



Effects of thalamic infarction on the structural and functional connectivity of the ipsilesional primary somatosensory cortex

Li Chen^{1,2} · Tianyou Luo² · Kangcheng Wang³ · Yong Zhang⁴ · Dandan Shi² · Fajin Lv² · Yang Li¹ · Yongmei Li² · Qi Li² · Weidong Fang² · Zhiwei Zhang² · Juan Peng² · Hanfeng Yang¹

Received: 4 September 2018 / Revised: 4 January 2019 / Accepted: 4 February 2019 / Published online: 6 March 2019
© European Society of Radiology 2019

Abstract

Objectives To identify regions causally influenced by thalamic stroke by measuring white matter integrity, cortical volume, and functional connectivity (FC) among patients with thalamic infarction (TI) and to determine the association between structural/functional alteration and somatosensory dysfunction.

Methods Thirty-one cases with TI-induced somatosensory dysfunction and 32 healthy controls underwent magnetic resonance imaging scanning. We reconstructed the ipsilesional central thalamic radiation (CTR) and assessed its integrity using fractional anisotropy (FA), assessed S1 ipsilesional changes with cortical volume, and identified brain regions functionally connected to TI locations and regions without TI to examine the potential effects on somatosensory symptoms.

Results Compared with controls, TI patients showed decreased FA ($F = 17.626, p < 0.001$) in the ipsilesional CTR. TI patients exhibited significantly decreased cortical volume in the ipsilesional top S1. Both affected CTR ($r = 0.460, p = 0.012$) and S1 volume ($r = 0.375, p = 0.049$) were positively correlated with somatosensory impairment in TI patients. In controls, the TI region was highly functionally connected to atrophic top S1 and less connected to the adjacent middle S1 region in FC mapping. However, TI patients demonstrated significantly increased FC between the ipsilesional thalamus and middle S1 area, which was adjacent to the atrophic S1 region.

Conclusions TI induces remote changes in the S1, and this network of abnormality underlies the cause of the sensory deficits. However, our other finding that there is stronger connectivity in pathways adjacent to the damaged ones is likely responsible for at least some of the recovery of function.

Key Points

- TI led to secondary impairment in the CTR and cortical atrophy in the ipsilesional top of S1.
- TI patients exhibited significantly higher functional connectivity with the ipsilateral middle S1 which was mainly located within the non-atrophic area of S1.
- Our results provide neuroimaging markers for non-invasive treatment and predict somatosensory recovery.

Keywords Thalamus · Stroke · Magnetic resonance imaging

Electronic supplementary material The online version of this article (<https://doi.org/10.1007/s00330-019-06068-0>) contains supplementary material, which is available to authorized users.

✉ Tianyou Luo
ltychy@sina.com

¹ Department of Radiology, Affiliated Hospital of North Sichuan Medical College, No. 63 Wenhua Street, Nanchong 637000, China

² Department of Radiology, The First Affiliated Hospital of Chongqing Medical University, No. 1 Youyi Road, Yuzhong District, Chongqing 400016, China

³ Department of Psychology, Southwest University, Chongqing, China

⁴ School of Foreign Languages, Southwest University of Political Science and Law, Chongqing, China

Abbreviations

CTR	Central thalamic radiation
DTI	Diffusion tensor imaging
FA	Fractional anisotropy
FC	Functional connectivity
FLA	Fugl-Meyer and Lindmark Assessment
FMA	Fugl-Meyer Assessment
fMRI	Functional magnetic resonance imaging
FWE	Familywise error
ICV	Intracranial volume
MNI	Montreal Neurological Institute
S1	Primary somatosensory cortex
SM1	Primary sensorimotor cortex
TI	Thalamic infarction
WD	Wallerian degeneration
WMHs	White matter hyperintensities

Introduction

Stroke is one of the most frequent conditions and a leading cause of disability. Stroke can cause normal locomotion and somatosensory impairments, thus impeding participation in activities of daily living [1, 2]. Somatosensory dysfunction is estimated to occur in up to half of stroke patients [3] and is characterized by reduced or no somatosensory experience, such as pain, touch, and proprioception. Stroke lesions in the thalamus, the sensory fibers of the top thalamocortical radiation, and the parietal operculum are linked to somatosensory deficits [4, 5]. The thalamus, a deep gray matter structure for receiving and relaying somatosensory signals to the primary somatosensory cortex (S1), plays a critical role in somatosensory function. Thalamic stroke patients exhibit varying degrees of somatosensory deficits [6]. Therefore, an investigation of patients with thalamic infarction (TI) may help elucidate brain dysfunction in stroke and the possible role of the thalamus in somatosensory function.

Central dysesthesia may be associated with hypoperfusion in the primary and secondary somatosensory cortices, mid-cingulate cortex, and adjacent supplementary motor area in patients with thalamic stroke [7]. Moreover, patients exhibit functional abnormality in unaffected thalamic nuclei [8] or show enhanced activation in the affected primary somatosensory cortex (S1) [9] and contralateral primary sensorimotor cortex (SM1) [10]. Within the somatosensory pathways, the thalamus receives information from the central thalamic radiation (CTR) and relays information to S1, a region with locally confined intrahemispheric anatomic connections to the thalamus. However, little is known regarding how TI affects the anatomic connectivity and function of the S1 and their relation with somatosensory dysfunction. Therefore, the objectives of this study are to determine whether TI is associated with

alterations in anatomical loss of S1 and intrinsic functional connectivity (FC) between the thalamus and S1 *in vivo*.

To meet these objectives, diffusion tensor imaging (DTI), cortical volume, and resting-state FC were used to investigate the abnormal neural system in stroke patients. DTI has been used to examine the relationship between white matter tracts and infarcts [11, 12] and to evaluate the white matter integrity of tracts by measuring fractional anisotropy (FA) [13]. Cortical volume changes are associated with loss of neurons, synapses, and nervous tissue rehabilitation [14], and cortical atrophy is correlated with long-term disability [15]. Resting-state FC is operationally defined as temporal correlations between spatially distinct brain regions [16] used to investigate dysfunctional mechanisms *in vivo* after stroke [17] and the neural substrates of stroke recovery [18]. Together, these methods and studies provide important insights. Thus, we hypothesized that TI may lead to decreased structural integrity of the CTR, which may subsequently cause somatosensory dysfunction and incite progressive functional coupling with the affected or unaffected regions of the ipsilesional S1.

Methods

Subjects

Patients with single unilateral ischemic thalamic stroke were recruited. All patients had brain infarcts observed on a diffusion-weighted MRI scan during the acute phase. The inclusion criteria for TI were as follows: (1) first-onset thalamic stroke patients with a contralateral somatosensory deficit, manifesting somatosensory deficit at stroke onset; (2) a single lesion restricted to the ventral posteromedial nucleus and neighboring regions; (3) more than 6 months after stroke onset to ensure that patients were at a stable chronic stage. Exclusion criteria for TI patients and controls were as follows: recurrent stroke after initial onset; cognitive impairments; other preexisting brain lesions visible on MRI; scale for white matter hyperintensities greater than 1; histories of any other neurologic or psychiatric disorders; and poor imaging quality. Hence, the final subjects were 31 TI patients and 32 age- and sex-matched healthy controls (21 males; mean age, 60.38 ± 6.06 years) in the study. None of the controls had neurological or psychiatric disorders. The lesion probability maps of TI patients are depicted in Fig. 1. Demographic and clinical data are described in Table 1.

Clinical evaluation

Clinical examinations were recorded before scanning and included the optimized Fugl-Meyer and Lindmark Assessment (FLA) [19] and Fugl-Meyer Assessment (FMA) [20], Barthel Index, and National Institutes of Health Stroke Scale. Patients

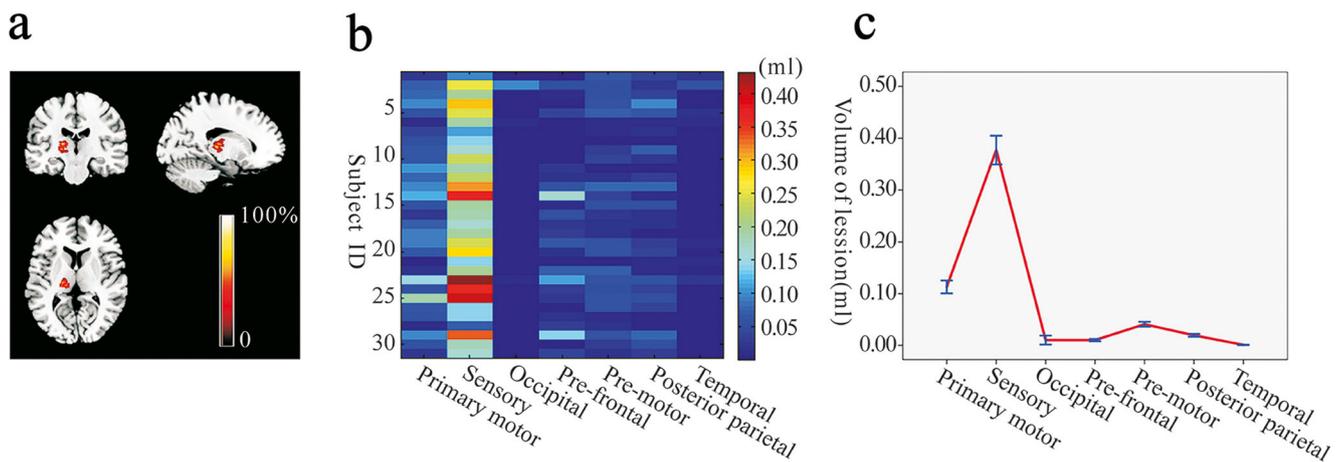


Fig. 1 Thalamic lesion distribution map. **a** The map of lesion probability in the thalamus. **b** The lesion volume of each thalamic subfield in every patient. A 25% threshold probabilistic atlas released in the FSL toolbox

with motor deficits were excluded based on the FMA. Somatosensory function was examined using the Fugl-Meyer and Lindmark Assessment, which includes a superficial sensory assessment (pain, temperature, and touch), proprioception (position sense and motion perception), and discriminative touch (two-point discrimination), for a total of 42 points.

Data acquisition

All MR images were acquired using GE Signa Hdxt 3-T scanner (General Electric Medical Systems) with a standard eight-channel head coil. The effect of scanner noise was decreased using earplugs. Head movement was reduced with foam padding. The scan parameters of the high-resolution 3D-T1 were previously described [21].

All subjects were asked to relax and remain still with their eyes closed while remaining awake (confirmed with a post-scan debriefing) during resting-state functional magnetic resonance imaging (fMRI) acquisition. The fMRI data were acquired with a gradient-echo image pulse sequence with the following parameters: axial slices = 33, thickness/gap = 4/0 mm, matrix = 64×64 , TR = 2000 ms, TE = 40 ms, flip angle = 90° , field of view = $240 \text{ mm} \times 240 \text{ mm}$, slices = 33, and volumes = 240.

In DTI acquisition, a single-shot, spin-echo planar imaging sequence was used in contiguous axial planes that covered the whole brain. Diffusion-sensitized gradients were applied along 30 non-collinear directions with a b value of 1000 s/mm^2 . In addition, eight sets of $b = 0$ images were obtained with the following imaging parameters: repetition time/echo time = $11,000/77.6 \text{ ms}$, field of view = $256 \text{ mm} \times 256 \text{ mm}$, matrix = 128×128 , flip angle = 90° , slice thickness/gap = $3/0 \text{ mm}$, and slices = 53.

No hemispheric asymmetry of the thalamocortical pathways was quantitatively observed [22], and the lateralization

was used to mask the thalamus subregions. **c** Averaged volume distribution (mean \pm SE) in each thalamic subfield in the TI group. The infarcts were mainly located in the sensory function subfield

of brain function was found at the cognitive networks [23]. We flipped the imaging data from right to left along the midline for the patients with right thalamus lesions. After flipping, the left side of the image corresponded to the ipsilesional hemisphere, and the right side corresponded to the contralesional hemisphere.

Measurement of stroke lesion volumes

Stroke lesion volumes of TI at both the acute and chronic phases were measured by using MRIcron software (available at www.nitrc.org/projects/mricron) based on the acute phase diffusion-weighted images and chronic T1-weighted images, respectively.

Data preprocessing

The DTI data were preprocessed using FMRIB's free software FSL (Oxford Center for Functional MRI of the Brain). The preprocessing for DTI data includes eddy current correction, brain extraction, reconstruction, registration, whole brain transform track, definition of region of interest (ROI), and tract CRT.

The cortical volume was calculated with FreeSurfer V.5.3.0 (Martinos Center for Biomedical Imaging center, MGH, <http://surfer.nmr.mgh.harvard.edu/>). The images were sequentially preprocessed as follows: skull stripping, intensity normalization, transformation into Talairach space, segmentation of subcortical white and gray matter structures, surface Atlas registration, surface extraction and calculating cortical volume.

Resting-state fMRI data were preprocessed with SPM8 (Wellcome Centre for Human Neuroimaging, UCL, <http://www.fil.ion.ucl.ac.uk/spm/software/spm8/>). The preprocessing for resting-state fMRI data includes slice

Table 1 Demographics and clinical information of the controls and patients with thalamic infarction

	Controls	TI patients	<i>p</i> value
Age (years)	60 ± 6	58 ± 9	0.245 ^a
Gender (female/male)	11/21	10/21	0.859 ^b
Systolic pressure (mmHg)	133 ± 13	136 ± 10	0.086 ^a
Diastolic pressure (mmHg)	77 ± 10	78 ± 8	0.187 ^a
Fast Glucose (mmol/L)	6.11 ± 2.02	6.54 ± 2.19	0.848 ^a
Smoking, current or quit < 5 years (no smoking/smoking)	15/17	12/19	0.513 ^b
Alcohol intake	8/24	6/25	0.590 ^b
Dyslipidemia	12/20	8/23	0.319 ^b
WMH grade	1.75 ± 0.96	1.65 ± 1.10	0.689 ^a
Duration (month)		8.58 (6.00–18.00)	
Lesion location (left/right)		16/15	
Lesion volume (cm ³)		0.40 (0.13–0.83)	
Somatosensory scores		27.65 ± 3.02	
Pain		3.68 ± 0.98	
Temperature		2.97 ± 0.80	
Touch		3.19 ± 0.00	
Proprioception		12.71 ± 1.60	
Stereognosis		1.77 ± 0.43	
Two-point discrimination		3.39 ± 0.62	

The continuous data are presented as the mean ± SD

TI thalamic infarction

^a Differences between the groups were assessed by *t* test

^b Differences between the groups were assessed by χ^2 test

timing, realign, normalize, smooth, detrend, nuisance regression, and filter.

Detailed descriptions of our preprocessing procedures for analyzing DTI, resting-state fMRI data, and cortical volume are in the online-only [Supplementary materials](#).

Multimodal MRI analyses

First, the general linear model was applied to quantitatively compare FA differences in the affected CTR between TI patients and healthy controls with age, gender, and intracranial volume (ICV) as nuisance variables ($p < 0.05$, Bonferroni corrected). The correlation between the FA values of the affected CTR and the somatosensory function score was analyzed in the TI group.

Second, we performed vertex- or voxel-wise comparisons between TI patients and healthy controls in terms of the cortical volume and resting-state FC in the ipsilateral hemisphere. The general linear model was used to test group differences in these measures using age, gender, and ICV as nuisance variables. Multiple comparisons were corrected using a familywise

error (FWE) with an initial height threshold of $p = 0.001$ and a cluster level corrected to $p < 0.05$.

The correlation between the volume of the S1 region and resting-state FC of the S1 and somatosensory function was explored in the TI group. For all correlation analyses, we used partial correlations to factor out age, gender, and ICV, and $p < 0.05$ was considered statistically significant.

Third, the script written by Preacher and Hayes [24] was used to conduct a mediation analysis using SPSS 16.0, which investigated whether the mediating variable affects the relation between an independent variable and dependent variable (for details, please see [supplementary materials](#)).

Results

Lesion distribution in the thalamic subregions

In our study, 31 patients had thalamic infarcts, which were mainly located in the ventral posterolateral nucleus and neighboring region. Figure 1a shows the probability map of a lesion in the thalamus in all patients. Behrens et al [25] identified seven specific subregions in the thalamus that connected to distinct cortices. In the present study, the region of the lesion was located at the sensory subregion of the thalamus with the highest probability, which was connected to the somatosensory cortices. We also calculated the volume of each thalamus subregion for every patient (Fig. 1b). As shown, lesions in the sensory subfield had the largest volume in every patient. Because of different sizes of each subregion within the thalamic connectivity atlas, we first divided the volume size of the lesion for each subject by the size of the template within each subregion of the thalamus and then averaged the percentage of the lesion in seven subregions (Fig. 1c) for the TI group. The result confirmed that the sensory subregion (mean = 37.74%) had the largest percentage of the lesion within seven subregions.

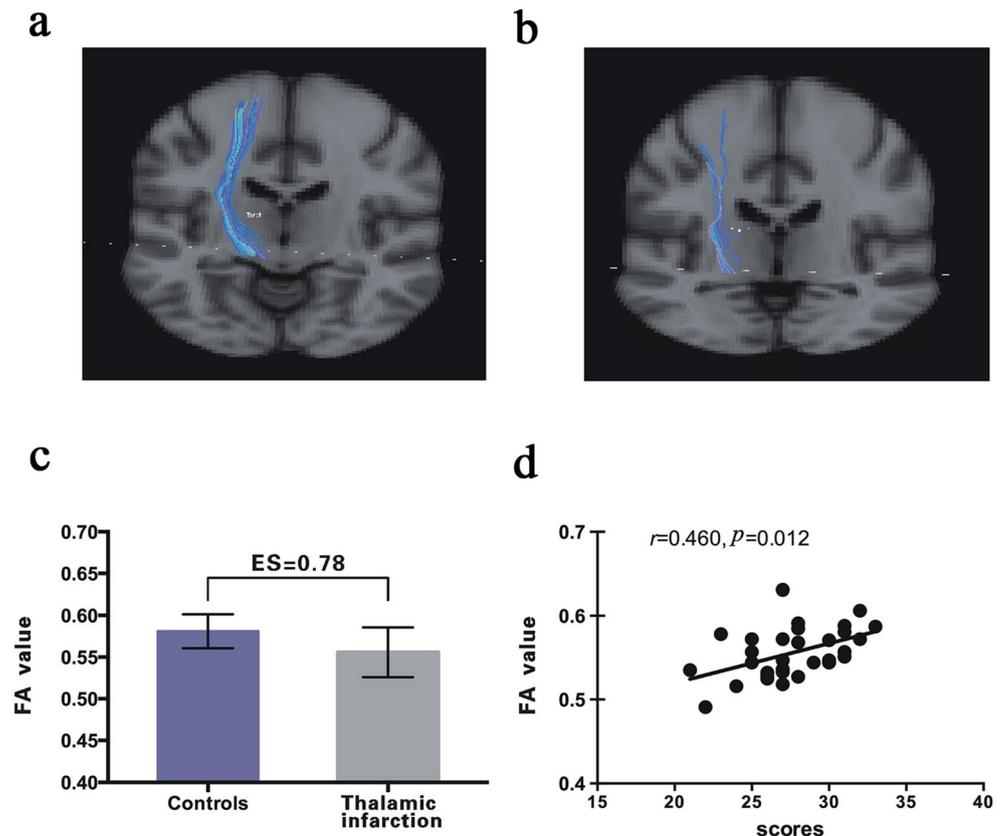
Structural connectivity within ipsilesional central thalamic radiation

An example of fiber tracts connecting the thalamus to the S1 is shown in Fig. 2a and b. The general linear model analysis showed that the TI patients had a significantly decreased FA ($F = 17.626$, $p < 0.001$, Fig. 2c) in the affected CTR. A significant positive correlation was found between the FA value of the affected CTR and the somatosensory function score ($r = 0.460$, $p = 0.012$, Fig. 2d).

Cortical volume analyses

Compared with the controls, the TI patients demonstrated reduced cortical volume in the ipsilesional top part of the S1 (top

Fig. 2 The changes in the integrity of the CTR and the association with somatosensory scores in the TI patients. **a** Fiber tractography between the left thalamus and primary somatosensory cortex in one control subject. **b** Fiber tractography between the ipsilesional thalamus and the primary somatosensory cortex in one patient with TI. **c** Compared with the controls, the patients with thalamic infarctions exhibited a decreased FA value of the affected CTR. **d** There was a significant positive correlation between the FA value of the CTR and the somatosensory function score in the TI patients. CTR, central thalamic radiation; FA, fractional anisotropy



S1 region, peak Talairach coordinates = $-16, -25, 68$; peak z score = 4.002; and cluster size = 653 mm^2) and ipsilesional lateral bottom S1 (peak Talairach coordinates = $-56, -19, 27$; peak z score = 5.401; and cluster size = 535 mm^2) (Fig. 3a). We then extracted and compared the mean cortical volumes of the ipsilesional top S1 region. The ipsilesional top S1 volume decreased in the TI group (Fig. 3b). The somatosensory function score was positively correlated with the ipsilesional top S1 volume in the TI patients ($r = 0.375, p = 0.049$) (Fig. 3c), suggesting that the smaller volume of the ipsilesional top S1 region corresponds to more severe somatosensory dysfunction.

Functional connectivity and statistical analysis of the thalamus

Figure 4b presents a connectivity map of a lesion with the rest of the whole brain in the control group. One dominant cortical connection within S1 was located at the top S1, which coincided with the atrophic region in S1. However, compared with the top S1 region, the middle and bottom of the S1 were less functionally connected to the lesion site of the thalamus.

Compared with the controls, the TI patients demonstrated increased FC between the ipsilesional non-infarcted thalamus (Fig. 4a) and ipsilesional middle and bottom of the S1/M1 (Montreal Neurological Institute (MNI) coordinates = $-39,$

$-36, 60$; peak z score = 4.14; and cluster size = 273 voxels), the contralesional S1/M1 (MNI coordinates = $21, -51, 72$; peak z score = 4.06; and cluster size = 1131 voxels), and the contralesional occipital middle gyrus/occipital bottom gyrus (MNI coordinates = $42, -87, -15$; peak z score = 4.42; and cluster size = 787 voxels) (Fig. 4c). We then extracted and compared the FC value of the ipsilesional top S1 region. The results showed that the FC value of the ipsilesional middle and bottom of the S1 increased in the TI group ($p < 0.001$). In addition, the somatosensory function score was positively correlated with the FC value between the ipsilesional thalamus and the middle S1 region ($r = 0.371, p = 0.048$, Fig. 4d), suggesting that higher connectivity with the ipsilesional middle and bottom S1 regions corresponds to less severe somatosensory dysfunction.

Relationship between structural and functional connectivity

The relationship among structural damage, FC, and anatomic connectivity in the CTR is presented in Fig. 5a, which shows that the decreased volume in the top S1 region is connected to the probability map of the ipsilesional CTR in the TI patients. The mediation analyses also revealed that the FA in the CTR had a significant indirect effect on somatosensory dysfunction via the ipsilesional top S1 volume (Fig. 5b). To examine

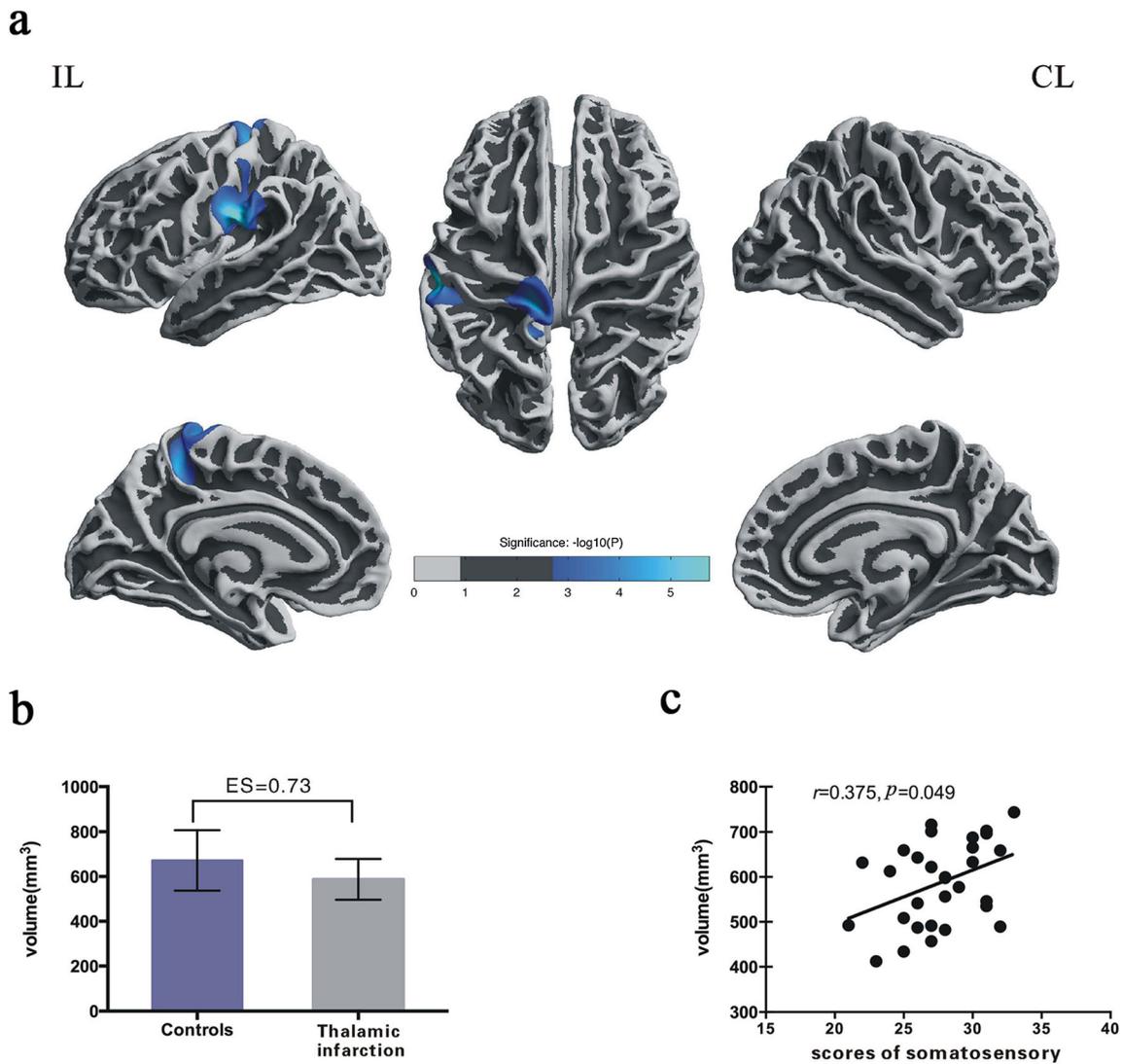


Fig. 3 The volume changes in the S1 and their associations with the somatosensory score in the thalamic infarction patients. **a** The white matter surface representations show a significant ($p < 0.05$ corrected) difference in the cortical volumes of the thalamic patients and control subjects. Cool colors (blue and green) indicate decreases in the thalamic infarction patients. Light gray areas represent gyri, and dark gray areas

represent sulci. **b** Compared with healthy controls, the patients with thalamic infarction exhibited decreased volume in the primary somatosensory cortex. **c** A significant positive correlation was observed between the reduction of the ipsilesional top S1 and somatosensory function in TI patients. CL, contralesional; IL, ipsilesional

whether the atrophic region would overlap with regions that showed increased FC with the ipsilesional thalamus, we mapped two results in Fig. 5c. The atrophic region (blue) did not overlap with the regions that showed increased FC with the ipsilesional thalamus (red).

Discussion

In this study, we used a lesion-inducing method to investigate remote structural and functional changes in the S1 and relationships among these alterations in the patients with TI. TI patients exhibited secondary impairment in the ipsilesional CTR and decreased cortical volume in the ipsilesional top

region of S1. Moreover, increased functional coupling between the ipsilesional thalamus and middle S1 regions occurred after TI. Surprisingly, the region exhibiting increased FC was adjacent to the region demonstrating decreased cortical volume in the TI patients. We found increased FC in the ipsilesional middle S1, indicating that this region is highly important in somatosensory recovery after stroke.

Our main findings were a marked decrease in FA in the ipsilesional CTR and decreased cortical volume in the ipsilesional top S1 region, which connected with the CTR in the TI patients. These results indicate that chronic TI led to secondary impairment in the CTR and top S1, which are in relationship with somatosensory dysfunction. As previously shown in neuropathological studies, degeneration of the distal

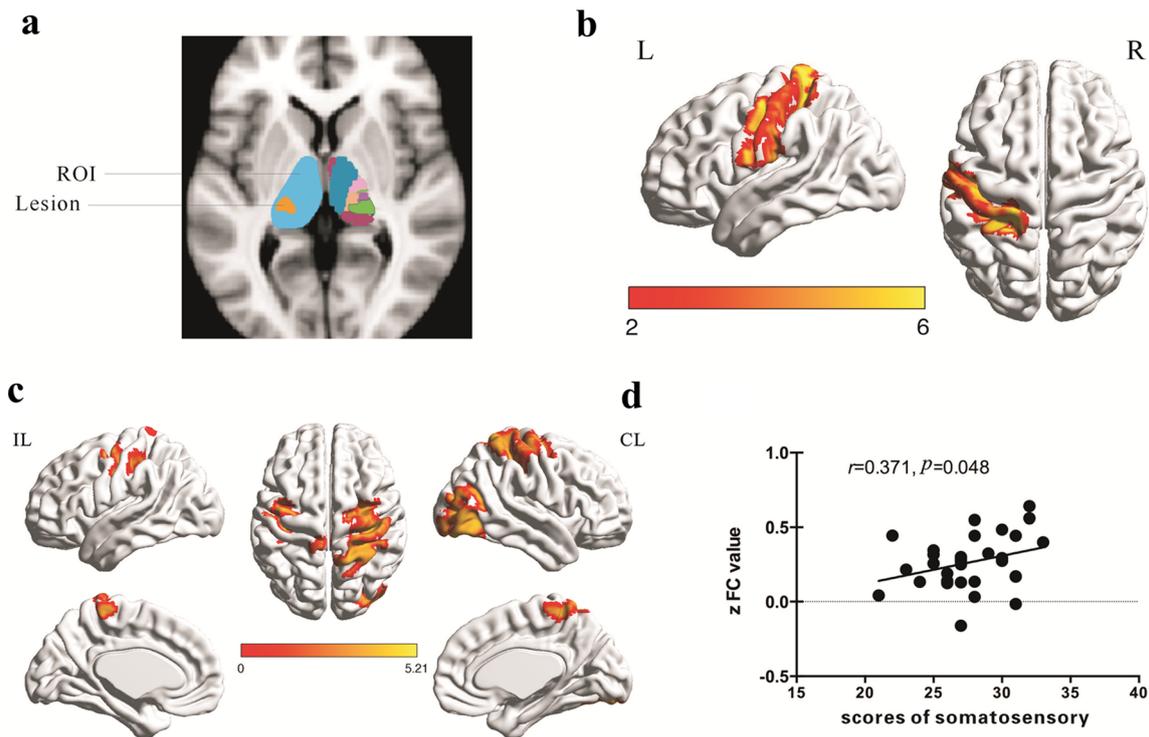


Fig. 4 The changes in resting-state FC and their associations with the somatosensory score in the TI patients. **a** The region with infarction in the left thalamus was labeled lesion (in orange), and the region with no infarction was labeled the ROI (in light blue). The lesion region in the left thalamus and sensory subregion in the right thalamus (in green) were symmetric. **b** One-sample *t* test showed the FC maps with the location of the lesion in the left thalamus as the seed in controls. The threshold was

set at $p < 0.05$, cluster size > 100 voxels. **c** Increased FC with the non-lesion region as the seed was found in the TI patients compared with that in the controls, which are indicated by warm colors. **d** Positive correlation of the FC values of the ipsilesional S1 and the somatosensory score in TI patients. CL, contralesional; FC, functional connectivity; IL, ipsilesional; L, left; R, right; ROI, region of interest

parts of nerves after injury to the proximal axon or cell body is referred to as Wallerian degeneration (WD), which occurs in both the peripheral and central nervous systems. In the central nervous system, WD is characterized by a highly stereotypical course, starting with disintegration of the axonal skeleton and membrane within days after injury, followed by degradation of the myelin sheath and infiltration by macrophages and microglia, with subsequent atrophy of the affected fiber tracts [26, 27]. Consistent with these studies, we found abnormal fiber integrity in the TI patients using FA, a common summary measure that reflects the directionality of molecular motion and is sensitive to the microstructural integrity of fibers. Taken together, the reduced FA in the ipsilesional CTR may reflect the phenomenon of WD to some extent.

The fibers of the ventral posterolateral thalamic nucleus via the posterior limbs of the internal capsule mainly project to the top and middle regions of the S1, which are responsible for somatosensory function. In the study, we found that patients with TI show somatosensory deficits and cortex atrophy in the top region of the S1. Therefore, we confirmed the thalamus-S1 pathway by using a lesion-inducing method and a non-invasive technique in vivo. This result was consistent with studies showing focal atrophy in cortical regions with a high probability of

connectivity with the incident infarct [28–31] and long-term disability in patients with subcortical stroke [15, 21, 28]. These results were also potentially due to secondary neurodegeneration, although the precise mechanism underlying the influence of TI on cortical atrophy has not been elucidated. In addition, the decreased FA of the CTR may have a direct or indirect effect on somatosensory deficits in TI individuals via decreased S1 volume, suggesting that TI may affect the CTR first, followed by the S1 area. However, more research is needed to determine the order of degeneration.

FC mapping of lesions in normal subjects revealed that the TI region was more connected to the atrophic top region of the S1 and less connected to the adjacent middle and bottom S1 regions. However, between-group comparisons of the non-lesioned thalamus demonstrated that the patients exhibited significantly increased FC between the ipsilesional thalamus and regions adjacent to the atrophic region in the ipsilesional S1. Several studies have demonstrated the contribution of the unaffected sensorimotor cortex to somatosensory and motor recovery after stroke [31–33]. And previous research have also suggested that the functional contribution of perilesional regions to language recovery [34] and increased FC is helpful to

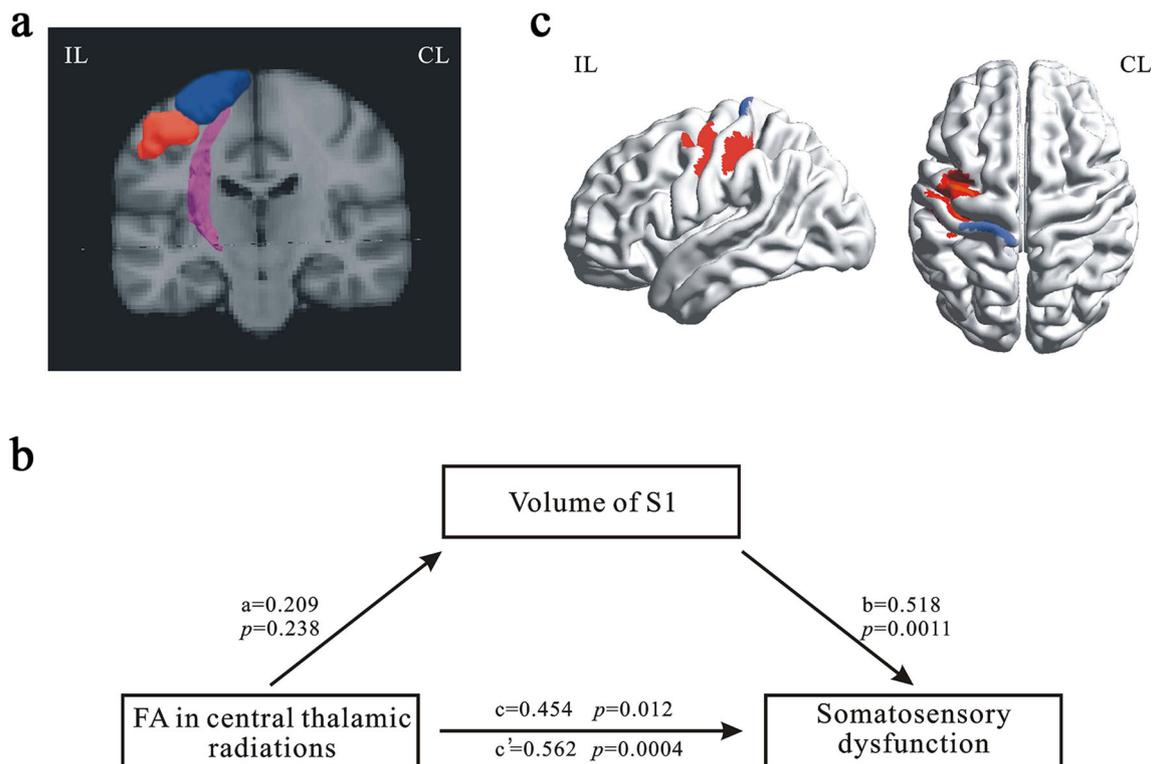


Fig. 5 Relationship between the structural and FC in the thalamic infarction patients. **a** Volume difference in the ipsilesional S1 and FC difference in the ipsilesional S1 and fiber tract in the affected CTR in the TI patients. **b** Mediation effects of the volume difference in the ipsilesional S1 on the relationship between the FA value of the affected

CTR and somatosensory dysfunction. **c** The relationship between the decreased volume and increased FC in the ipsilesional S1. CL, contralesional; CTR, central thalamic radiation; FA, fractional anisotropy; FC, functional connectivity; IL, ipsilesional; S1, primary somatosensory cortex

restoration of motor function in the chronic poststroke phase [35–37]. Using PET, Weder et al [38] reported that patients with chronic thalamic or basal ganglia infarcts showed activation of the bilateral sensorimotor cortex during the performance of a somatosensory discrimination task using the area contralateral to the affected hand. Interestingly, in the present study, the region that did not overlap with structurally damaged top S1 also showed enhanced FC with the ipsilesional thalamus, suggesting that increased FC occurred in the ipsilesional unaffected S1 area. Increased FC in the non-atrophic S1 region might be related to axons sprouting to establish new connections and novel projection patterns [39, 40]. However, the concept of a compensatory effect is still speculative and requires further evidence. Another possibility is that the increased activity with the sensory cortex not only served as compensation but also might reflect a primary pathophysiological change in TI, as a consequence of abnormal thalamic outflow. Because other diseases, such as Parkinson's disease [41], show increased cerebro-cerebellum FC in patients as a result of abnormal activity of the thalamus, these results might reflect pathophysiological change. In addition, the TI patients demonstrated increased FC between the ipsilesional thalamus and contralesional occipital

middle and bottom gyri. Recent DTI tractography research predominantly revealed direct white matter pathways between the thalamus and occipital cortex [25, 42]. Arcaro et al [43] reported that the pulvinar of the thalamus was functionally connected with the occipital cortex. Lam et al [44] demonstrated that resting-state connectivity within and between motor and frontoparietal networks is associated with motor outcome. Thus, the increased FC with the occipital cortex might be similar with increased coupling with S1 in this study, suggesting a compensation effect or a pathophysiological change in TI.

A major limitation of the present study is the lack of information about the other senses, namely, sight, smell, taste, and hearing. We considered only the evaluation of sensory experiences associated with somatosensory dysfunction (pain, temperature, touch, proprioception, two-point discrimination, and stereognosis) and did not measure other senses. However, our results may be reflective of the neuroimaging mechanisms underlying the dysfunctional somatic sensation. Second, the present research adopted FC methods to show higher FC between the unaffected region and the affected thalamus, which was associated with better somatosensory function; however, the corresponding neurobiological basis is poorly understood. Further work is needed, and a longitudinal sample of stroke

patients with somatosensory deficits and more behavioral measures would help validate the findings and explore their clinical implications.

Conclusions

In conclusion, thalamic lesions were not only associated with microstructural white matter injury in the CTR and impaired cortical volume of the S1 but also resulted in increased functional coupling to the non-atrophic S1 region. However, the enhanced middle S1 FC which is adjacent to the damaged ones may be responsible for at least some of the recovery of somatosensory function.

Funding This study was supported by the National Natural Science Foundation of China (81671666), the Doctoral Scientific Funds of North Sichuan Medical College (CBY16-QD04), Key Project Sichuan Provincial Department of Education (18ZA0211), Postgraduate Science Innovation Foundation of Chongqing (CYB16061), Fundamental Research Funds for the Central Universities (SWU1709569), and Chongqing Scientific and Technological Talents Program (kjxx2017011).

Compliance with ethical standards

Guarantor The scientific guarantor of this publication is Tianyou Luo.

Conflict of interest The authors of this manuscript declare no relationships with any companies whose products or services may be related to the subject matter of the article.

Statistics and biometry No complex statistical methods were necessary for this paper.

Informed consent Written informed consent was obtained from all subjects in this study.

Ethical approval Institutional Review Board approval was obtained.

Methodology

- Prospective
- Case-control study
- Performed at one institution

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

References

1. Kessner SS, Bingel U, Thomalla G (2016) Somatosensory deficits after stroke: a scoping review. *Top Stroke Rehabil* 23:136–146
2. Leoni RF, Paiva FF, Kang BT et al (2012) Arterial spin labeling measurements of cerebral perfusion territories in experimental ischemic stroke. *Transl Stroke Res* 3:44–55
3. Feigensohn JS, McCarthy ML, Greenberg SD, Feigensohn WD (1977) Factors influencing outcome and length of stay in a stroke rehabilitation unit. Part 2. Comparison of 318 screened and 248 unscreened patients. *Stroke* 8:657–662
4. Meyer S, Kessner SS, Cheng B et al (2016) Voxel-based lesion-symptom mapping of stroke lesions underlying somatosensory deficits. *Neuroimage Clin* 10:257–266
5. Preusser S, Thiel SD, Rook C et al (2015) The perception of touch and the ventral somatosensory pathway. *Brain* 138:540–548
6. Kim JH, Greenspan JD, Coghill RC, Ohara S, Lenz FA (2007) Lesions limited to the human thalamic principal somatosensory nucleus (ventral caudal) are associated with loss of cold sensations and central pain. *J Neurosci* 27:4995–5004
7. Kishi M, Sakakibara R, Nagao T, Terada H, Ogawa E (2009) Thalamic infarction disrupts spinothalamic projection to the mid-cingulate cortex and supplementary motor area. *J Neurol Sci* 281:104–107
8. Ohara S, Lenz FA (2001) Reorganization of somatic sensory function in the human thalamus after stroke. *Ann Neurol* 50:800–803
9. Staines WR, Black SE, Graham SJ, McIlroy WE (2002) Somatosensory gating and recovery from stroke involving the thalamus. *Stroke* 33:2642–2651
10. Lee MY, Kim SH, Choi BY, Chang CH, Ahn SH, Jang SH (2012) Functional MRI finding by proprioceptive input in patients with thalamic hemorrhage. *NeuroRehabilitation* 30:131–136
11. Kunitatsu A, Aoki S, Masutani Y, Abe O, Mori H, Ohtomo K (2003) Three-dimensional white matter tractography by diffusion tensor imaging in ischaemic stroke involving the corticospinal tract. *Neuroradiology* 45:532–535
12. Lee JS, Han MK, Kim SH, Kwon OK, Kim JH (2005) Fiber tracking by diffusion tensor imaging in corticospinal tract stroke: topographical correlation with clinical symptoms. *Neuroimage* 26:771–776
13. Stinear CM, Barber PA, Smale PR, Coxon JP, Fleming MK, Byblow WD (2007) Functional potential in chronic stroke patients depends on corticospinal tract integrity. *Brain* 130:170–180
14. Maguire EA, Gadian DG, Johnsrude IS, et al (2000) Navigation-related structural change in the hippocampi of taxi drivers. *Proc Natl Acad Sci U S A* 97:4398–4403
15. Seghier ML, Ramsden S, Lim L, Leff AP, Price CJ (2014) Gradual lesion expansion and brain shrinkage years after stroke. *Stroke* 45:877–879
16. Barkhof F, Haller S, Rombouts SA (2014) Resting-state functional MR imaging: a new window to the brain. *Radiology* 272:29–49
17. Liu J, Qin W, Zhang J, Zhang X, Yu C (2015) Enhanced interhemispheric functional connectivity compensates for anatomical connection damages in subcortical stroke. *Stroke* 46:1045–1051
18. Dijkhuizen RM, Zaharchuk G, Otte WM (2014) Assessment and modulation of resting-state neural networks after stroke. *Curr Opin Neurol* 27:637–643
19. Lindmark B, Hamrin E (1988) Evaluation of functional capacity after stroke as a basis for active intervention. Presentation of a modified chart for motor capacity assessment and its reliability. *Scand J Rehabil Med* 20:103–109
20. Fugl-Meyer AR, Jääskö L, Leyman I, Olsson S, Stegling S (1975) The post-stroke hemiplegic patient. 1. A method for evaluation of physical performance. *Scand J Rehabil Med* 7:13–31
21. Chen L, Luo T, Lv F et al (2016) Relationship between hippocampal subfield volumes and memory deficits in patients with thalamus infarction. *Eur Arch Psychiatry Clin Neurosci* 266:543–555
22. Wilkinson M, Kane T, Wang R, Takahashi E (2016) Migration pathways of thalamic neurons and development of thalamocortical connections in humans revealed by diffusion MR tractography. *Cereb Cortex* 27:5683–5695
23. Wang D, Buckner RL, Liu H (2014) Functional specialization in the human brain estimated by intrinsic hemispheric interaction. *J Neurosci* 34:12341–12352
24. Preacher KJ, Hayes AF (2008) Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models. *Behav Res Methods* 40:879–891

25. Behrens TE, Johansen-Berg H, Woolrich MW et al (2003) Non-invasive mapping of connections between human thalamus and cortex using diffusion imaging. *Nat Neurosci* 6:750–757
26. Silasi G, Murphy TH (2014) Stroke and the connectome: how connectivity guides therapeutic intervention. *Neuron* 83:1354–1368
27. Yoon H, Kim J, Moon WJ et al (2017) Characterization of chronic axonal degeneration using diffusion tensor imaging in canine spinal cord injury: a quantitative analysis of diffusion tensor imaging parameters according to histopathological differences. *J Neurotrauma* 34:3041–3050
28. Cheng B, Schulz R, Bönstrup M et al (2015) Structural plasticity of remote cortical brain regions is determined by connectivity to the primary lesion in subcortical stroke. *J Cereb Blood Flow Metab* 35:1507–1514
29. Duering M, Righart R, Csanadi E et al (2012) Incident subcortical infarcts induce focal thinning in connected cortical regions. *Neurology* 79:2025–2028
30. Duering M, Righart R, Wollenweber FA, Zietemann V, Gesierich B, Dichgans M (2015) Acute infarcts cause focal thinning in remote cortex via degeneration of connecting fiber tracts. *Neurology* 84:1685–1692
31. Zhang J, Meng L, Qin W, Liu N, Shi FD, Yu C (2014) Structural damage and functional reorganization in ipsilesional m1 in well-recovered patients with subcortical stroke. *Stroke* 45:788–793
32. Carter AR, Astafiev SV, Lang CE et al (2010) Resting interhemispheric functional magnetic resonance imaging connectivity predicts performance after stroke. *Ann Neurol* 67:365–375
33. Park CH, Chang WH, Ohn SH et al (2011) Longitudinal changes of resting-state functional connectivity during motor recovery after stroke. *Stroke* 42:1357–1362
34. Hartwigsen G, Saur D (2017) Neuroimaging of stroke recovery from aphasia - insights into plasticity of the human language network. *Neuroimage* S1053–8119:31000–31005
35. Grefkes C, Fink GR (2014) Connectivity-based approaches in stroke and recovery of function. *Lancet Neurol* 13:206–216
36. Grefkes C, Ward NS (2014) Cortical reorganization after stroke: how much and how functional. *Neuroscientist* 20:56–70
37. Thiel A, Vahdat S (2015) Structural and resting-state brain connectivity of motor networks after stroke. *Stroke* 46:296–301
38. Weder B, Knorr U, Herzog H et al (1994) Tactile exploration of shape after subcortical ischaemic infarction studied with PET. *Brain* 117(Pt 3):593–605
39. Carmichael ST (2006) Cellular and molecular mechanisms of neural repair after stroke: making waves. *Ann Neurol* 59:735–742
40. Carmichael ST (2008) Themes and strategies for studying the biology of stroke recovery in the poststroke epoch. *Stroke* 39:1380–1388
41. Wu T, Hallett M (2013) The cerebellum in Parkinson's disease. *Brain* 136:696–709
42. Zhang D, Snyder AZ, Shimony JS, Fox MD, Raichle ME (2010) Noninvasive functional and structural connectivity mapping of the human thalamocortical system. *Cereb Cortex* 20:1187–1194
43. Arcaro MJ, Pinsk MA, Kastner S (2015) The anatomical and functional organization of the human visual pulvinar. *J Neurosci* 35:9848–9871
44. Lam TK, Dawson DR, Honjo K et al (2018) Neural coupling between contralesional motor and frontoparietal networks correlates with motor ability in individuals with chronic stroke. *J Neurol Sci* 384:21–29