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Efficient organisation of the contralateral hemisphere connectome is associated with improvement in intelligence quotient after paediatric epilepsy surgery

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ABSTRACT

Objective: Aims of epilepsy surgery in childhood include optimising seizure control and facilitating cognitive development. Predicting which children will improve cognitively is challenging. We investigated the association of the pre-operative structural connectome of the contralateral non-operated hemisphere with improvement in intelligence quotient (IQ) post-operatively.
Methods: Consecutive children who had undergone unilateral resective procedures for epilepsy at a single centre were retrospectively identified. We included those with pre-operative volume T1-weighted non-contrast brain magnetic resonance imaging (MRI), no visible contralateral MRI abnormalities, and both pre-operative and two years post-operative IQ assessment. The MRI of the hemisphere contralateral to the side of resection was anatomically parcellated into 34 cortical regions and the covariance of cortical thickness between regions was used to create binary and weighted group connectomes.
Results: Eleven patients with a post-operative IQ increase of at least 10 points at two years were compared with twenty-four patients with no change in IQ score. Children who gained at least 10 IQ points post-operatively had a more efficiently structured contralateral hemisphere connectome with higher global efficiency (0.74) compared to those whose IQ did not change at two years (0.58, $p = 0.014$). This was consistent across thresholds and both binary and weighted networks. There were no statistically significant group differences in age, sex, age at onset of epilepsy, pre-operative IQ, mean cortical thickness, side or site of procedure, two year post-operative Engel scores or use of anti-seizure medications between the two groups.
Conclusions: Surgical procedures to reduce or stop seizures may allow children with an efficiently structured contralateral hemisphere to achieve their cognitive potential.

1. Introduction

Medically resistant epilepsy in children requires significant health and social care resources and can affect quality of life due to poor seizure control and developmental and cognitive deterioration or delay. The frequency of cognitive impairment in epilepsy varies with aetiology, with low grade neoplasms being associated with a very low likelihood of intellectual disability and epileptic encephalopathies being highly associated with cognitive dysfunction [1]. An early age of epilepsy onset, longer duration of epilepsy, increased seizure frequency, and anti-seizure medication (ASM) are all associated with worse cognition regardless of the epilepsy aetiology [1–3]. Cognitive impairment in epilepsy may therefore result from a combination of aetiological, genetic, environmental, seizure-related, and therapeutic factors [1].

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Children with medically resistant epilepsy referred for epilepsy surgery have a high frequency of cognitive dysfunction with around 60 % having a pre-operative intelligence quotient (IQ) lower than 80 [2,4]. Meta-analyses of post-operative changes in IQ following epilepsy surgery have reported pooled estimates of a 16–19 % chance of a significant gain in IQ post-operatively [5,6]. Macroscopic structural abnormalities, such as gliosis, infarcts, and cortical abnormalities in the non-operated hemisphere have been associated with poorer cognitive outcomes following hemispherectomy [7,8]. Widespread microstructural changes such as reduced fractional anisotropy (FA), decreased thalamic volumes, and cortical thinning in both the ipsilateral and contralateral hemispheres have been identified in focal onset epilepsies also [9–11]. This suggests that brain microstructure is affected beyond the macroscopically or electrically abnormal focal epileptogenic region, and these microstructural abnormalities might also contribute to outcomes following surgery.

The structure of the brain can be modelled as a network, or connectome, with anatomical regions as nodes and either white matter streamlines or covariance of region of interest (RoI) thickness or volume as edges [12]. Networks can be mathematically analysed using graph theory [12], and global changes in brain structure in epilepsy may be reflected in alterations in structural connectomes. The average path length of a network is the average of the shortest path lengths between any two nodes in the network, and the global efficacy is the inverse relation of this, measuring efficiency of network information transfer [13]. We hypothesised that a pre-existing more efficient structural network may facilitate a greater gain in cognitive function following epilepsy surgery when the impact of uncontrolled seizures is mitigated. This study aims to assess whether the pre-operative network global efficiency in the contralateral non-operated hemisphere is associated with a post-operative improvement in IQ in children undergoing resective epilepsy surgery.

2. Materials and methods

We performed a retrospective cross-sectional between-group comparison of the global efficiency of the pre-operative structural contralateral hemisphere connectome between children whose IQ scores improved two years following epilepsy surgery and those whose IQ scores did not improve. This manuscript was prepared according to the STROBE guidelines [14]. The study was considered by the Dutch Medical Ethics Committee and it was confirmed that the Medical Research Involving Human Subjects Act did not apply and written informed consent from the participants for retrospective data analysis was not necessary.

2.1. Patient identification and inclusion

Consecutive patients between the ages of one and 17 years who had undergone unilateral resective epilepsy surgery for focal onset epilepsy in the Dutch collaborative national paediatric epilepsy surgery programme between 2004 and 2014 were identified from the records of the University Medical Centre, Utrecht. All participants had a confirmed diagnosis of a focal onset epilepsy refractory to medical therapy and underwent a unilateral resective procedure. We only included those with a macroscopically normal contralateral hemisphere on MRI as reported clinically by the reporting radiologist and confirmed by second review of imaging for this study. We excluded participants who did not have a suitable 3D T1-weighted volumetric non contrast-enhanced sequence performed prior to surgery, and those with excessive movement or other artefacts. Those without documentation of pre-operative and post-operative IQ scores, and those who scored below the assessable range of the IQ instruments were also excluded to allow quantifiable assessment of IQ change.

Clinical and demographic data were sourced from patient records and included: age at operation, gender, duration of epilepsy, age at onset of epilepsy, aetiology of epilepsy, results of relevant investigations, site, side, and extent of procedure undertaken, Engel classification of seizure outcome and ASM status two years post-operatively.

2.2. Neuropsychological analyses

Neuropsychological testing was carried out pre and post-operatively by trained clinical paediatric neuropsychologists. Age and developmental stage appropriate testing methods were used to evaluate IQ (Weschler Intelligence Scales for Children (23), Snijders-Oomen Niet-verbale Intelligentietest (5), Bayley Scales of Infant Development (3), Kaufman Adolescent and Adult Intelligence Test (3), Wechsler Adult Intelligence Scales (1)). All children were tested post-operatively at two years with the same test as pre-operatively. The difference between pre-operative and post-operative scores was calculated as the post-operative score minus the pre-operative score. The participants were divided into those with and without a clinically meaningful increase of at least 10 IQ points post-operatively, which is an increase larger than twice the standard error of measurement [6].

2.3. MRI processing

All 3D T1-weighted sequences were acquired at 1.5 T with one of the following two similar protocols: (1) Philips Achieva with SENSE head coil, repetition time (TR): 25 ms; echo time (TE): 4.6 ms; flip angle: 30°; field of view (FOV) 256x256; voxel size: 0.9x0.9x1mm (28 participants); or (2) Philips Intera with SENSE head coil (TR: 30 ms; TE: 4.6 ms; flip angle: 30°, FOV: 256x256, voxel size: 1x1x1mm (7 participants). Freesurfer software (http://surfer.nmr.mgh.harvard.edu/) was used for brain extraction, volumetric segmentation of deep grey and white matter structures, surface based registration, and cortical parcellation using the Desikan-Killiany atlas [15,16]. Cortical thickness at each surface vertex was calculated as the distance from the grey-white boundary to the grey-cerebrospinal fluid boundary [16]. All segmentations and parcellations were manually checked for quality and accuracy and corrected where necessary. Manual editing was performed to achieve accurate segmentation and parcellation of the non-operated hemisphere only, and hemispheres were processed separately where this was necessary due to anatomical abnormalities preventing accurate processing of the pathological hemisphere.

Mean hemisphere cortical thickness measurements were calculated across each of the 34 regions of the Desikan-Killiany atlas [15]. Group cortical thickness networks were constructed using these regions as network nodes and the pearson product moment correlation coefficient of the cortical thickness at each cortical region as the edge weight [17–20]. Self-self connections were set to zero and negative correlations were removed as these cannot be used in graph theory analysis and do not biologically represent the same information as the original positive weights when converted to absolute values [12,13,20]. Matrices were thresholded in a stepwise manner using absolute thresholds to remove all edges with weights below the threshold value in steps of 0.05. Network metrics were analysed at two different thresholds. The first was the highest threshold value that maintained a completely connected network without any disconnected nodes [17,21]. The second threshold was chosen to create sparse networks with a density of 0.2 for comparison with previous studies of structural brain connectomes [22,23]. Binary networks were created by setting all existing edge weights to one and non-existent edges to zero. An overview of the processing pipeline is in Fig. 1.

Connectivity matrices were analysed using the Brain Connectivity Toolbox [13] in Matlab Release 2015b (The Mathworks Inc, Massachusetts, United States). Network measures calculated were: network density – the number of edges present as a proportion of all possible edges; average node degree – the average number of edges connected to each node; mean node strength - the mean sum of weights connected to each node; mean edge weight – the mean of all network edge weights;

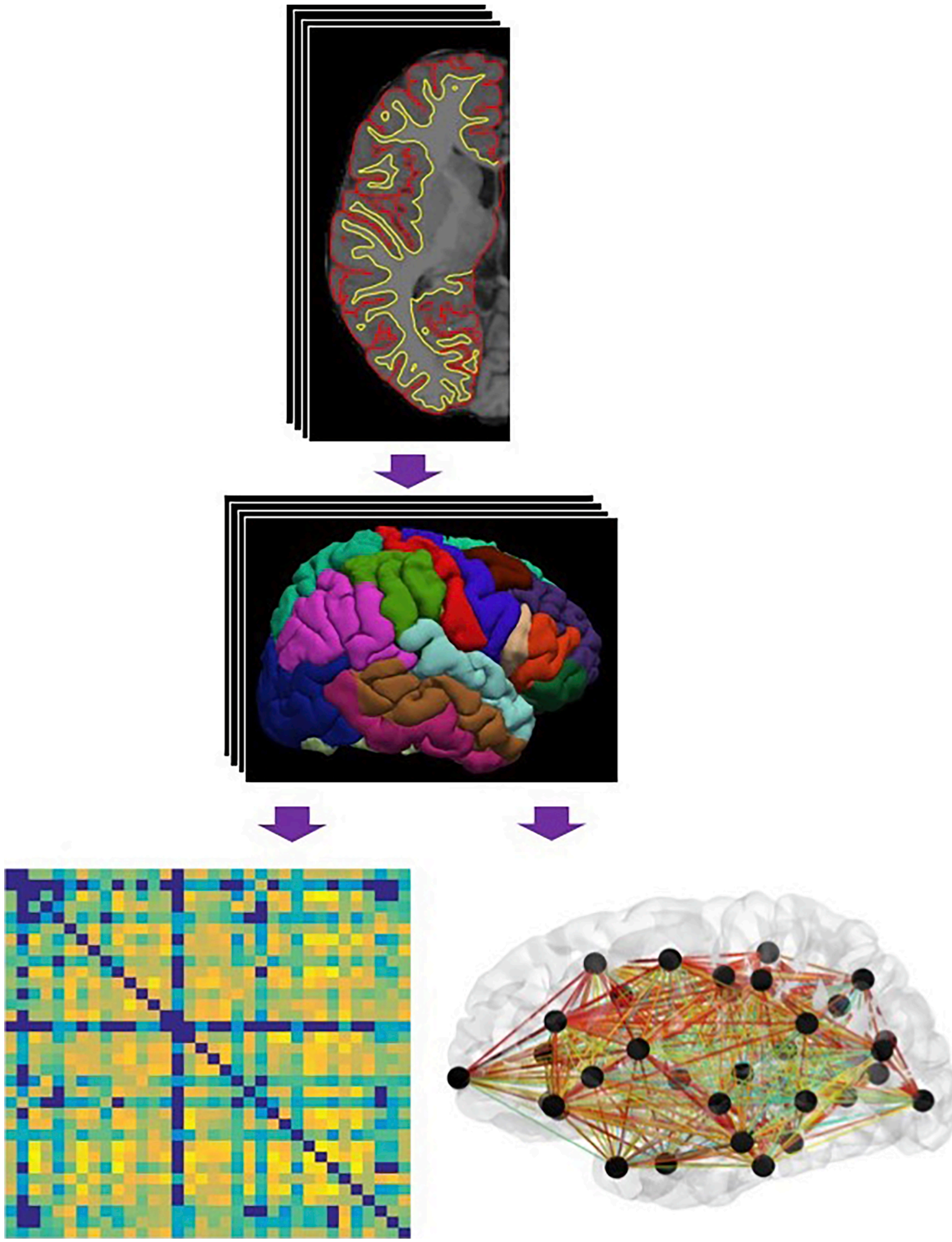

Fig. 1. Creation of cortical thickness connectomes. Each participant's T1-weighted volumetric MRI of the contralateral non-operated hemisphere was segmented into grey matter, white matter and CSF and then parcellated into the 34 cortical regions of the Desikan-Killiany atlas using Freesurfer. Cortical thickness measurements in each region were correlated within the groups and the correlation coefficient was used as the edge weight between each region to create a connectivity matrix or within-hemisphere connectome for each group. (MRI: magnetic resonance imaging; CSF: cerebrospinal fluid).

global efficiency – mean inverse shortest path between all nodes in the network; normalised clustering coefficient – the fraction of neighbours of a node connected to each other (binary), or the average geometric mean of the product of edge weights of triangles surrounding the node (weighted) [13]. The clustering coefficient was normalised by dividing by the mean clustering coefficient of 1000 randomly rewired networks with the same number of nodes, edges, and node degrees [13]. Global efficiency was chosen as the measure of integration as cortical thickness networks can disconnect at lower densities, leading to problems calculating average path lengths due to values of infinity in the distance matrix [24].

2.4. Statistical analysis

Data analysis was carried out using R version 3.4.0 "You Stupid Darkness" (The R Foundation for Statistical Computing, 2017) and Matlab Release 2015b. Group cortical thickness network measures were compared using permutation testing. The subjects were permuted into 1000 random group allocations and network measures were computed for these random permuted group networks. The *p* values were calculated as the number of times the absolute difference between the randomly permuted groups was greater than the absolute difference between the experimental groups divided by the 1000 permutations, and were corrected for multiple comparisons using the false discovery rate at 5 % [25]. Comparison of demographic and clinical features between the two groups was carried out using t tests for normally distributed data, Mann Whitney U tests for numerical data that did not follow a normal distribution, and X^2 tests for categorical data.

3. Results

Of 242 patients within the age of 1–17 years, we identified 35 patients who fulfilled the inclusion criteria. Reasons for exclusion were: lack of available 3D T1 non contrast enhanced MRI (117), artefact on MRI (15), bilateral pathological changes on MRI (11), lack of available pre and post operative IQ test results (47), and scoring below the assessable range on IQ testing (17). There were 11/35 (31 %) patients with a post-operative increase in IQ of at least 10 points, and 24/35 (69 %) patients whose IQ did not change more than 10 points. No patient had a greater than 10 point decrease in IQ post-operatively and no patient had a change of exactly 10 points. Table 1 compares the clinical features of the two groups. Those with an increase in IQ post-operatively had a significantly shorter duration of epilepsy pre-operatively, but similar age at onset of epilepsy (median 3.0 years vs 2.8 years). There were no patients with hippocampal sclerosis in the group that improved more than 10 points post-operatively, and slightly more with focal cortical dysplasia (55 % vs 33 %, see Table 1). Two years post-operatively there was a higher proportion of patients who were seizure free (82 % vs 58 %) and ASM free (36 % vs 21 %) in the group with an improvement in IQ but this did not reach statistical significance (see Table 1). Mean cortical thickness measurements were similar between the two groups.

Table 1
Comparison of demographic and clinical features by change in IQ.

	Group		*p*
	change IQ ≥ 10	change IQ < 10	
	n = 11	n = 24	
Pre-operative			
female	6 (54.5 %)	11 (45.8 %)	*0.909*
age at Operation (years)	8.2 (5.0–13.1)	11.4 (7.1–13.9)	*0.234*
age at first seizure (years)	3.0 (2.0–6.8)	2.8 (1.0–5.0)	*0.454*
duration of epilepsy (years)	3.1 (2.0–5.4)	5.8 (3.2–12.0)	*0.033*
left hemisphere operation	5 (45.5 %)	11 (45.8 %)	*1.00*
single lobe operation	10 (90.9 %)	22 (91.7 %)	*1.00*
aetiology			*0.559*
cortical dysplasia	6 (54.5 %)	8 (33.3 %)	
hippocampal sclerosis	0 (0 %)	4 (16.7 %)	
neurocutaneous	1 (9.1 %)	1 (4.2 %)	
tumour	3 (27.3 %)	7 (29.2 %)	
vascular	1 (9.1 %)	2 (8.3 %)	
unknown	0 (0 %)	2 (8.3 %)	
mean cortical thickness (mm)	2.9 (0.39)	2.8 (0.26)	*0.478*
pre-op IQ	72.2 (14.5)	78.0 (19.4)	*0.336*
Two years post-operative			
change in IQ	19.6 (9.5)	2.3 (11.3)	*<0.001*
Engel score 1A	9 (81.8 %)	14 (58.3 %)	*0.329*
ASM free	4 (36.4 %)	5 (20.8 %)	*0.576*

Patients with a post-operative IQ score more than 10 points above their pre-operative IQ score are compared to those without a change in IQ. Data are count (percentage) for categorical data, median (IQR) for age and years, and mean (SD) for cortical thickness and IQ scores.
(IQ: intelligence quotient; IQR: interquartile range; SD: standard deviation; ASM: anti-seizure medication).

Network global efficiency across all threshold values was higher in the group with a greater than 10 point post-operative increase in IQ. This was true for both weighted networks and binary networks (see Fig. 2). The highest threshold that maintained a completely connected network with no disconnected nodes in both groups was a threshold value of 0.3. Thresholding networks to remove all edge weights below an absolute value led to networks with a higher density in the group with an increase in post-operative IQ at all threshold levels (see Table 2). This suggests there are a higher number of connections of greater weights in the group with an increase in IQ. Group cortical thickness networks for the two groups are shown in Fig. 3. These show a higher number of edges with greater edge weights in the group with an increase in post-operative IQ. Network mean node strength and degree and network mean edge weight and density were higher in both the dense and the sparse networks in those whose IQ increased, but these differences were not statistically significant using group permutation testing (Table 2).

The group whose IQ increased more than 10 points post operatively had significantly higher weighted global efficiency in both the dense and the sparse networks. Binary global efficiency was higher in both the dense and sparse networks but only statistically significant in the sparse networks, which also had a much higher difference in network density and degree. A higher network density and degree will lead to a higher network global efficiency due to the increased number and strength of connections. The normalised clustering coefficient (γ) was not markedly different between the group with or without an increase in IQ post-operatively, suggesting that network segregation is similar between the two groups.

To assess whether the lower contralateral network efficiency in the group of patients without significant IQ improvement could be directly explained by a longer duration of epilepsy pre-operatively, we computed group networks for the dichotomised groups with a pre-operative duration of epilepsy shorter or longer than five years. Global efficiency of the weighted contralateral network in those with a duration of epilepsy longer than five years was similar to that of those with a shorter duration (n = 16, Eglob: 0.28 vs n = 19, Eglob:0.32, $p = 0.865$, threshold = 0.8). As a higher proportion of those whose IQ increased by more than 10 points were also seizure free post operatively, we also compared contralateral network global efficiency between those who were both seizure and ASM free post-operatively to those who were not. Those who were seizure and ASM free had a higher global efficiency (n = 9, Eglob: 0.67), compared to those who were not (n = 26, Eglob: 0.22, p = 0.06, threshold = 0.8).

4. Discussion

Children who had an increase of at least 10 points in IQ score two years following resective epilepsy surgery had higher global efficiency in the pre-operative cortical thickness connectome within their contralateral hemisphere compared to children whose IQ did not change. This finding was present in both dense and sparse networks, and in both weighted and binary networks.

To our knowledge there have not been any previous studies of the association between pre-operative structural network global efficiency in the contralateral hemisphere and change in IQ following epilepsy surgery. Our results are consistent with the finding that contralateral macroscopic structural MRI abnormalities are associated with a lower chance of cognitive improvement following hemispherectomy [7,8], and the observation that differences in the strength of functional connectivity within epileptic networks correlate with cognitive outcomes following epilepsy surgery [26,27]. Higher network average path length in whole brain structural connectomes has also previously been

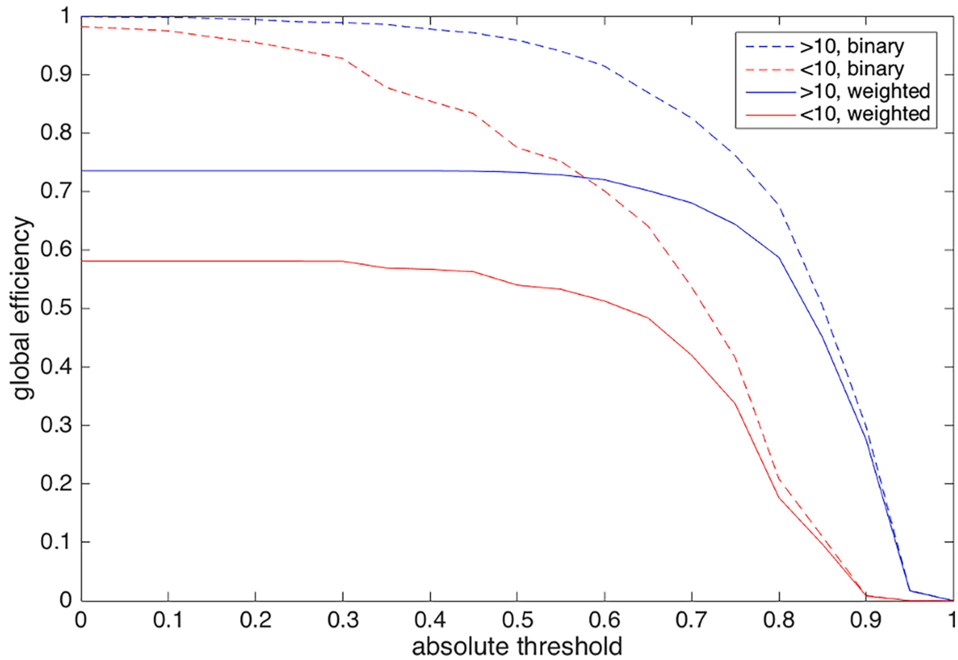

Fig. 2. Network global efficiency. Network global efficiency was compared between the group with an increase of at least 10 points post-operatively (blue line) and the group without an increase in IQ post-operatively (red line). Both binary (dotted lines) and weighted (solid lines) networks were analysed. Global efficiency was calculated for networks thresholded to remove all values between zero and one in steps of 0.05. The group with a greater than 10 point increase in IQ post-operatively has a higher global efficiency across the range of threshold values in both binary and weighted networks. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 2
Global network characteristics by change in IQ.

	dense networks, t = 0.3		*p*	sparse networks, t = 0.8		*p*
	change IQ ≥ 10	change IQ < 10		change IQ ≥ 10	change IQ < 10	
binary networks						
density	0.98	0.86	*0.113*	0.39	0.12	*0.139*
degree	32.3	28.4	*0.114*	13.06	4.00	*0.140*
γ	1.00	0.99	*0.960*	1.27	1.58	*0.690*
EGlob	0.99	0.93	*0.228*	0.68	0.21	*0.042*
weighted networks						
S	24.0	18.0	*0.145*	11.3	3.38	*0.142*
EW	0.75	0.64	*0.138*	0.87	0.84	*0.370*
γ	1.00	1.01	*0.960*	1.28	1.59	*0.690*
EGlob	0.74	0.58	*0.014*	0.59	0.18	*0.044*

Contralateral hemisphere network characteristics for those with a post-operative change in IQ of at least 10 points and those without a change in IQ. Network measures were calculated from both the binary and weighted networks. All edge weights below 0.3 were removed to create dense completely connected networks with no disconnected nodes. Sparse networks were created by removing all edge weights below 0.8. Permutation testing using 1000 group permutations was used to calculate *p* values. The group with a post-operative increase in IQ of at least 10 points has a statistically significant higher global efficiency in all network types except the dense binary networks.
(t: threshold value; IQ: intelligence quotient, γ: normalised clustering coefficient; E_{Glob}: global efficiency; S: mean network strength; EW: mean network edge weight).

associated with lower IQ scores or cognitive impairment in patients with epilepsy [18,28,29]. Pre-operative structural and functional connectome findings and predicted changes in connectomes following surgical resection have also been associated with seizure freedom following epilepsy surgery [30–35]. Therefore, our finding that contralateral structural connectome efficiency is associated with post-operative improvement in IQ is consistent with previous findings of predictors of IQ change following epilepsy surgery.

Children whose IQ improved post-operatively had better seizure control, lower ASM load post-operatively, a shorter duration of epilepsy pre-operatively, and were slightly younger. This is consistent with previous studies of associations with IQ change following paediatric epilepsy surgery [6,7,36,37]. The group with epilepsy for more than five years pre-operatively did not have a difference in their group contralateral cortical thickness connectome global efficiency compared to the group with epilepsy for less than five years pre-operatively, which suggests that the difference in global efficiency between those with and without an improvement in post-operative IQ is not due to the group difference in duration of epilepsy. During childhood and adolescence the cortex thins [38,39]. Thinner cortex and faster thinning of the cortex are associated with higher IQ [38]. In addition, structural brain networks derived from white matter show increased correlation with IQ as children develop through adolescence [39]. In our study those whose IQ improved were slightly younger at the time of surgery compared to those who did not (mean 8 years vs mean 11 years). However, the mean cortical thickness was similar (2.9 mm vs 2.8 mm, see Table 1), so our findings are unlikely to be driven by differences in pre-operative age.

As better seizure control is associated with better cognition, it was not possible to find a group in whom cognition improved but seizures did not. Cortical thickness networks are group networks rather than individual networks so we used permutation testing for statistical analysis and could not perform regression to assess for the relative influence of post-operative seizure freedom. Instead we investigated those who were seizure and ASM free post-operatively, and also found higher pre-operative contralateral network global efficiency. It is likely that there is a relationship between contralateral network global efficiency, post-operative seizure and ASM freedom, and post-operative cognitive improvement [1]. As seizure burden, microstructural anatomical changes, functional and structural connectivity and ASM burden are all associated with cognition in epilepsy, it is possible that more efficient structural connectomes pre-operatively facilitate the chances of improvement post-operatively [1,18,28,29].

The higher intra-hemisphere global efficiency in the group network

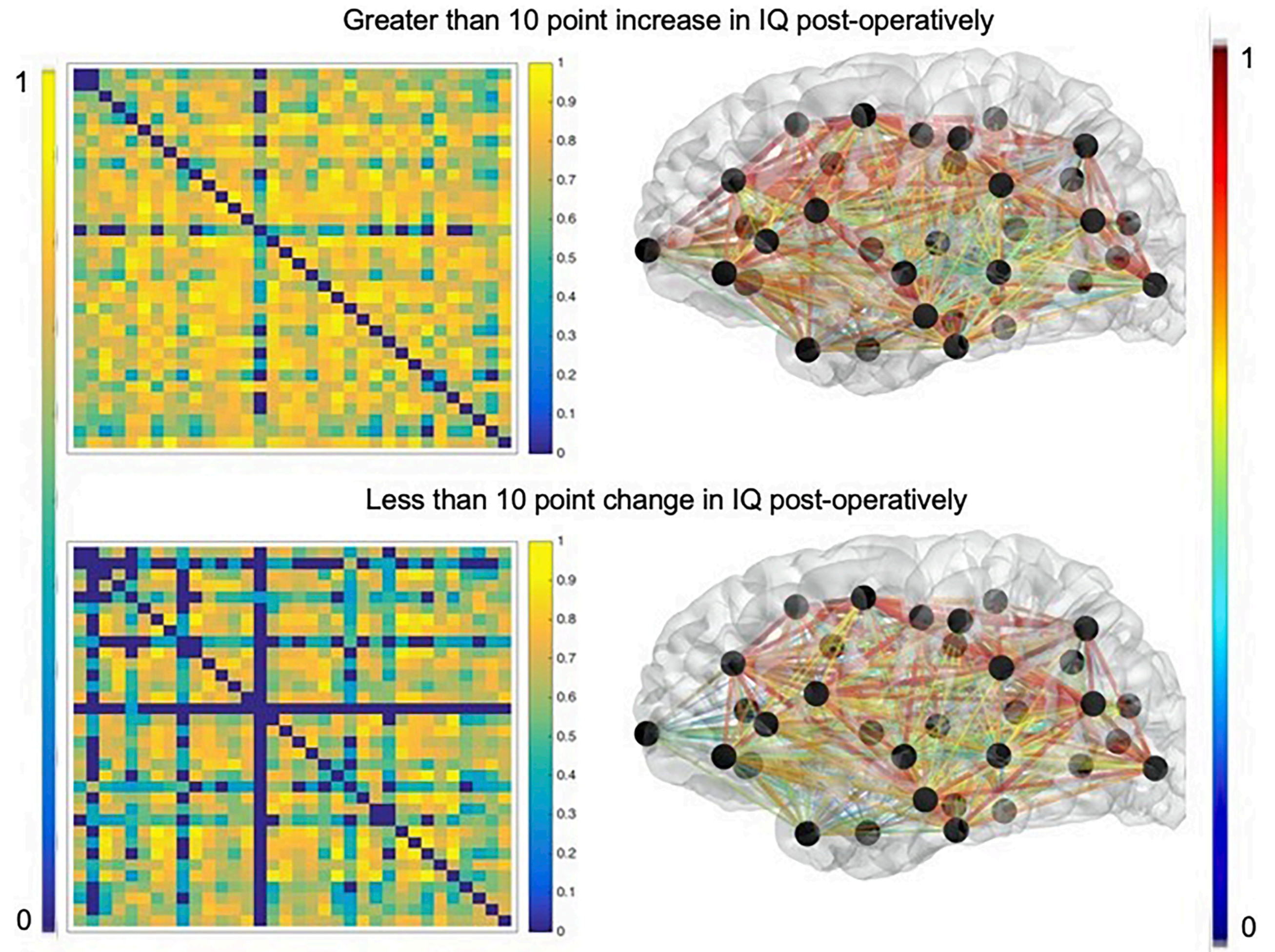

Fig. 3. Group cortical thickness networks. Group cortical thickness networks for the group with a greater than 10 point increase in IQ post-operatively (above) and the group with a less than 10 point change (below). Connectivity matrices (left) and networks overlaid on left hemisphere anatomical regions (right). Negative and self-self connections have been removed and networks are thresholded to remove all edge weights below 0.3. Connectivity matrices have Desikan-Killiany cortical regions along the left and bottom axes and region cortical thickness correlations within the matrices. Correlations range from zero (blue) to one (yellow) as shown in the left hand colour bar key. Cortical thickness correlations in the anatomical networks range from zero (blue) to one (red) as per the right hand colour bar key, and thicker lines represent higher edge weights. All regions are represented by circles of the same size. The connectome representations show the group with a greater than 10 point increase in IQ has a larger number of higher edge weights. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

of those whose IQ increased at least 10 points post-operatively could be accounted for by the higher network density, mean node degree, mean node strength, and mean edge weight. However, the normalised clustering coefficient was similar between groups, and a difference in clustering might also be expected if the findings were due only to network density. The greater number and strength of connections was not caused by any difference in overall cortical thickness as mean cortical thickness measurements were similar between the two groups, or in thresholding, as the same threshold was applied to both groups for analyses. The larger magnitude of the between group difference in global efficiency compared to the non-significant differences in number and weight of connections therefore suggests that the increased network efficiency is not only due to an increased number and weight of connections, but is also likely due to the arrangement of those connections.

Cortical thickness and patterns have long been linked to brain function [40,41]. Changes in regional correlations in cortical thickness have been attributed to environmental influences, such as learning, or to genetic and developmental influences [20,42,43]. Lower global efficiency within the contralateral hemisphere of the group without an increase in IQ post-operatively could represent a lack of development of correlations that enable efficient brain function. This could be as a result of uncontrolled seizure activity preventing usual development or the underlying epilepsy aetiology causing both disordered cortical thickness correlations and epilepsy.

Surgical resection for focal epilepsy aims to remove the epileptogenic focus and prevent seizures spreading but does not alter the underlying pathological process that has led to epilepsy. Our group comparisons show that increased efficiency in the contralateral hemisphere is associated with cognitive improvement following resective epilepsy surgery, but we are unable to provide values or cut offs for individual predictions. Improved understanding of whether cognitive function is constrained by the structural organisation of the brain could help in identifying structural correlates of cognitive function that have the potential to serve as radiological biomarkers of outcome following epilepsy surgery, and contribute to individual counselling and predictions.

The strengths of this study are the validated standardised methods of IQ assessment and imaging analysis and standardised clinical data collection and follow up as part of an epilepsy surgery programme. However, the retrospective nature of patient identification and requirement for complete data for analysis led to a relatively small cohort that may be underpowered to detect small between group differences. Our small cohort is demographically comparable to those undergoing surgery as part of the Dutch collaborative national epilepsy surgery programme (median age 10 years; median age at seizure onset 2 years; 48 % female) [44]. However, our cohort has higher representation of tumours, focal cortical dysplasia and hippocampal sclerosis, and slightly better seizure outcomes than the overall cohort [44], as expected when selecting those with a structurally normal contralateral hemisphere. The proportion whose IQ score increased post-operatively is similar to the Dutch and other series and *meta*-analyses suggesting around 30 % improve post-operatively [5,6,45]. Although this suggests our sample is representative, our preliminary findings only apply to those with an IQ within the measurable range of standard IQ assessment tools, and a macroscopically structurally normal contralateral hemisphere.

We analysed within hemisphere contralateral connectomes rather than whole brain connectomes to avoid the influence of structural abnormalities within the operated hemisphere. We did not analyse post-operative connectomes, so we cannot comment on any potential for plastic network remodelling post-operatively. Our study was restricted to two year follow up, and improvements in IQ have been reported over five years post-operatively [3]. We cannot assess whether longer term cognitive outcomes are associated with pre-operative structural connectomes. We chose to construct networks from covariance of cortical thickness rather than using white matter streamlines. Cortical thickness networks have similar patterns of connectivity to networks constructed from diffusion tensor imaging, tract tracing data, or anatomical data [20,41,46–50] and do not have difficulties of under-representation of long range connections or dealing with crossing fibres [46,47,50,51]. We used the 1.5 T anatomical imaging available in this retrospective observational study and analytical methods designed using 1.5 T imaging [15,16]. Analysing 3 T imaging, structural networks derived from white matter tracts, and functional networks in future studies could corroborate our results.

In conclusion, this study shows that the structural organisation of the contralateral non-operated hemisphere is associated with change in IQ following childhood resective epilepsy surgery. Increased network global efficiency is related to a post-operative increase of at least 10 points in IQ.

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Author contributions

All authors were involved in: experimental design, data acquisition, and analysis and interpretation of data; drafting or critically revising the article with respect to intellectual content; and have read and approved the submitted manuscript.

Data Availability Statement

Retrospective anonymised data were used for this publication. No permission was given for sharing of data.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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