were corrected with the CUDA 8.0 implementation of the eddy command in the FSL software library (version 6.0) with the following parameters: 4 standard deviations as criterion for classifying a slice as outlier (ol_nstd=4), 10 slice to volume iterations (s2v_niter=10), 6 smoothing iterations, during which a filter width of 10, 6, 4, 2, 0, 0 mm for each subsequent smoothing iterations was used. Next, FA and mean diffusivity (MD) maps were calculated by running the *dtifit* command in FSL on the motion corrected DTI dataset; tensors were fitted with a weighted least squared algorithm. DTI data were further processed by the Bayesian multi-fiber estimation method BedpostX (CUDA 8.0 implementation for FSL 6.0), estimating up to 3 fiber populations per voxel (Hernandez et al. 2013).

**Graph theory parameters**

**Global and nodal efficiency**

The networks ability to transfer information in parallel was quantified by calculating the weighted global efficiency, which is the reciprocal of the harmonic mean of the shortest weighted path length. Networks that have a short average shortest path length between two nodes are considered topologically integrated and efficient (Latora et al. 2001). Global efficiency for a weighted graph $G$ was calculated based on the following equation

$$E_{global}(G) = \frac{1}{N(N-1)} \sum_{i \neq j \in G} \frac{1}{d_{i,j}}$$
where $N$ is the total number of nodes in the network $G$; $d_{i,j}$ is the weighted shortest paths length between nodes $i$ and $j$ (Latora et al. 2003). Accordingly, weighted nodal efficiency was calculated as nodal counterpart of the weighted global efficiency. Nodal efficiency quantifies the integration of a specific node with all other nodes in the network. It is the normalized sum of the inverse of the shortest path length $d_{i,j}$ of a specific node $i$ to all other nodes (Latora et al. 2003).

$$E_{nodal}(i) = \frac{1}{N-1} \sum_{j \in G} \frac{1}{d_{i,j}}$$

We expect global and nodal efficiency to increase during neonatal brain development (Cao et al. 2017).

**Local efficiency**

Local efficiency as opposed to nodal efficiency quantifies the integration of a specific node within a subgraph $G_i$, encompassing all nodes that are immediate neighbours of the node (Latora et al. 2001, Latora et al. 2003). Thus, local efficiency is a measure of structural segregation.

$$E_{local}(i) = \frac{1}{N} \sum_{i \in G} E_{global}(G_i)$$

The average local efficiency across all nodes serves as global measure of the local efficiency of a network. Local efficiency is expected to decrease during neonatal brain development (Cao et al. 2017).

**Strength**

By summing the edge weights ($w_{i,j}$) of all edges connected to a node, nodal strength was calculated. Global strength was measured by averaging the strength of all nodes in the network (Barrat et al. 2004) and is expected to increase with brain network development.

$$s_i = \sum_{j \in G} w_{i,j}$$

**Transitivity**

Transitivity, which is sometimes also referred to as clustering coefficient, quantifies the probability that the nodes $j$ and $h$, which are directly connected to node $i$ are also directly connected with each other (Barrat et al. 2004). For global transitivity the number of connected triangles is divided by the number of connected triplets. For the nodal counterpart the weighted transitivity was calculated following the generalization by Barrat et al. (Barrat et al. 2004). $w_{i,h}$
is the edge weight; $s_i$ is the sum of all neighboring edge weights; $k_i$ is the vertex degree, i.e. the number of all edges connected to that node; $a_{ij}$ denotes the element in the adjacency matrix.

$$\text{transitivity}_i = \frac{1}{s_i(k_i - 1)} \sum_{j,h} \frac{w_{ij} w_{ih}}{2} a_{ij} a_{ih} a_{jh}$$

Transitivity as measure of structural segregation is expected to decrease with brain network development (Cao et al. 2017).
Supplementary Figure 1

Flow chart of included subjects and available connectomes.
### Supplementary Table 1

| Lobe   | Region  | Threshold* | $\beta^*$ | SE*     | 95% CI* | $P_{\text{lat}}^*$ | Amtpc | Acrit |
|--------|---------|------------|-----------|---------|---------|-------------------|-------|-------|
|        |         | Controls > CHD                                                                                  |       |         |
|        |         | Nodal efficiency                                                                                 |       |         |
|        |         |                                                     |       |         |
|        |         | Frontal                                             |       |         |
|        |         | SFGdor.L 0.18, 0.029, 0.0054 [0.017; 0.042] 1.6E-06 0.48 0.25 |       |         |
|        |         | SFGdor.R 0.18, 0.028, 0.0054 [0.016; 0.04] 0.000003 0.38 0.25 |       |         |
|        |         | ORBsup.L 0.15, 0.038, 0.0068 [0.023; 0.053] 1.2E-06 0.71 0.25 |       |         |
|        |         | ORBsup.R 0.08, 0.029, 0.006 [0.016; 0.043] 0.000021 0.63 0.25 |       |         |
|        |         | ORBmid.L 0.11, 0.074, 0.012 [0.046; 0.1] 2.4E-07 0.89 0.25 |       |         |
|        |         | OLF.L 0.18, 0.02, 0.0043 [0.01; 0.03] 0.000014 0.27 0.25 |       |         |
|        |         | OLF.R 0.18, 0.022, 0.0041 [0.013; 0.031] 1.9E-06 0.45 0.25 |       |         |
|        |         | SFGmed.L 0.15, 0.035, 0.007 [0.019; 0.051] 5.1E-06 0.29 0.25 |       |         |
|        |         | Insula                                             |       |         |
|        |         | INS.L 0.18, 0.022, 0.0044 [0.013; 0.032] 3.3E-06 0.69 0.25 |       |         |
|        |         | INS.R 0.18, 0.026, 0.0041 [0.016; 0.035] 1.5E-07 0.69 0.25 |       |         |
|        |         | Limbic                                             |       |         |
|        |         | ACG.R 0.18, 0.027, 0.005 [0.015; 0.038] 1.9E-06 0.59 0.25 |       |         |
|        |         | DCG.L 0.18, 0.026, 0.0046 [0.016; 0.037] 6.5E-07 0.43 0.25 |       |         |
|        |         | DCG.R 0.18, 0.028, 0.005 [0.017; 0.039] 8.8E-07 0.43 0.25 |       |         |
|        |         | PCG.L 0.17, 0.032, 0.0054 [0.02; 0.045] 4.3E-07 0.71 0.25 |       |         |
|        |         | PCG.R 0.18, 0.042, 0.0063 [0.028; 0.056] 3.2E-08 0.88 0.25 |       |         |
|        |         | Occipital                                          |       |         |
|        |         | CAL.R 0.14, 0.021, 0.0044 [0.011; 0.031] 0.000013 0.56 0.25 |       |         |
|        |         | MOG.R 0.13, 0.026, 0.0062 [0.012; 0.04] 0.000068 0.25 0.25 |       |         |
|        |         | IOG.R 0.13, 0.038, 0.007 [0.022; 0.054] 1.7E-06 0.52 0.25 |       |         |
|        |         | FFG.R 0.07, 0.032, 0.0074 [0.016; 0.049] 0.00015 0.62 0.25 |       |         |
|        |         | Parietal                                           |       |         |
|        |         | ANG.R 0.18, 0.023, 0.0041 [0.014; 0.032] 8.8E-07 0.31 0.25 |       |         |
|        |         | SCGM                                              |       |         |
|        |         | PUT.L 0.18, 0.021, 0.0043 [0.011; 0.031] 7.2E-06 0.37 0.25 |       |         |
|        |         | PUT.R 0.18, 0.022, 0.0046 [0.012; 0.033] 7.5E-06 0.41 0.25 |       |         |
|        |         | Temporal                                          |       |         |
|        |         | HES.L 0.18, 0.021, 0.0046 [0.011; 0.031] 0.000013 0.27 0.25 |       |         |
|        |         | STG.L 0.18, 0.02, 0.0042 [0.01; 0.029] 0.00009 0.27 0.25 |       |         |
|        |         | ITG.R 0.13, 0.025, 0.0053 [0.013; 0.037] 0.00015 0.34 0.25 |       |         |
|        |         | Strength                                           |       |         |
|        |         | Frontal                                             |       |         |
|        |         | ORBsup.L 0.13, 1.6, 0.32 [0.89; 2.4] 0.00003 0.86 0.21 |       |         |
|        |         | ORBsup.R 0.1, 1.4, 0.3 [0.74; 2.1] 0.000072 0.65 0.21 |       |         |
|        |         | ORBmid.L 0.18, 1.4, 0.29 [0.73; 2] 0.000069 0.74 0.21 |       |         |
|        |         | ORBmid.R 0.18, 1.5, 0.33 [0.7; 2.2] 0.00013 0.71 0.21 |       |         |
|        |         | SFGmed.L 0.15, 1.3, 0.26 [0.74; 1.9] 0.000027 0.51 0.21 |       |         |
|        |         | SFGmed.R 0.03, 1.2, 0.25 [0.68; 1.8] 0.000037 0.23 0.21 |       |         |
|        |         | Limbic                                             |       |         |
|        |         | PCG.R 0.18, 4.4, 0.66 [2.9; 5.9] 3.3E-08 0.84 0.21 |       |         |
|        |         | Occipital                                          |       |         |
|        |         | IOG.R 0.17, 1.3, 0.28 [0.66; 1.9] 0.000084 0.41 0.21 |       |         |
|        |         | CHD > Controls                                     |       |         |
|        |         | Nodal efficiency                                   |       |         |
|        |         |                                                     |       |         |
|        |         | Transitivity                                        |       |         |
|        |         | Frontal                                             |       |         |
|        |         | SFGdor.L 0.13, 0.13, 0.025 [0.072; 0.19] 5.1E-06 0.37 0.16 |       |         |
|        |         | SFGdor.R 0.11, 0.15, 0.035 [0.075; 0.23] 0.00006 0.34 0.16 |       |         |
|        |         | Insula                                             |       |         |
|        |         | INS.R 0.07, 0.15, 0.031 [0.08; 0.22] 0.000031 0.49 0.16 |       |         |
| Region  | Lesion  | Local Efficiency | Strength |
|---------|---------|-----------------|----------|
| SCGM    | PAL.R   | 0.14 0.091 0.21 | 0.000038 0.17 0.16 |
| Limbic  | PreCG.L | 0.03 0.94 0.2  | 0.00023 0.23 0.14 |
| PreCG.R | 0.04 1 0.23 | [0.48; 1.5] | 0.00053 0.15 0.14 |
| SFGdor.L | 0.13 0.63 0.14 | [0.32; 0.94] | 0.00002 0.28 0.14 |
| SFGdor.R | 0.11 0.71 0.15 | [0.38; 1] | 0.000019 0.41 0.14 |
| SMA.R   | 0.09 0.81 0.19 | [0.37; 1.3] | 0.00019 0.34 0.14 |
| Insula  | INS.L   | 0.04 0.52 0.14 | 0.0036 0.5 0.14 |
| INS.R   | 0.06 0.67 0.14 | [0.34; 0.99] | 0.00011 0.74 0.14 |
| Limbic  | ACG.L   | 0.14 0.59 0.11 | [0.34; 0.84] | 0.000002 0.31 0.14 |
| DCG.L   | 0.06 0.63 0.11 | [0.27; 0.78] | 0.00011 0.65 0.14 |
| DCG.R   | 0.09 0.45 0.084 | [0.25; 0.64] | 0.000013 0.59 0.14 |
| PCG.L   | 0.18 0.42 0.069 | [0.26; 0.58] | 2.8E-07 0.58 0.14 |
| PCG.R   | 0.15 0.47 0.076 | [0.29; 0.64] | 1.5E-07 0.41 0.14 |
| HIP.L   | 0.06 0.42 0.12 | [0.15; 0.69] | 0.0017 0.42 0.14 |
| HIP.R   | 0.05 0.53 0.12 | [0.26; 0.8] | 0.00049 0.7 0.14 |
| PHG.L   | 0.06 0.42 0.16 | [0.052; 0.78] | 0.018 0.29 0.14 |
| AMYG.L  | 0.15 0.6 0.13 | [0.3; 0.9] | 0.00002 0.2 0.14 |
| Occipital | CUN.L  | 0.18 0.36 0.07 | [0.2; 0.51] | 1.7E-06 0.19 0.14 |
| LING.L  | 0.14 0.5 0.1 | [0.26; 0.73] | 7.9E-06 0.2 0.14 |
| SOG.R   | 0.1 0.59 0.17 | [0.2; 0.99] | 0.0017 0.14 0.14 |
| Parietal | PoCG.R  | 0.03 0.64 0.2 | [0.19; 1.1] | 0.012 0.3 0.14 |
| SMG.R   | 0.12 0.71 0.19 | [0.27; 1.1] | 0.00063 0.19 0.14 |
| PCUN.L  | 0.08 0.43 0.11 | [0.19; 0.68] | 0.00029 0.18 0.14 |
| PCUN.R  | 0.03 0.38 0.16 | [0.018; 0.75] | 0.049 0.36 0.14 |
| PCL.L   | 0.04 0.92 0.2 | [0.47; 1.4] | 0.00018 0.28 0.14 |
| SCGM    | CAU.R   | 0.08 0.5 0.12 | [0.23; 0.78] | 0.00025 0.32 0.14 |
| PUT.L   | 0.04 0.63 0.1 | [0.4; 0.87] | 4.5E-07 0.59 0.14 |
| PUT.R   | 0.05 0.45 0.097 | [0.23; 0.67] | 0.00037 0.52 0.14 |
| PAL.L   | 0.08 0.62 0.13 | [0.31; 0.92] | 0.0000064 0.35 0.14 |
| PAL.R   | 0.14 0.48 0.078 | [0.3; 0.65] | 1.3E-07 0.43 0.14 |
| Temporal | THA.L   | 0.14 0.34 0.062 | [0.2; 0.48] | 1.1E-06 0.51 0.14 |
| THA.R   | 0.06 0.38 0.084 | [0.19; 0.57] | 0.00014 0.5 0.14 |
| HES.L   | 0.04 0.45 0.2 | [-0.0028; 0.89] | 0.05 0.23 0.14 |
| MTG.R   | 0.05 0.55 0.16 | [0.17; 0.92] | 0.0044 0.18 0.14 |
| ITG.L   | 0.18 0.46 0.082 | [0.27; 0.64] | 5.3E-07 0.16 0.14 |
Supplementary Table 1 Significant nodal level differences between preoperative CHD neonates and healthy controls as revealed by MTPC. As two one-sided tests were performed to determine the direction of the effects, results are grouped by the contrast “Controls > CHD” or “CHD > Controls”. *Threshold indicates the cost threshold at which the strongest β coefficient was observed. Statistical parameters are given for that threshold. *P_fdr is the threshold-specific P-value corrected for multiple comparison across all 90 ROIs by means of the Benjamini Hochberg procedure. Amtpc and Acrit denote the results of the overall MTPC comparison across the whole range of thresholds. SCGM, subcortical gray matter.

| THA.R | 0.09 | 1.6  | 0.32  | [0.92; 2.4] | 0.000051 | 0.48  | 0.23  |
Supplementary Table 2

| Abbreviation | Name                                      | Lobe     |
|--------------|-------------------------------------------|----------|
| PreCG        | Precentral gyrus                          | Frontal  |
| SFGdor       | Superior frontal gyrus (dorsolateral)     | Frontal  |
| ORBsup       | Superior frontal gyrus (orbital part)     | Frontal  |
| MFG          | Middle frontal gyrus                      | Frontal  |
| ORBmid       | Middle frontal gyrus (orbital part)       | Frontal  |
| IFGoperc     | Inferior frontal gyrus (opercular part)   | Frontal  |
| IFGtriang    | Inferior frontal gyrus (triangular part)  | Frontal  |
| ORBinf       | Inferior frontal gyrus (orbital part)     | Frontal  |
| ROL          | Rolandic operculum                        | Frontal  |
| SMA          | Supplementary motor area                  | Frontal  |
| OLF          | Olfactory cortex                          | Frontal  |
| SFGmed       | Superior frontal gyrus (medial)            | Frontal  |
| ORBsupmed    | Superior frontal gyrus (medial orbital)    | Frontal  |
| REC          | Rectus gyrus                              | Frontal  |
| INS          | Insula                                    | Insula   |
| ACG          | Anterior cingulate and paracingulate gyri | Limbic   |
| DCG          | Median cingulate and paracingulate gyri   | Limbic   |
| PCG          | Posterior cingulate gyrus                 | Limbic   |
| HIP          | Hippocampus                               | Limbic   |
| PHG          | Parahippocampal gyrus                     | Limbic   |
| AMYG         | Amygdala                                  | Limbic   |
| CAL          | Calcarine fissure and surrounding cortex  | Occipital|
| CUN          | Cuneus                                    | Occipital|
| LING         | Lingual gyrus                             | Occipital|
| SOG          | Superior occipital gyrus                  | Occipital|
| MOG          | Middle occipital gyrus                    | Occipital|
| IOG          | Inferior occipital gyrus                  | Occipital|
| FFG          | Fusiform gyrus                            | Occipital|
| PoCG         | Postcentral gyrus                         | Parietal |
| SPG          | Superior parietal gyrus                   | Parietal |
| IPL          | Inferior parietal, supramarginal and angular gyri | Parietal |
| SMG          | Supramarginal gyrus                       | Parietal |
| ANG          | Angular gyrus                             | Parietal |
| PCUN         | Precuneus                                 | Parietal |
| PCL          | Paracentral lobule                        | Parietal |
| CAU          | Caudate nucleus                           | SCGM     |
| PUT          | Lenticular nucleus, putamen               | SCGM     |
| PAL          | Lenticular nucleus, pallidum              | SCGM     |
| THA          | Thalamus                                  | SCGM     |
| HES          | Heschl gyrus                              | Temporal |
| STG          | Superior temporal gyrus                   | Temporal |
| TPOsup       | Temporal pole: superior temporal gyrus     | Temporal |
| MTG          | Middle temporal gyrus                     | Temporal |
**Supplementary Table 2** List of node abbreviations parcellated with the Automated Anatomical Labeling. Abbreviations are appended by .L for left hemispheric and .R for right hemispheric regions.

| Abbreviation | Description                                      | Hemisphere |
|--------------|--------------------------------------------------|------------|
| TPOmid       | Temporal pole: middle temporal gyrus             | Temporal   |
| ITG          | Inferior temporal gyrus                          | Temporal   |
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