Received: 29 March 2022 | Revised: 11 April 2022 | Accepted: 24 April 2022

DOI: 10.1111/ane.13631

Acta Neurologica Scandinavica WILEY

ORIGINAL ARTICLE

Cortical remodeling before and after successful temporal lobe epilepsy surgery

Wei Li[1] | Yuchao Jiang[2] | Yingjie Qin[1] | Xiuli Li[3] | Du Lei[3] | Heng Zhang[4] | Cheng Luo[2] | Qiyong Gong[3] | Dong Zhou[1] | Dongmei An[1]

[1]Department of Neurology, West China Hospital, Sichuan University, Chengdu, China

[2]MOE Key Lab for Neuroinformation, Center for Information in Medicine, School of life Science and technology, The Clinical Hospital of Chengdu Brain Science Institute, University of Electronic Science and Technology of China, Chengdu, China

[3]Department of Radiology, Huaxi MR Research Center, West China Hospital, Sichuan University, Chengdu, China

[4]Department of Neurosurgery, West China Hospital, Sichuan University, Chengdu, China

Correspondence
Dongmei An and Dong Zhou, Department of Neurology, West China Hospital, Sichuan University, Chengdu, Sichuan, China.
Emails: andongmei2010@gmail.com (D.A.); zhoudong66@yahoo.de (D.Z.)

Qiyong Gong, Huaxi MR Research Center, Department of Radiology, Center for Medical Imaging, West China Hospital, Sichuan University, Chengdu, Sichuan, China.
Email: qiyonggong@hmrrc.org.cn

Funding information
National Natural Science Foundation of China, Grant/Award Number: 81771402, 82171443 and 81871017; Sichuan International Science and Technology Innovation Cooperation / Hong Kong, Macao and Taiwan Science and Technology Innovation Cooperation Project, Grant/Award Number: 2021YFH0136; 1.3.5 project of disciplines of excellence-clinical research incubation project, West China Hospital, Sichuan University, Grant/Award Number: 2019HXFH047; 1.3.5 project for disciplines of excellence of West China Hospital at Sichuan University, Grant/Award Number: ZY2017305

Objectives: To explore dynamic alterations of cortical thickness before and after successful anterior temporal lobectomy (ATL) in patients with unilateral mesial temporal lobe epilepsy (mTLE).

Materials and Methods: High-resolution T1-weighted MRI was obtained in 28 mTLE patients who achieved seizure freedom for at least 24 months after ATL and 29 healthy controls. Patients were scanned at five timepoints, including before surgery, 3, 6, 12 and 24 months after surgery. Preoperative cortical thickness of mTLE patients were compared with healthy controls. Dynamic alterations of cortical thickness before and after surgery were compared among five scans using linear mixed models.

Results: Patients with mTLE showed cortical thinning pre-surgically in ipsilateral entorhinal cortex, parahippocampal gyrus, inferior parietal cortex, lateral occipital cortex; contralateral pericalcarine cortex (PCC); and bilateral caudal middle frontal gyrus (cMFG), paracentral lobule, precentral gyrus (PCG), superior parietal cortex. Cortical thickening was observed in contralateral rostral anterior cingulate cortex (rACC). Patients showed postsurgical cortical thinning in ipsilateral temporal lobe, fusiform gyrus, caudal anterior cingulate cortex, lingual gyrus, and insula. Ipsilateral cMFG, PCC, and contralateral PCG showed significant cortical thickening after surgery. In addition, contralateral rACC showed cortical thickening at 3 months follow-up, however, with obvious cortical thinning at 24 months follow-up.

Conclusions: Mesial temporal lobe epilepsy patients showed widespread cortical thinning before and after anterior temporal lobectomy. Progressive cortical thinning mainly existed in neighboring regions of resection. Postoperative cortical thickening may indicate cortical remodeling after successful surgery.

KEYWORDS
cortical thickness, remodeling, structural MRI, surgery, temporal lobe epilepsy

1 | INTRODUCTION

Mesial temporal lobe epilepsy (mTLE) is the most common type of drug-resistant epilepsy in adults,[1] of which anterior temporal lobectomy (ATL) is a well-established and effective treatment,[2] offering a seizure-free rate of about 60%–70%.[3]

It has been well acknowledged that mTLE is a network disorder involving widespread cortical and subcortical regions, even far beyond the mesial temporal structures.[4,5] Structural MRI have revealed extensive gray matter atrophy[6–9] and cortical thinning[10–12] in mTLE. Longitudinal study demonstrated that mTLE may lead to progressive gray matter atrophy with the course of epilepsy,[13] even in patients who achieved seizure freedom for at least 2 years through antiseizure medications (ASMs) therapy[14] or epilepsy surgery,[15] suggesting a probable underlying pathological mechanism other than ongoing seizures. In addition, it was reported that progressive cortical thinning advanced in focal epilepsy patients at a rate more than twice that of normal aging, especially in the first five years after epilepsy onset.[16]

Thus, how to prevent progressive neurodegenerative process in mTLE has become an important issue in clinical practice. Previous voxel-based morphometry (VBM) studies revealed increased gray matter volume (GMV) at some postoperative timepoint in seizure-free patients, indicating cortical reorganization after successful TLE surgery.[17,18] However, postsurgical GMV increase was not consistently found in other studies. Surface-based morphometry (SBM) analysis, which has improved inter-subject spatial alignment, may be more sensitive to reveal cortical remodeling after successful surgery. In a recent well-designed longitudinal study, no more progressive thinning than that observed during normal aging was found in postoperative seizure-free TLE patients, suggesting successful epilepsy surgery might prevent progressive cortical thinning.[19] In another study, no significant cortical thinning except for cortices near the resected areas were observed and some presurgical cortical atrophy recovered after successful ATL.[20] However, it remains unclear how the cortices remodels after successful surgery, let alone the dynamic changing process.

We previously studied dynamic changes of white matter diffusion, gray matter volume, and intrinsic brain activity in mTLE patients who achieved seizure freedom after ATL at five serial timepoints: before surgery, 3, 6, 12 and 24 months after surgery.[21,22] In the current study, we aimed to explore dynamic cortical thickness alterations after successful TLE surgery and to confirm postoperative cortical remodeling.

2 | MATERIALS AND METHODS

2.1 | Participants

Intractable unilateral mTLE patients who underwent ATL in West China Hospital were consecutively enrolled from April 2014 to October 2018. Diagnosis was made based on multimodal information including seizure semiology, ictal and interictal EEG, structural MRI and positron emission tomography/computed tomography (PET/CT) if available, according to the International League Against Epilepsy (ILAE) criteria.[23] All patients were diagnosed as medical intractable mTLE, with a negative structural MRI or evidence of unilateral hippocampal sclerosis (HS) concordant with EEG findings. The diagnosis of mTLE with normal MRI was made according to typical semiology including epigastric or psychic auras, loss of consciousness, oral alimentary and manual automatisms, as well as specific interictal spike waves and ictal rhythmic theta activity in unilateral anterior temporal regions on EEG. All patients achieved standard unilateral ATL by one experienced surgeon to reduce surgical removal differences as much as possible. Post-surgical outcome was assessed according to the ILAE classification[3] every 3 months after surgery. All patients achieved seizure freedom for at least 24 months after ATL. Patients were excluded for any of the following reasons: (1) with other neurological or psychiatric disorders; (2) with alcohol or other substances abuse; (3) with other structural lesions except HS confirmed by postoperative histopathological examination according to ILAE classification[24]; (4) lost to follow-up.

Age- and gender-matched healthy controls (HC) were also recruited. This study was approved by the local ethics committee on human experimentation protocols of West China Hospital, and informed consent was obtained from all participants.

2.2 | Image acquisition

High-resolution 3D T1-weighted MRI data were acquired on a 3.0 T MRI system (Trio; Siemens) with an 8-channel phased array head coil at West China Hospital. MTLE patients were scanned at five timepoints (before surgery, 3, 6, 12 and 24 months after surgery) using the same protocol, while healthy controls were only scanned at one timepoint. Images were obtained in sagittal orientation using a spoiled gradient-recalled sequence with the following parameters: repetition time (TR) = 1900 ms; echo time (TE) = 2.26 ms; flip angle = 9°; slice thickness = 1 mm; field of view (FOV) = 256 × 256 mm^2; and voxel size = 1.0 × 1.0 × 1.0 mm^3. A standard birdcage head coil and a restraining foam pad were used to minimize the head motion. Earplugs were used to reduce the noise.

2.3 | Image processing

SPM12 (http://www.fil.ion.ucl.ac.uk/spm/) was applied for preprocessing. We flipped T1 images of right-sided mTLE patients (9/28) and according matched HC to obtain the ipsilateral and contralateral datasets, similar to our previous study.[22] There was evidence that gray matter structural compromise equally distributed in left and right TLE.[25] Preoperative images were co-registered to a symmetric Montreal Neurological Institute (MNI) template using a nonlinear transformation function. This template was created by averaging MNI template and its left–right flipped counterpart. Surgical

resections of all patients were manually delineated in native space. The resection masks and postoperative images were registered to the corresponding preoperative images using affine registration to reduce possible stretching of non-resected tissue and then normalized to the symmetric MNI template using the same nonlinear transformation function. We used a group-level resection mask including all voxels within individual resection mask to remove analysis within it to avoid possible effect of resection differences.

The regional cortical thickness was characterized with the Computational Anatomy Toolbox (CAT12; http://dbm.neuro.uni-jena.de/cat12/) within SPM12. Default parameters of CAT12 for the preprocessing procedure were applied, including bias field correction, spatial normalization, segmentation (gray matter, white matte, and cerebrospinal fluid), and resampling to $2\times2\times2\,mm^3$. Cortical thickness maps were smoothed with a 10 mm surface-based kernel, while postoperative images were smoothed after masking out the resection areas. Gyral-based regions of interest (ROIs) were extracted as described by Desikan et al.[26] Mean cortical thickness of each ROI was calculated for further statistical analysis.

2.4 | Statistical analysis

Independent two-sample *t*-tests were used to compare the cortical thickness between preoperative mTLE patients and HC, with age and gender as covariates. $p<.05$ was considered as statistical significance. Linear mixed models were used to find out brain regions with significant cortical thickness changes among pre- and postoperative scans in mTLE patients. Post hoc t test was used to depict the dynamic cortical thickness alterations at different timepoints. $p<.05$ was considered statistically significant after Bonferroni correction for multiple comparisons.

3 | RESULTS

3.1 | Clinical data

Finally, 28 mTLE patients (12 males) were enrolled. The mean age at surgery was 25.9 years old (range: 15–44 years old), and mean duration of epilepsy was 13 years (range: 2–31 years). All patients underwent standard unilateral ATL (19/9, L/R) by one surgeon and achieved ILAE class 1 after surgery for at least 24 months. The median follow-up time was 35 months (range: 27–52 months). The antiseizure medications in the first 2 years after surgery remained the same as those prior to surgery. Postoperative histopathological test confirmed hippocampal sclerosis in 17 patients and gliosis in the other 11 patients. Preoperative structural MRI data were acquired in all 28 patients while postoperative data were acquired in 16/17/20/24 patients at 3 m/6 m/12 m/24 m follow-up, respectively. Detailed clinical characteristics of patients were summarized in Table 1.

Furthermore, 29 healthy controls (13 males) were enrolled with a mean age of 27.5 years old (range: 19–42 years old). There was no statistical difference in age and gender between the patient and control group. All participants were native Chinese speakers and right-handed assessed by the Edinburgh Inventory handedness test. All participants were the same as our previous study[22] exploring structural and functional reorganization of contralateral hippocampus after TLE surgery.

3.2 | Cortical thickness changes before surgery

As shown in Table 2, mTLE patients showed cortical thinning in ipsilateral entorhinal cortex (EC), parahippocampal gyrus (PHG), inferior parietal cortex (IPC), lateral occipital cortex (LOC); contralateral pericalcarine cortex (PCC); and bilateral caudal middle frontal gyrus (cMFG), paracentral lobule (PCL), precentral gyrus (PCG), and superior parietal cortex (SPC). Cortical thickening was observed in contralateral rostral anterior cingulate cortex (rACC).

In addition, we explored cortical thickness differences between mTLE patients with HS and gliosis only confirmed by histopathological test. Presurgical cortical thinning was more obvious in gliosis patients than HS patients in ipsilateral postcentral gyrus, precuneus, PCL, PCG, SPC, and contralateral cMFG ($p<.05$) (Table S1).

3.3 | Cortical thickness changes after surgery

As shown in Figure 1 and Table 3, ipsilateral superior temporal gyrus (STG), fusiform gyrus (FG), inferior temporal gyrus (ITG), middle temporal gyrus (MTG), caudal anterior cingulate cortex (cACC), lingual gyrus (LG), and insula (INS) showed significant cortical thinning after surgery. Thereinto, ipsilateral FG, cACC, LG, and INS showed progressive cortical thinning from 3 to 24 months follow-up.

Ipsilateral caudal middle frontal gyrus, pericalcarine cortex, and contralateral precentral gyrus showed significant cortical thickening after surgery.

Contralateral anterior cingulate cortex showed cortical thickening at 3 months after surgery, however, with obvious cortical thinning at 24 months follow-up.

Furthermore, we also explored postsurgical cortical thickness differences between HS and gliosis patients. No obvious difference was found in postsurgical cortical thinning between two groups ($p>.05$). However, compared with HS patients, gliosis patients showed more obvious cortical thickening in ipsilateral caudal middle frontal gyrus at 6, 12, and 24 months after surgery ($p = .001, .02, .02$).

4 | DISCUSSION

The present study explored longitudinal dynamic cortical thickness alterations in mTLE patients who achieved seizure freedom after ATL for at least 24 months at five serial timepoints. Presurgical cortical thinning was found in several regions involving bilateral hemispheres. Cortical thickening was observed in contralateral rACC.

TABLE 1 Demographic and clinical characteristics of mTLE patients

Subject	Sex	Age at surgery (year)	Disease duration (years)	Seizure type	Seizure frequency	Seizure focus	Pathology (ILAE classification)
TLE_01	M	22	14	FS	Monthly	L	HS
TLE_02	F	22	10	FS, FBTCS	Weekly	L	Gliosis
TLE_03	F	26	17	FS	Weekly	L	HS
TLE_04	F	35	31	FS, FBTCS	Monthly	L	Gliosis
TLE_05	M	20	4	FS, FBTCS	Weekly	L	HS
TLE_06	F	25	15	FS, FBTCS	Monthly	L	HS
TLE_07	F	26	6	FS, FBTCS	Daily	L	Gliosis
TLE_08	M	22	10	FS	Daily	R	Gliosis
TLE_09	F	41	10	FS	Weekly	R	HS
TLE_10	M	17	8	FS, FBTCS	Monthly	L	Gliosis
TLE_11	M	20	14	FS, FBTCS	Monthly	R	Gliosis
TLE_12	F	38	27	FS	Monthly	R	Gliosis
TLE_13	F	19	12	FS	Weekly	R	HS
TLE_14	M	28	21	FS, FBTCS	Monthly	L	Gliosis
TLE_15	M	18	4	FS	Monthly	L	HS
TLE_16	M	20	19	FS, FBTCS	Monthly	L	Gliosis
TLE_17	M	22	22	FS, FBTCS	Daily	R	HS
TLE_18	M	17	7	FS	Monthly	L	HS
TLE_19	M	41	13	FS	Monthly	L	HS
TLE_20	F	23	2	FS, FBTCS	Monthly	R	HS
TLE_21	F	25	14	FS, FBTCS	Weekly	L	Gliosis
TLE_22	F	26	9	FS, FBTCS	Daily	L	HS
TLE_23	F	39	21	FS, FBTCS	Weekly	R	HS
TLE_24	F	33	18	FS	Monthly	R	Gliosis
TLE_25	F	15	3	FS, FBTCS	Weekly	L	HS
TLE_26	F	19	18	FS, FBTCS	Monthly	L	HS
TLE_27	F	22	14	FS, FBTCS	Monthly	L	HS
TLE_28	M	44	15	FS, FBTCS	Monthly	L	HS

Abbreviations: F, female; FBTCS, focal to bilateral tonic–clonic seizure; FS, focal seizure; HS, hippocampal sclerosis; ILAE, International League Against Epilepsy; L, left; M, male; R, right; TLE, temporal lobe epilepsy.

Further postsurgical cortical thinning was observed in cortices in ipsilateral hemisphere. Furthermore, significant cortical thickening was observed in ipsilateral cMFG, PCC, and contralateral PCG after successful surgery. These findings extended our understanding of dynamic structural alterations in epileptic brain following ATL and confirmed cortical remodeling after successful surgery.

Widespread cortical thinning was found pre-surgically in mTLE patients, including ipsilateral EC, PHG, IPC, LOC; contralateral PCC; and bilateral cMFG, PCL, PCG, and SPC. These results were in keeping with previous findings that cortical thinning was bilateral and located beyond the epileptic focus,[7,10,11,16,27] indicating extensive neuronal loss and neurodegeneration in mTLE patients.[28] It reinforced the concept that mTLE is indeed a sophisticated network disorder. The underlying mechanisms may be the acute effect of repetitive seizures or chronic effect of epilepsy itself. Besides, we found cortical thickening in contralateral rACC, which was not reported before and might suggest a structural compensation in contralateral hemisphere.

Ipsilateral STG, FG, ITG, MTG, cACC, LG, and INS showed cortical thinning after surgery. Thereinto, ipsilateral FG, cACC, LG, and INS showed progressive cortical thinning from 3 to 24 months follow-up. Postoperative cortical thinning maybe the results of tissue shrinkage in the remnant of ipsilateral temporal lobe and ongoing Wallerian degeneration in nerve bundles disconnected by resection.[16,18,21,29] In addition, direct surgical effect often occurred immediately after surgery and lasted from months to years; thus, ipsilateral temporal lobe showed cortical thinning at 3-month follow-up and remained relatively stable thereafter. Interestingly, although with favorable seizure outcome, our patients showed progressive cortical thinning in ipsilateral FG, cACC, LG, and INS from 3 to 24 months after surgery, which was inconsistent with the recent finding that no more progressive thinning was found

TABLE 2 Regions with significant cortical thickness alterations before surgery

Region	CT of mTLE	CT of HC	T value	*p* Value
Ipsilateral hemisphere				
Entorhinal cortex	4.17 ±0.48	4.42 ±0.34	−2.24	.03
Parahippocampal gyrus	2.67 ±0.14	2.77 ±0.16	−2.57	.01
Inferior parietal cortex	2.70 ±0.13	2.78 ±0.11	−2.44	.02
Lateral occipital cortex	2.27 ±0.13	2.37 ±0.15	−2.70	.01
Caudal middle frontal gyrus	2.88 ±0.15	2.98 ±0.12	−2.68	.01
Paracentral lobule	2.58 ±0.16	2.70 ±0.12	−3.06	.00
Precentral gyrus	2.65 ±0.17	2.75 ±0.14	−2.41	.02
Superior parietal cortex	2.43 ±0.16	2.53 ±0.10	−2.66	.01
Contralateral hemisphere				
Pericalcarine cortex	1.80 ±0.17	1.89 ±0.14	−2.16	.04
Caudal middle frontal gyrus	2.94 ±0.15	3.03 ±0.13	−2.34	.02
Paracentral lobule	2.58 ±0.15	2.67 ±0.14	−2.31	.02
Precentral gyrus	2.62 ±0.19	2.72 ±0.15	−1.98	.04
Superior parietal cortex	2.47 ±0.13	2.53 ±0.09	−2.05	.04
Rostral anterior cingulate cortex	3.25 ±0.17	3.03 ±0.19	4.42	.00

Abbreviation: CT, cortical thickness.

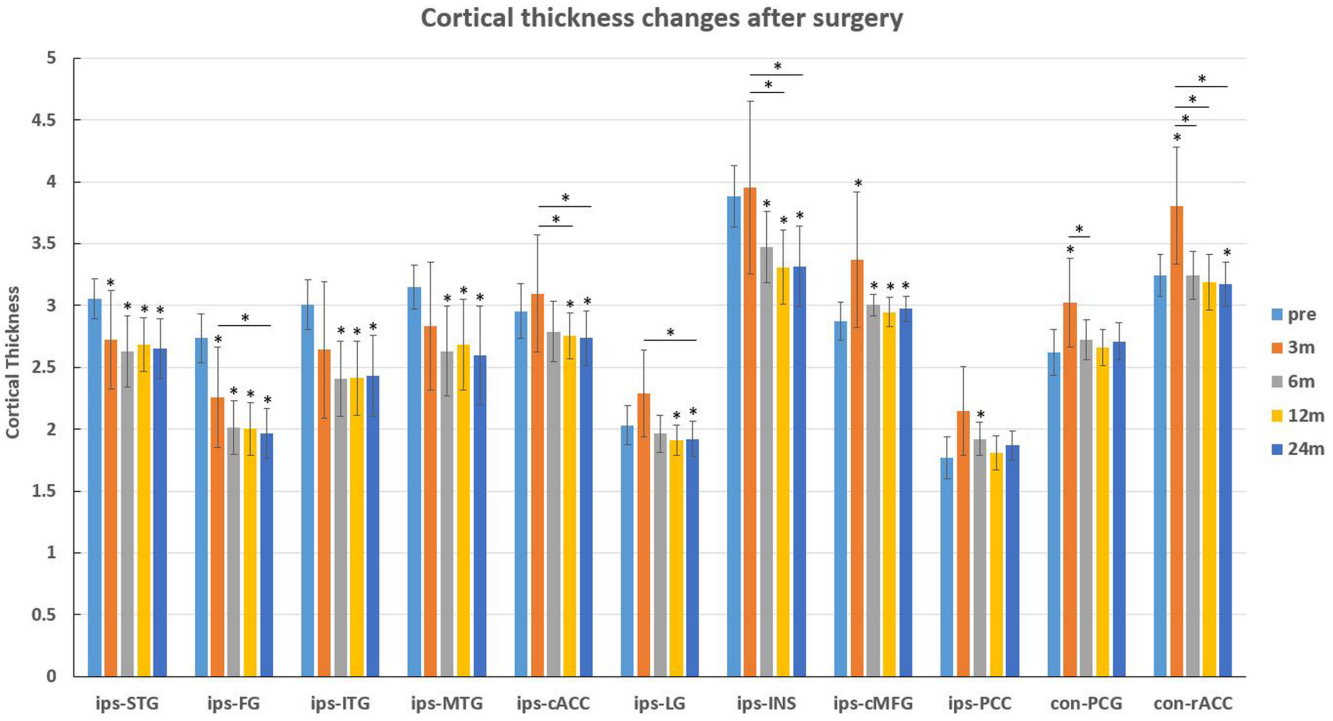

FIGURE 1 Cortical thickness changes after successful surgery (*$p < .05$, Bonferroni correction; separate asterisks indicated significant differences with preoperative scan). Abbreviations: 12 m, 12 months after surgery; 24 m, 24 months after surgery; 3 m, 3 months after surgery; 6 m, 6 months after surgery; cACC, caudal anterior cingulate cortex; cMFG, caudal middle frontal gyrus; con, contralateral; FG, fusiform gyrus; INS, insula; ips, ipsilateral; ITG, inferior temporal gyrus; LG, lingual gyrus; MTG, middle temporal gyrus; PCC, pericalcarine cortex; PCG, precentral gyrus; pre, preoperative, rACC, rostral anterior cingulate cortex; STG, superior temporal gyrus

in postoperative seizure-free TLE patients.[16] Previously, we also found progressive gray matter atrophy in ipsilateral insula in patients achieved seizure freedom after surgery.[15] The possible reason of progressive cortical thinning may be the underlying pathologic mechanism of mTLE, similarly to the progression of gray matter atrophy in seizure-free TLE patients.[14] Another possibility may be the effects of ASMs since ASMs were thought to be associated with reduced cortical thickness and brain volume.[14,30]

TABLE 3 Cortical thickness comparisons (T value) between different time points

Region	3 m/ pre	6 m/ pre	12 m/ pre	24 m/ pre	6 m/ 3 m	12 m/ 3 m	24 m/ 3 m	12 m/ 6 m	24 m/ 6 m	24 m/ 12 m
ips-STG	−3.78*	−7.45*	−9.80*	−10.17*	−2.55	−0.94	−1.08	1.24	1.32	−0.15
ips-FG	−4.41*	−11.26*	−14.68*	−15.33*	−3.06	−1.79	−3.53*	0.81	−0.35	−1.32
ips- ITG	−2.88	−8.58*	−8.14*	−8.51*	−2.73	−1.27	−2.33	0.69	0.57	1.53
ips-MTG	−3.23	−8.76*	−7.93*	−8.60*	−2.72	−1.28	−2.57	0.85	0.04	−1.15
ips-cACC	1.51	−2.83	−7.28*	−6.84*	−3.53*	−2.47	−3.59*	0.46	−1.39	−0.15
ips-LG	2.43	−1.65	−4.39*	−3.58*	−3.26	−3.04	−3.43*	−1.82	−1.52	0.57
ips-INS	0.14	−6.68*	−8.75*	−7.75*	−3.44*	−2.71	−4.03*	−1.29	−2.42	−0.83
ips-cMFG	3.59*	7.45*	5.72*	4.64*	−3.26	−2.43	−3.11	0.04	−1.24	−0.14
ips-PCC	3.06	3.66*	1.84	2.96	−2.69	−2.62	−2.78	−2.12	−1.56	1.64
con-PCG	3.45*	2.80	2.74	2.71	−3.46*	−2.89	−3.36	−0.38	−0.15	1.01
con-rACC	4.23*	−1.08	−2.58	−4.51*	−4.06*	−3.86*	−4.43*	−0.81	−2.22	−0.64

Abbreviations: 6 m, 6 months after surgery; 12 m, 12 months after surgery; 24 m, 24 months after surgery; 3 m, 3 months after surgery; ACC, caudal anterior cingulate cortex; cMFG, caudal middle frontal gyrus; con, contralateral; FG, fusiform gyrus; INS, insula; ips, ipsilateral; ITG, inferior temporal gyrus; LG, lingual gyrus; MTG, middle temporal gyrus; PCC, pericalcarine cortex; PCG, precentral gyrus; pre, preoperative; rACC, rostral anterior cingulate cortex; STG, superior temporal gyrus.

*$p < .05$, Bonferroni correction.

All our patients kept the same ASMs within the first 2 years after surgery.

More importantly, postoperative cortical thickening was found in ipsilateral cMFG, PCC, and contralateral PCG, which was rarely reported in the literature. These findings may imply the cortical remodeling after successful TLE surgery, which might result from a neuroplastic mechanism generated by the new state of seizure control.[18] Previous studies[10–12,17,31] mostly focused on preoperative cortical abnormalities or reflected postoperative cortical alterations at one single timepoint, which may not completely reflect the dynamic changes of cortical thickness before and after surgery. Recent TLE study with two postsurgical timepoints (≥3 months and ≥12 months) revealed focal postsurgical cortical thickening in right postcentral gyrus in right TLE patients achieved seizure freedom.[16] In our study, ipsilateral cMFG showed consistently cortical thickening at all postoperative scans when compared with preoperative scan, suggesting the cortical remodeling was relatively stable and reliable. Similarly, Doucet et al.[18] found postsurgical gray matter volume increase in ipsilateral frontal cortex within good outcome patients, indicating ipsilateral frontal cortex played important roles in postsurgical structural reconstruction in TLE. Moreover, ipsilateral PCC and contralateral PCG also showed obvious cortical thickening at 3–6 months after surgery when compared with preoperative scan. Since pericalcarine cortex located nearby the primary visual cortex,[32] there was a possibility that the cortical thickening in ipsilateral PCC might contribute to visual and verbal memory reorganizations after successful surgery. Further visual and memory tests were needed to verify it. Cortical thickening in contralateral precentral gyrus after surgery indicated cortical remodeling in contralateral hemisphere, which was consistent with previous findings of postoperative gray matter concentration primarily in contralateral hemisphere in seizure-free cases.[17] Although our controls were only scanned once, we could not exclude subtle normal variations with time; however, previous studies only found aging-related cortical thinning in healthy volunteers.[16] It was more likely that our findings of postoperative cortical thickening resulted from postoperative cortical remodeling rather than normal variations. In another word, successful surgery might prevent, even reverse, progressive cortical thinning.

In addition, contralateral rACC showed significant cortical thickening before surgery, further cortical thickening at 3 months after surgery, however, with obvious cortical thinning at 24 months follow-up. The fluctuation of cortical thickness in contralateral rACC may reflect the reversible influence of seizures and surgery to contralateral hemisphere.

Furthermore, our subgroup analysis indicated that gliosis patients showed more obvious cortical thinning before surgery and more obvious cortical thickening in ipsilateral caudal middle frontal gyrus after successful surgery than HS patients. These results provided preliminary evidence of structural and remodeling differences between mTLE patients with different pathology. Further studies with more patients with persistent seizures after surgery were needed to confirm whether these differences were related to seizure or cognitive outcomes.

4.1 | Limitations

There were several limitations in this study. Firstly, our sample size was relatively small. Secondly, we right–left flipped images to combine analysis, ignoring different functions of left and right hemisphere. Thirdly, not all patients were scanned five times and healthy controls were only scanned once, which may cause inter-group

imbalance. Further study with more patients and more longitudinal scans for controls was needed to increase our statistical power and to analyze in each hemisphere independently.

ACKNOWLEDGEMENT

This study was supported by National Natural Science Foundation of China (NSFC, Grant No. 81771402, 82171443, 81871017), Sichuan International Science and Technology Innovation Cooperation / Hong Kong, Macao and Taiwan Science and Technology Innovation Cooperation Project (2021YFH0136), 1.3.5 project of disciplines of excellence-clinical research incubation project, West China Hospital, Sichuan University (2019HXFH047) and 1.3.5 project for disciplines of excellence of West China Hospital at Sichuan University (ZY2017305). We wish to thank all our subjects and colleagues for their assistances and cooperation.

AUTHOR CONTRIBUTIONS

Wei Li collected and interpreted the data and drafted the manuscript. Yuchao Jiang and Cheng Luo performed the data analysis and results visualization. Yingjie Qin and Xiuli Li helped collect clinical and neuroimaging data. Du Lei helped interpret the results. Heng Zhang performed the surgery and helped postsurgical follow-up. Qiyong Gong, Dong Zhou and Dongmei An designed the study and revising the manuscript.

CONFLICT OF INTEREST

All authors have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ORCID

Qiyong Gong https://orcid.org/0000-0002-5912-4871
Dong Zhou https://orcid.org/0000-0001-7101-4125

REFERENCES

1. Kwan P, Schachter SC, Brodie MJ. Drug-resistant epilepsy. *N Engl J Med*. 2011;*365*(10):919-926.
2. de Tisi J, Bell GS, Peacock JL, et al. The long-term outcome of adult epilepsy surgery, patterns of seizure remission, and relapse: a cohort study. *Lancet*. 2011;*378*(9800):1388-1395.
3. Wieser HG, Blume WT, Fish D, et al. ILAE commission report. Proposal for a new classification of outcome with respect to epileptic seizures following epilepsy surgery. *Epilepsia*. 2001;*42*(2):282-286.
4. Jin SH, Jeong W, Chung CK. Mesial temporal lobe epilepsy with hippocampal sclerosis is a network disorder with altered cortical hubs. *Epilepsia*. 2015;*56*(5):772-779.
5. Hetherington HP, Kuzniecky RI, Vives K, et al. A subcortical network of dysfunction in TLE measured by magnetic resonance spectroscopy. *Neurology*. 2007;*69*(24):2256-2265.
6. Bernasconi N, Duchesne S, Janke A, Lerch J, Collins DL, Bernasconi A. Whole-brain voxel-based statistical analysis of gray matter and white matter in temporal lobe epilepsy. *Neuroimage*. 2004;*23*(2):717-723.
7. Bonilha L, Keller SS. Quantitative MRI in refractory temporal lobe epilepsy: relationship with surgical outcomes. *Quant Imaging Med Surg*. 2015;*5*(2):204-224.
8. Li J, Zhang Z, Shang H. A meta-analysis of voxel-based morphometry studies on unilateral refractory temporal lobe epilepsy. *Epilepsy Res*. 2012;*98*(2–3):97-103.
9. Keller SS, Roberts N. Voxel-based morphometry of temporal lobe epilepsy: an introduction and review of the literature. *Epilepsia*. 2008;*49*(5):741-757.
10. Kemmotsu N, Girard HM, Bernhardt BC, et al. MRI analysis in temporal lobe epilepsy: cortical thinning and white matter disruptions are related to side of seizure onset. *Epilepsia*. 2011;*52*(12):2257-2266.
11. Whelan CD, Altmann A, Botía JA, et al. Structural brain abnormalities in the common epilepsies assessed in a worldwide ENIGMA study. *Brain*. 2018;*141*(2):391-408.
12. Raj A, Mueller SG, Young K, Laxer KD, Weiner M. Network-level analysis of cortical thickness of the epileptic brain. *Neuroimage*. 2010;*52*(4):1302-1313.
13. Caciagli L, Xiao F, Wandschneider B, Koepp MJ. Imaging biomarkers of anti-epileptic drug action: insights from magnetic resonance imaging. *Curr Pharm des*. 2017;*23*(37):5727-5739.
14. Alvim MK, Coan AC, Campos BM, et al. Progression of gray matter atrophy in seizure-free patients with temporal lobe epilepsy. *Epilepsia*. 2016;*57*(4):621-629.
15. Li W, Jiang Y, Qin Y, et al. Dynamic gray matter and intrinsic activity changes after epilepsy surgery. *Acta Neurol Scand*. 2021;*143*(3):261-270.
16. Galovic M, de Tisi J, McEvoy AW, et al. Resective surgery prevents progressive cortical thinning in temporal lobe epilepsy. *Brain*. 2020;*143*(11):3262-3272.
17. Yasuda CL, Valise C, Saúde AV, et al. Dynamic changes in white and gray matter volume are associated with outcome of surgical treatment in temporal lobe epilepsy. *Neuroimage*. 2010;*49*(1):71-79.
18. Doucet GE, He X, Sperling M, Sharan A, Tracy JI. Frontal gray matter abnormalities predict seizure outcome in refractory temporal lobe epilepsy patients. *Neuroimage Clin*. 2015;*9*:458-466.
19. Galovic M, van Dooren VQH, Postma TS, et al. Progressive cortical thinning in patients with focal epilepsy. *JAMA Neurol*. 2019;*76*(10):1230-1239.
20. Zhao Y, Zhang C, Yang H, et al. Recovery of cortical atrophy in patients with temporal lobe epilepsy after successful anterior temporal lobectomy. *Epilepsy Behav*. 2021;*123*:108272.
21. Li W, An D, Tong X, et al. Different patterns of white matter changes after successful surgery of mesial temporal lobe epilepsy. *Neuroimage Clin*. 2019;*21*:101631.
22. Li W, Jiang Y, Qin Y, et al. Structural and functional reorganization of contralateral hippocampus after temporal lobe epilepsy surgery. *Neuroimage Clin*. 2021;*31*:102714.
23. Engel J Jr. International League Against Epilepsy (ILAE). A proposed diagnostic scheme for people with epileptic seizures and with epilepsy: report of the ILAE task force on classification and terminology. *Epilepsia*. 2001;*42*(6):796-803.
24. Blümcke I, Thom M, et al. International consensus classification of hippocampal sclerosis in temporal lobe epilepsy: a task force report from the ILAE commission on diagnostic methods. *Epilepsia*. 2013;*54*(7):1315-1329.
25. Liu M, Bernhardt BC, Bernasconi A, Bernasconi N. Gray matter structural compromise is equally distributed in left and right temporal lobe epilepsy. *Hum Brain Mapp*. 2016;*37*(2):515-524.
26. Desikan RS, Ségonne F, Fischl B, et al. An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. *Neuroimage*. 2006;*31*(3):968-980.
27. Bernhardt BC, Bernasconi N, Concha L, Bernasconi A. Cortical thickness analysis in temporal lobe epilepsy: reproducibility and relation to outcome. *Neurology*. 2010;*74*(22):1776-1784.

28. Fischl B, Dale AM. Measuring the thickness of the human cerebral cortex from magnetic resonance images. *Proc Natl Acad Sci USA*. 2000;*97*(20):11050-11055.
29. Mueller SG, Laxer KD, Barakos J, Cheong I, Garcia P, Weiner MW. Widespread neocortical abnormalities in temporal lobe epilepsy with and without mesial sclerosis. *Neuroimage*. 2009;*46*(2):353-359.
30. Pardoe HR, Berg AT, Jackson GD. Sodium valproate use is associated with reduced parietal lobe thickness and brain volume. *Neurology*. 2013;*80*(20):1895-1900.
31. Coan AC, Appenzeller S, Bonilha L, Li LM, Cendes F. Seizure frequency and lateralization affect progression of atrophy in temporal lobe epilepsy. *Neurology*. 2009;*3*(11):834-842.
32. Bedny M, Pascual-Leone A, Dodell-Feder D, Fedorenko E, Saxe R. Language processing in the occipital cortex of congenitally blind adults. *Proc Natl Acad Sci U S A*. 2011;*108*(11):4429-4434.

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

How to cite this article: Li, W., Jiang, Y., Qin, Y., Li, X., Lei, D., Zhang, H., Luo, C., Gong, Q., Zhou, D. & An, D. (2022). Cortical remodeling before and after successful temporal lobe epilepsy surgery. *Acta Neurologica Scandinavica*, *00*, 1–8. doi:10.1111/ane.13631