Crossed Cerebellar Diaschisis: Risk Factors and Prognostic Value in Medically Intractable Epilepsy by ^{18}F-FDG PET/CT

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Abstract

Purpose Crossed cerebellar diaschisis (CCD) has been widely studied in hemispheric stroke but is less characterized in epilepsy. In this study, we used ^{18}F-FDG positron emission tomography (PET)/computed tomography (CT) to investigate the risk factors for CCD and its prognostic value for intractable epilepsy.

Methods One hundred medically intractable epilepsy patients pathologically diagnosed with focal cortical dysplasia (FCD) postoperatively were included and classified into two groups: CCD+ and CCD-. All patients underwent ^{18}F-FDG PET/CT preoperatively. PET/CT images were analysed qualitatively by visual assessment and semi-quantitatively using the absolute asymmetry index (|AI|). Clinical factors, including age, sex, body mass index (BMI), age at seizure onset, epilepsy duration, seizure type, epilepsy severity, electroencephalography(EEG) and brain magnetic resonance imaging (MRI), were retrospectively assessed from medical records. Follow-up outcomes were evaluated according to the Engel classification at 3, 6, 12, 24 and 36 months postoperatively.

Results Of the 100 patients, 77 (77%) were classified as CCD-, and 23 (23%) were classified as CCD+. CCD+ patients had a higher number of lobes involved on PET (3.61±2.16 vs 2.26±1.01, P<0.001) and more cases of occipital hypometabolism (21.74% vs 5.19%, P=0.03) than CCD- patients. CCD- patients showed more negative MRI results than CCD+ patients (P=0.02). Patients with a poor prognosis had more cases of parietal hypometabolism on PET (P=0.02). At 12 months postoperatively, 71%(29/41) of CCD- patients and 31%(4/13) of CCD+ patients presented a favourable prognosis (P=0.02). Significant differences in the average |AI| values in the posterior frontal and anterior temporal lobes were found between CCD+ and CCD- patients (P<0.05), but no significant correlation of the |AI| between supratentorial regions and the contralateral cerebellum was identified in CCD+ patients.

Conclusion The number of lobes involved on PET, structural anomalies on MRI, the lesion location on PET, the |AI| values in the posterior frontal and anterior temporal lobes may be predisposing factors for CCD. CCD occurrence may help predict the prognosis of FCD patients at 12 months postoperatively, and parietal hypometabolism on PET may indicate a poor prognosis.

Introduction

Epilepsy is the most common, chronic, serious neurological disease, with 65 million people affected worldwide [1]. However, almost 30% of seizures cannot be controlled with antiepileptic drugs [2], reflecting medically intractable epilepsy. Focal cortical dysplasia (FCD) is one of the most common causes of medically intractable epilepsy, which can be effectively treated by surgery [3]. However, a significant portion of patients continue experiencing seizures following surgery; thus, preoperative evaluation of the epileptogenic onset zone (EON) is particularly important. Magnetic resonance imaging (MRI), positron emission tomography (PET)/computed tomography (CT) and electroencephalogram have been widely used for presurgical localization of the EON. The sensitivity of ^{18}F-FDG PET, as a form of functional imaging, for localizing the EON has been reported to be 85%-94% [4, 5]. ^{18}F-FDG, as the most commonly

used PET tracer, was used to measure glucose metabolism related to the synaptic and neuronal activity of brain tissue [6]. Interictal ^{18}F-FDG PET often showed hypometabolism of the EON. In addition to the EON, hypometabolism is sometimes displayed in remote sites, such as the contralateral cerebellum and ipsilateral thalamus, which is called "diaschisis".

In 1914, von Monakow coined the term “diaschisis” to describe the neurophysiological changes that occur distant to a focal brain lesion, and many years later, in 1981, Baron described the occurrence of crossed cerebellar diaschisis (CCD) after hemispheric stroke [7]. CCD is a phenomenon including decreases in metabolism and blood flow in the cerebellar hemisphere contralateral to a supratentorial lesion. In the following decades, this concept attracted clinical interest, with researchers attempting to investigate associated biomarkers and the mechanism and clinical role of CCD using single-photon emission computed tomography (SPECT), PET or MRI. These studies focused mainly on cerebrovascular diseases, especially cerebral infarction. Although many studies on the CCD phenomenon have been conducted in other supratentorial lesions, such as epilepsy, tumours, and cerebral trauma, most published literature on the topic includes case reports with limited patient populations. Biersack first reported three cases of CCD in epilepsy patients using ^{99m}Tc-HMPAO SPECT before and during the Wada test in 1987 [8]. To date, no systematic analysis of medically intractable epilepsy caused by FCD with CCD using ^{18}F-FDG PET/CT has been performed, and no study has detected associations between CCD and surgery outcomes. This study was designed to clarify relevant factors for CCD and investigate the relationship between CCD occurrence and the prognosis of epilepsy surgery.

Materials And Methods

Subjects

Patients with medically intractable epilepsy who had undergone ^{18}F-FDG PET/CT preoperatively between April 2015 and July 2018 were retrospectively reviewed. One hundred (30 females and 70 males; mean age ± standard deviation (SD), 24.18 ± 9.22 y) patients with medically intractable epilepsy caused by FCD were included in this study. We classified all the patients into two groups depending on the PET/CT images: CCD positive (CCD+) and CCD negative (CCD-). Patients were pathologically diagnosed with FCD postoperatively. Clinical factors, including age, sex, body mass index (BMI), age at seizure onset, epilepsy duration, seizure type, epilepsy severity, electroencephalography (EEG), and brain MRI, were reviewed. The severity of epilepsy was classified as severe, moderate, or mild; patients who had more than 20 seizures per year were considered “severe”, those who had less than 20 per year were considered “moderate”, and those without seizures in the past 12 months were considered “mild” [9]. Epileptic seizure types were classified as “motor onset” or “non-motor onset” according to the 2017 International League Against Epilepsy (ILAE) guidelines [10]. Epileptiform discharges revealed by EEG were classified as focal (seizures originating in a single lobe) or non-focal (seizures originating in more than two lobes, bilateral seizures, or generalized seizures).

The inclusion criteria were as follows: clinical diagnosis of epilepsy [11]; failure of more than two kinds of antiepileptic drugs; epileptic seizure-free status in excess of 24 h before ^{18}F-FDG PET/CT [12]; and available follow-up data for the Engel classification of postoperative outcomes [13]. The exclusion criteria were as follows: diabetes, hypertension, smoking, cerebrovascular disease, such as infarct or cerebrovascular stenosis found by MRI, magnetic resonance angiography (MRA) or computed tomography angiography (CTA), pathology-detected FCD with hippocampal sclerosis (HS), tumours, heterotopic grey matter, cerebrovascular malformation and so on, and a clinical history of febrile convulsion or head trauma.

PET/CT imaging

All PET/CT scans were performed on a uMI 510 PET/CT scanner (United Imaging Healthcare, Shanghai, China). ^{18}F-FDG was produced on site in a radiochemistry laboratory, and the radiochemical purity of the tracer was greater than 98%. Interictal ^{18}F-FDG PET/CT brain scans were acquired 40 minutes after intravenous injection of the radiotracer ^{18}F-FDG (3.7 ~ 7.4 MBq/kg). All patients were instructed to fast for 4 to 6 hours before injection. After injection, the patients were asked to keep their eyes closed and remain quiet during the 40-minute uptake period. The scan protocol included low-dose CT acquisition, which was used for attenuation correction and localization. The CT image parameters were a slice thickness of 3.0 mm and a scanning time of 11.4 s. A single PET bed position was subsequently acquired for 15 minutes. Iterative reconstruction was performed with a matrix size of 128 × 128 and a slice thickness of 2.44 mm.

Qualitative analysis. Two nuclear medicine physicians analysed the ^{18}F-FDG PET/CT images by visual assessment. The brain was classified into 14 regions: six in each supratentorial cerebral hemisphere (anterior and posterior frontal, anterior and posterior temporal, parietal and occipital lobes) and one in each cerebellar hemisphere [14]. Each brain region was assessed separately. We defined hypometabolic brain regions as brain regions showing decreased radiotracer uptake in more than two positions and a percentage standardized uptake value (SUV) reduction ≥ 10% on two continuous images compared with the contralateral symmetrical areas. When a diagnostic disagreement occurred between the two readers, a discussion ensued until a consensus was reached.

Semi-quantitative analysis. Semi-quantitative analysis was completed by two experienced scientists (one from the nuclear medicine department and one from united imaging) who were double-blinded to the results of the qualitative analysis. The region of interest (ROI) of each brain region was drawn along the outline of the grey matter cortex and mirrored to the contralateral side manually (see Fig. 1). The mean SUV of each ROI was quantitatively measured and recorded. The difference between the abnormal side and the normal side of the brain cortex is expressed by the absolute asymmetry index (|AI|). We adopted the average count of each ROI. The |AI| was calculated as follows: |AI|=|(left - right)/([left + right]/2)|. CCD was considered positive if the |AI| of a certain zone was greater than 0.1 [15].

Follow-up

After surgery, all patients were followed up from 3 months to 36 months via outpatient visits or telephone interviews. According to the Engel classification, seizure outcomes were classified into classes I-IV as follows [16]: Engel class I: completely seizure free, auras only, or convulsions with drug withdrawal only; Engel class II: rare seizures; Engel class III: meaningful improvement; and Engel class IV: no significant improvement or worse. Engel class I had a good prognosis, and Engel classes II ~ IV had a poor prognosis.

Statistical analysis

All data were analysed using SPSS software (version 21.0; IBM SPSS Statistics). Unless otherwise stated, values are reported as the mean ± SD. The numbers of hypometabolic regions in the cerebral hemisphere on PET images between CCD + and CCD- patients were compared using the χ^2 test. A comparison of sex, MRI (negative/positive), EEG (focal/non-focal), seizure type (motor onset/non-motor onset), seizure severity (severe/moderate), FCD type (FCD I/FCD II/FCD III), and the prognosis of epilepsy surgery between CCD + and CCD- patients was also performed using the χ^2 test. A two-sample t test was used to compare age, BMI, onset age, epilepsy duration and hypometabolic regions on PET images between CCD + and CCD- patients. The |AI| values in different brain regions among CCD + and CCD- patients were compared using the independent-samples Mann-Whitney test. Analysis of the correlation of the |AI| between different supratentorial regions and the contralateral cerebellum in CCD + patients was performed using Spearman correlation coefficients. A *P* value less than 0.05 ($P < 0.05$) was considered statistically significant.

Results

Patients were classified as having three types of FCD according to the pathology results. The most common type was FCD I (64/100, 64%), followed by FCD II (25/100, 25%) and FCD III (11/100, 11%). The EON defined by surgery was most frequently located in a single lobe of the cerebrum; for example, almost 50% (45/90) of seizures began in the temporal lobe, 39% (35/90) began in the frontal lobe, 10% (9/90) began in the parietal lobe, and only 1% (1/90) began in the occipital lobe. Ten patients had epileptic foci originating in two lobes of the brain (7 began in the temporal and frontal lobes, 2 began in the temporal and occipital lobes, and 1 began in the parietal and occipital lobes).

PET/CT reading and statistical analysis were used to classify CCD; 77 patients (77%) were classified as CCD- (mean age 23.95 ± 9.72 y), and 23 patients (23%) were classified as CCD+ (mean age 24.96 ± 7.51 y). In total, we found 220 hypometabolic regions by qualitative analysis of the interictal PET/CT images. The most common location of hypometabolic regions was the anterior temporal lobe (37.27%), followed by the anterior frontal lobe (23.64%) (Table 1, Fig. 2–4). When comparing different regions in patients with CCD + and CCD-, a significant difference was identified in the occipital lobe ($P = 0.03$) (Table 2).

Table 1

^{18}F-FDG PET/CT qualitative analysis showed hypometabolic regions in 100 FCD patients

Brain regions	Number (n)	n%
Anterior frontal	52	23.64
Posterior frontal	30	13.64
Parietal	31	14.09
Anterior temporal	82	37.27
Posterior temporal	16	7.27
Occipital	9	4.09
Total	220	100

Table 2

Comparison of the number of hypometabolic brain regions in the cerebral hemisphere involved on PET scans between patients with CCD (CCD + vs CCD-) and prognosis (poor vs good)

Brain region	CCD n(n%)			Prognosis n(n%)		
	+(n = 23)	-(n = 77)	*P*	Poor(n = 35)	Good(n = 65)	*P*
Anterior frontal	16(69.57)	36(46.75)	0.06	22(62.86)	30(46.15)	0.08
Posterior frontal	10(43.48)	20(25.97)	0.13	12(34.29)	18(27.69)	0.49
Parietal	10(43.48)	21(27.27)	0.20	16(45.71)	15(23.08)	**0.02**
Anterior temporal	21(91.30)	61(79.22)	0.31	31(88.57)	51(78.46)	0.21
Posterior temporal	7(30.43)	9(11.69)	0.07	9(25.71)	7(10.77)	0.05
Occipital	5(21.74)	4(5.19)	**0.03**	6(17.14)	3(4.62)	0.06
CCD: crossed cerebellar diaschisis; +: CCD+; -: CCD-						

Comparison between clinical characteristics and the presence of CCD

CCD + patients had more lobes involved on PET than CCD- patients ($P < 0.001$). MRI showed more negative results in CCD- patients than in CCD + patients ($P = 0.02$) (Table 3). No significant differences in age, sex, BMI, onset age, epilepsy duration, EEG type, seizure type, seizure severity or FCD type were found between CCD + and CCD- patients (all $P > 0.05$).

Table 3
Comparison between clinical characteristics and CCD presence in 100 FCD patients

Clinical characteristic	CCD+ (n = 23)	CCD- (n = 77)	*P* value
Sex			0.95
male/female	16/7	54/23	
Age (y)	24.96 ± 7.51	23.95 ± 9.72	0.65
BMI	22.65 ± 4.02	22.74 ± 5.20	0.94
Age of onset (y)	11.08 ± 7.14	11.77 ± 7.52	0.69
Duration of epilepsy	13.86 ± 9.34	12.21 ± 7.96	0.40
Lobes involved on PET	3.61 ± 2.16	2.26 ± 1.01	**< 0.001**
MRI	11	57	**0.02**
negative	12	20	
positive			
EEG	5	16	0.56
focal	18	61	
non-focal			
Seizure type	20	73	0.20
motor onset	3	4	
non-motor onset			
Seizure severity	19	55	0.21
severe	4	22	
moderate	0	0	
mild			
FCD type	12	52	0.31
FCD I	5	20	
FCD II	6	5	
FCD III			

CCD: crossed cerebellar diaschisis; FCD: focal cortical dysplasia; BMI: body mass index; MRI: magnetic resonance imaging; EEG: electroencephalography

Correlations between the Engel class and CCD

The 100 FCD patients with medically intractable epilepsy were followed up at 3, 6, 12, 24 and 36 months postoperatively. Sixty-five patients were classified as Engel class I, 12 as Engel class II, 13 as Engel class III, and 10 as Engel class IV. In summary, 65% of the patients presented a favourable prognosis, and 35% of the patients presented a poor prognosis. When comparing different regions in patients with different prognostic outcomes, a significant difference was identified in the parietal lobe ($P = 0.02$) (Table 2).

Fifty-four patients were followed up at 12 months after surgery: 41 were classified as CCD-, and 13 were classified as CCD+. At 12 months postoperatively, 71% (29/41) of CCD- patients had a good prognosis, whereas 31% (4/13) of CCD + patients had a good prognosis ($P = 0.02$) (Fig. 5). Thirteen patients were followed up at 3 months after surgery, 14 patients were followed up at 6 months after surgery, 16 patients were followed up at 24 months after surgery, and 3 patients were followed up at 36 months after surgery. No significant differences at 3, 6, 24, or 36 months were observed between CCD- and CCD + patients (all $P > 0.05$).

Semi-quantitative PET analysis

No significant difference in the |AI| was noted between the two experienced scientists ($P = 0.66$). The average |AI| values in different ROIs are shown in Table 4. We found significant differences in the average |AI| values in the posterior frontal and anterior temporal lobes ($P < 0.05$) between CCD + and CCD- patients, but no significant difference was found in the anterior frontal, parietal, posterior temporal or occipital lobe (Fig. 6). No significant correlation of the |AI| between supratentorial regions and the contralateral cerebellum was identified in CCD + patients (Fig. 7).

Table 4
The average |AI| in different ROIs

ROI	AI (mean ± SD)
Anterior frontal	0.21 ± 0.11
Posterior frontal	0.21 ± 0.08
Parietal	0.20 ± 0.08
Anterior temporal	0.23 ± 0.11
Posterior temporal	0.21 ± 0.09
Occipital	0.22 ± 0.09
AI: asymmetry index; ROI: region of interest	

Based on the average |AI|, 51 brain regions showed mild hypometabolism, 115 brain regions showed moderate hypometabolism, and 54 brain regions showed severe hypometabolism. When analysing the correlations between the grade of hypometabolism and CCD in different brain regions and in the whole

brain, significant differences were detected in the frontal and temporal lobes and the whole brain (P< 0.05), but no significant correlations were found between the grade of hypometabolism and outcomes and seizure severity (Table 5).

Discussion

We retrospectively analysed the results of the interictal ^{18}F-FDG PET/CT brain scans of 100 FCD patients. CCD was observed in 23% of FCD patients in this study. This rate is lower than the previously reported prevalence of CCD in patients with ictal epileptic seizures and after stroke [15, 17–19]. In addition, our study demonstrated that the number of lobes involved on PET, structural anomalies on MRI, the lesion location on PET, the |AI| in the posterior frontal and anterior temporal lobes may be predisposing factors for CCD, the presence of CCD may affect the prognosis of FCD patients at 12 months postoperatively, and parietal hypometabolism on PET may indicate a poor prognosis. To the best of our knowledge, this is the first interictal ^{18}F-FDG PET/CT study to investigate the incidence of CCD, identify risk factors for seizure-related CCD, and determine the correlation between CCD and prognosis in patients with FCD confirmed by postoperative pathology.

Our results suggest that the number of lobes involved on PET and the lesion location on PET are related to the appearance of CCD. Previous studies have uncovered possible risk factors associated with the presence of stroke-related CCD, but conflicting results still exist. A recent survey of 108 patients with ischaemic stroke within 6 h of onset found no significant differences in the distribution of supratentorial ischaemic lesions between CCD + and CCD- patients using whole-brain volume perfusion CT (CTP) [20]. Kim et al [21] hypothesized that the location rather than the extent of a lesion may be the primary determinant for the occurrence of CCD in patients with cerebral infarction. They found that CCD + was significantly higher when infarctions were located in the frontoparietal lobes or the deep middle cerebral artery territory compared to other regions (11/19 vs 1/7, P = 0.048). In this study, a significant difference was found between CCD + and CCD- when a hypometabolic brain region was located in the occipital lobe (P = 0.04). The pathophysiologic distinction may need to be studied further to explain the difference. Kunz et al [22] found no significant association between CCD + and infarction volume (P = 0.972). Conversely, Jeon et al [23] demonstrated that the supratentorial ischaemic volume on each CTP map did not differ significantly between CCD + and CCD- groups (P > 0.05), but a correlation analysis of the supratentorial ischaemic volume on each CTP map showed a positive and significant linear correlation (P < 0.05). In our study, the CCD + group had a higher number of hypometabolic regions on PET than the CCD- group (P = 0.00), which can be regarded as equal to the volume of the EON. However, the range of hypometabolic regions on PET is always greater than that in the EON [5, 24]; thus, these results do not imply the real volume of the EON. In the future, we need quantitative methods to calculate the real volume of the EON.

We found that the average |AI| values in the posterior frontal and anterior temporal lobes in the CCD + group were significantly higher than those in the CCD- group, but no correlation of the |AI| between supratentorial regions and the contralateral cerebellum was found in CCD + patients. Jeon et al [23] found

that the supratentorial degree of perfusion reduction and the infratentorial asymmetry index were strongly and significantly ($P < 0.05$) correlated with each other in CCD + patients. Kunz et al [22] showed that CCD + patients had larger supratentorial cerebral blood flow deficits than CCD- patients (median: 164 ml vs. 115 ml; $P = 0.001$) by CT perfusion imaging among acute ischaemic stroke patients. To date, most studies on CCD have focused on cerebral perfusion, and studies on cerebral metabolism are lacking. Cerebral blood flow perfusion and cerebral glucose metabolism reflect different brain physiological states, and a direct integrated study of brain perfusion and metabolism should be performed.

To date, this study is the first to investigate the prognostic value of CCD in FCD patients postoperatively; however, pioneering studies have explored its clinical significance in ischaemic patients. Sin et al [15] hypothesized that CCD was associated with poor motor recovery after 6 months in patients with haemorrhagic stroke assessed with the Fugl-Meyer Assessment (FMA) and the Korean version of the Modified Barthel Index (K-MBI) score, which is consistent with Small et al [25] who concluded that the occurrence of CCD had a close association with motor recovery using functional MRI. Sebök et al [19] included 25 cases with symptomatic unilateral cerebrovascular steno-occlusive disease and concluded that CCD + patients were in poorer clinical condition than CCD- patients after a 3-month follow-up: National Institutes of Health Stroke Scale (NIHSS) 2 vs 0, $P = 0.02$; modified Rankin Scale (mRS) 1 vs 0, $P = 0.04$. Other authors demonstrated that CCD has no prognostic value for stroke outcomes. Zhang et al [20] found no difference in the NIHSS score between CCD + and CCD- patients with acute ischaemic stroke, which is similar to the result obtained by Kunz et al [22]. In summary, CCD is not only a concomitant symptom in diseases such as cerebral infarction and epilepsy but also an important indicator for functional recovery and prognosis. We need a more exact evaluation index in addition to the Engel class to explore the value of CCD in patients with epilepsy at baseline and during follow-ups.

The underlying pathophysiologic mechanism of CCD due to cerebral infarction is functional disruption of the cortico-ponto-cerebellar (CPC) pathways [26, 27]. Recently, Hong demonstrated that FCD lesions can influence whole-brain network integrity using structural equation modelling [28]. CCD + patients showed more significant structural anomalies on MRI and a higher rate of the “severe” grade of hypometabolism in the frontal and temporal lobes and the whole brain than CCD- patients ($P < 0.05$), and parietal hypometabolism on PET may indicate a poor prognosis (P = 0.02), which are interesting findings of our study. We thought that these findings were closely related to the CPC pathways. Massaro [29] found CCD in patients with status epilepticus by MRI and attributed the finding to excessive neuronal transmission caused by prolonged excitatory synaptic activity from the supratentorial hemisphere to the contralateral cerebellum through the CPC pathway, resulting in increased energy metabolism and cerebral blood flow. Ictal ^{18}F-FDG PET showed hypermetabolism, whereas hypometabolism is observed on interictal imaging. Sebök et al [19] found that CCD + patients showed more severely impaired supratentorial cerebrovascular reactivity than CCD- patients. Lindenberg et al [30] found that the integrity of motor fibre tracts was positively correlated with stroke recovery in 35 chronic stroke patients undergoing diffusion tensor imaging (DTI). In the next step, we will analyse differences in fibre tracts in CPC pathways between CCD

+ and CCD- epilepsy patients using integrated ^{18}F-FDG PET/MR-DTI and determine the correlation between the grade of hypometabolism and the integrity of motor fibre tracts.

Some limitations exist in this retrospective research. First, the checkout offset cannot be avoided completely. Second, in this study, we performed only a semi-quantitative analysis to evaluate the severity of CCD and not a quantitative analysis. Despite these limitations, the population in this retrospective study was sufficiently large to investigate the predictors and clinical value of CCD and may provide a basis for further prospective research.

Conclusion

The number of lobes involved on PET, structural anomalies on MRI, the lesion location on PET, the |AI| values in the posterior frontal and anterior temporal lobes may be predisposing factors for CCD. The CCD phenomenon may be helpful for predicting the prognosis of FCD patients at 12 months postoperatively, and parietal hypometabolism on PET may indicate a poor prognosis.

Declarations

Ethics approval and consent to participate The subjects provided written informed consent for the study protocols, which were approved by the ethics committee of Xuanwu Hospital and conducted in accordance with the Declaration of Helsinki. Consent to participate was obtained from all individual participants included in the study.

Consent for publication Not applicable

Availability of data and material The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests The authors declare that they have no competing interests.

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Authors' contributions Yaqin Hou, Guoguang Zhao and Jie Lu contributed to the concept and study design. Xiaotong Fan, Yongzhi Shan and Guoguang Zhao were responsible for patient management. Yaqin Hou, Kun Guo, Kun Shang, Jingjuan Wang, and Zhenming Wang contributed to data acquisition and analysis. Yaqin Hou, and Jie Lu drafted the manuscript, tables and figures. Jie Lu contributed to critical revision of the manuscript. All authors approved the final version.

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Figures

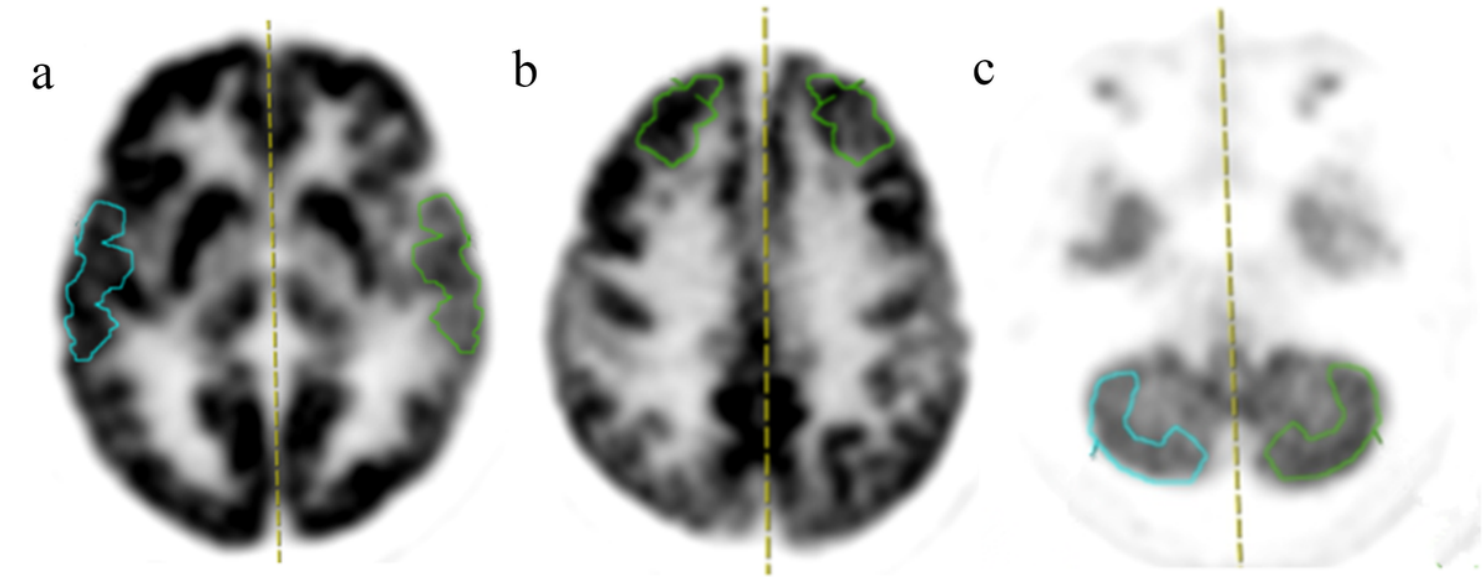

Figure 1

Three examples of mirrored ROI segmentations demonstrating the approach to |AI| calculation. a: anterior temporal lobe; b: anterior frontal lobe; c: cerebellum.

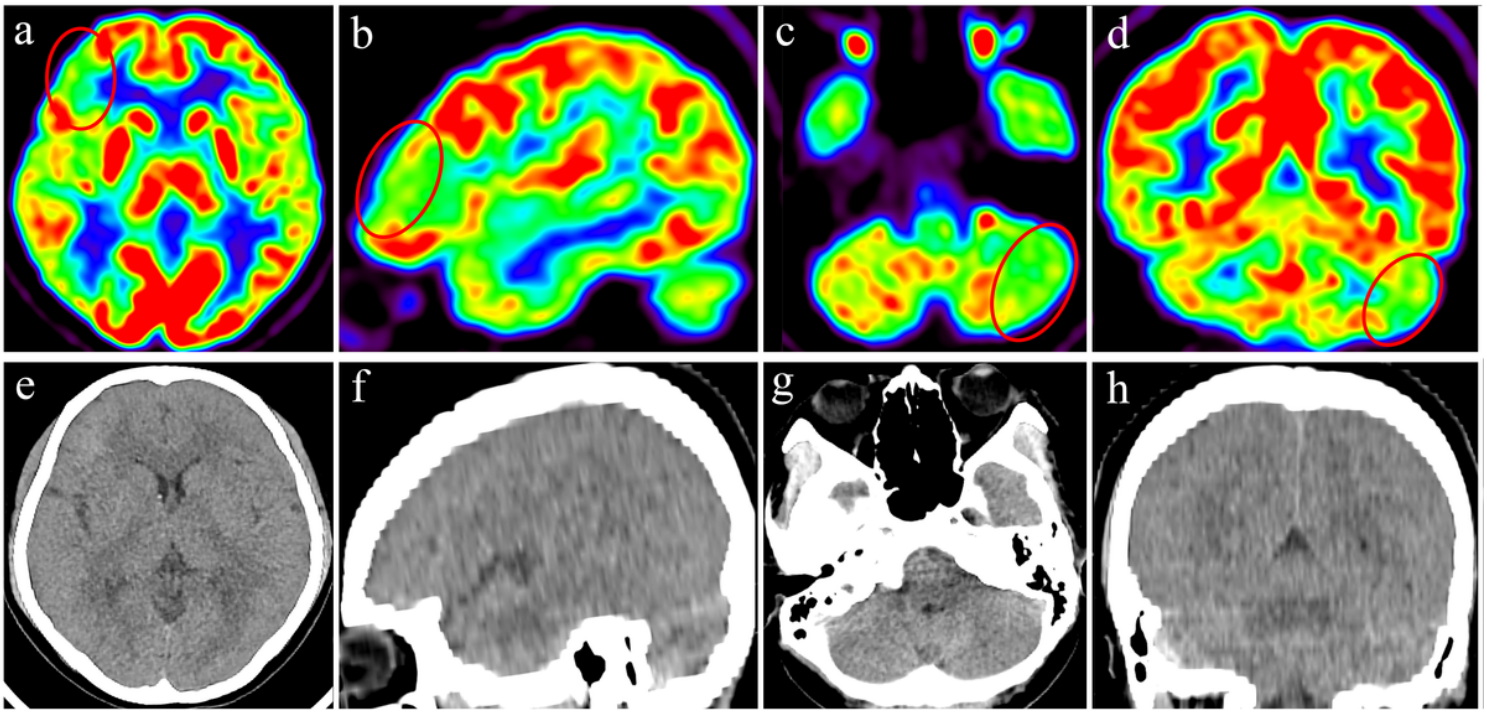

Figure 2

Male, 27 y, age of onset 20 y, and duration of epilepsy 7 y. Interictal 18F-FDG PET/CT images show hypometabolism in the left anterior temporal lobe (ellipse; a: axial, b: coronal) and contralateral

cerebellum (ellipse; c: axial, d: coronal) on PET images, without significant abnormalities on CT images (e-h). The pathology after surgery was FCD IIIb in the left anterior temporal lobe.

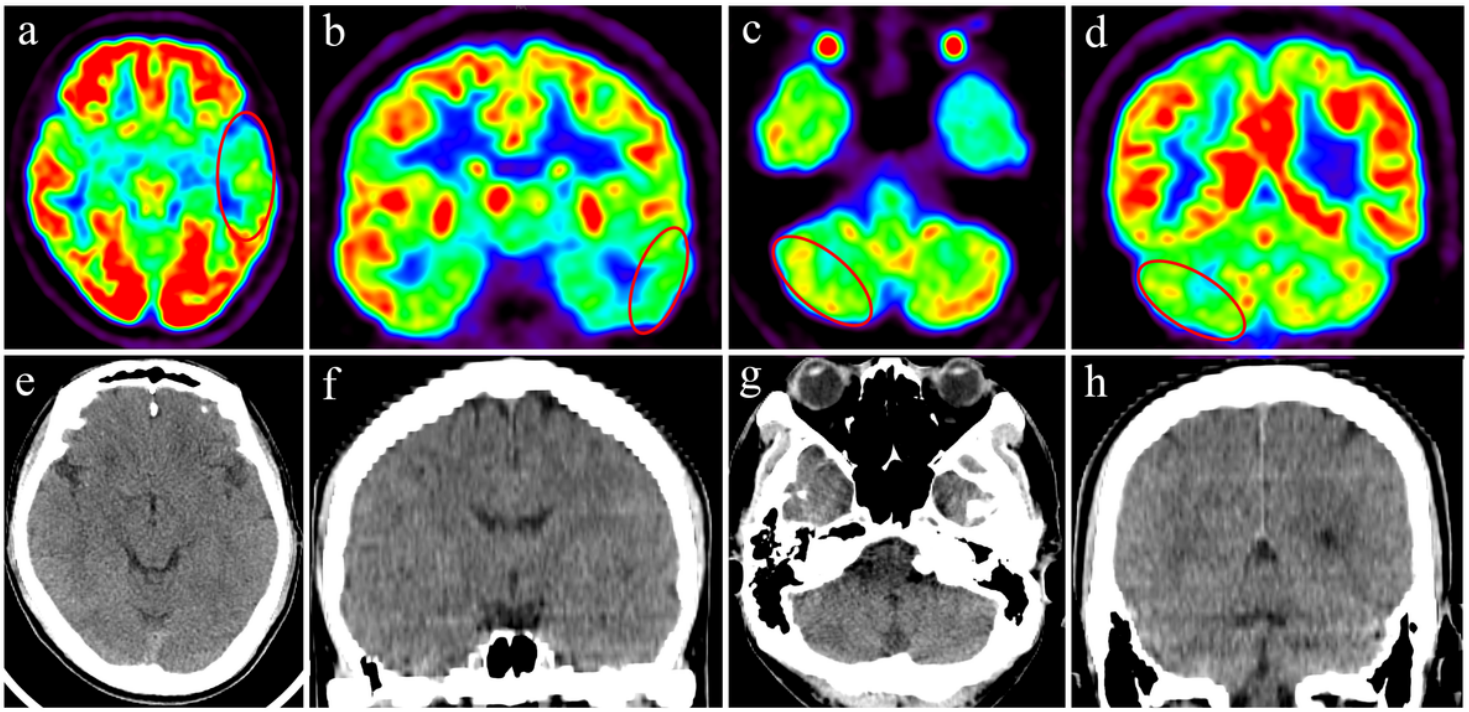

Figure 3

Female, 17 y, age of onset 13 y, and duration of epilepsy 4 y. Interictal 18F-FDG PET/CT shows hypometabolism in the right anterior frontal lobe (ellipse; a: axial, b: sagittal) and contralateral cerebellum (ellipse; c: axial, d: coronal) on PET images, without significant abnormalities on CT images (e-h). The pathology after surgery was FCD IIb in the right anterior frontal lobe.

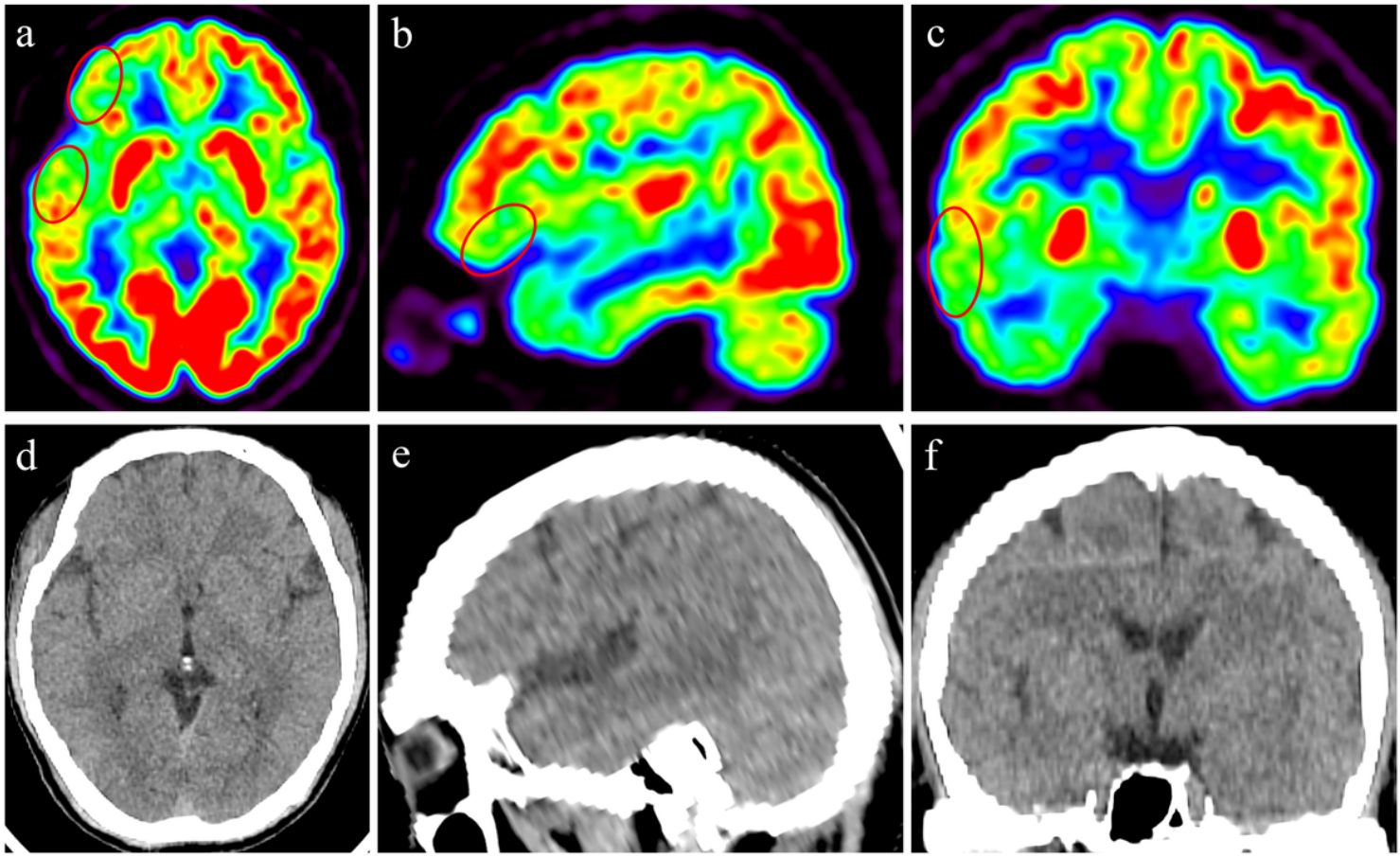

Figure 4

Male, 45 y, age of onset 15 y, and duration of epilepsy 30 y. Interictal 18F-FDG PET/CT shows hypometabolism in the right anterior frontal and temporal lobes (ellipse; a: axial, b: sagittal, c: coronal) on PET images, without significant abnormalities on CT images (d-f). The pathology after surgery was FCD Ib in the right anterior frontal and temporal lobes.

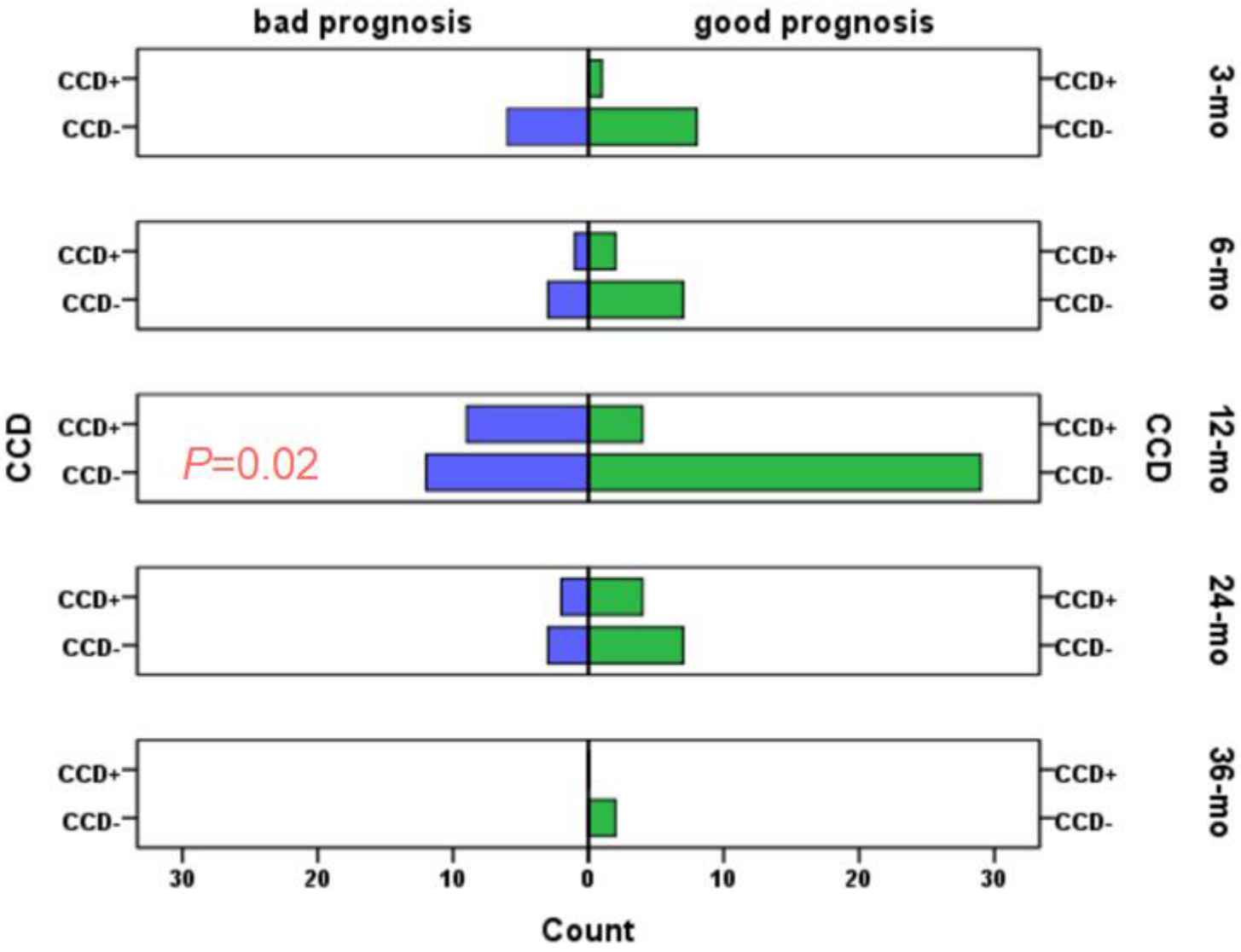

Figure 5

Comparison of the outcomes between CCD+ and CCD- patients. Forty-one CCD- and 13 CCD+ patients showed a significant difference after 12 months of follow-up. No significant differences at 3, 6, 24, or 36 months were found between CCD- and CCD+ patients.

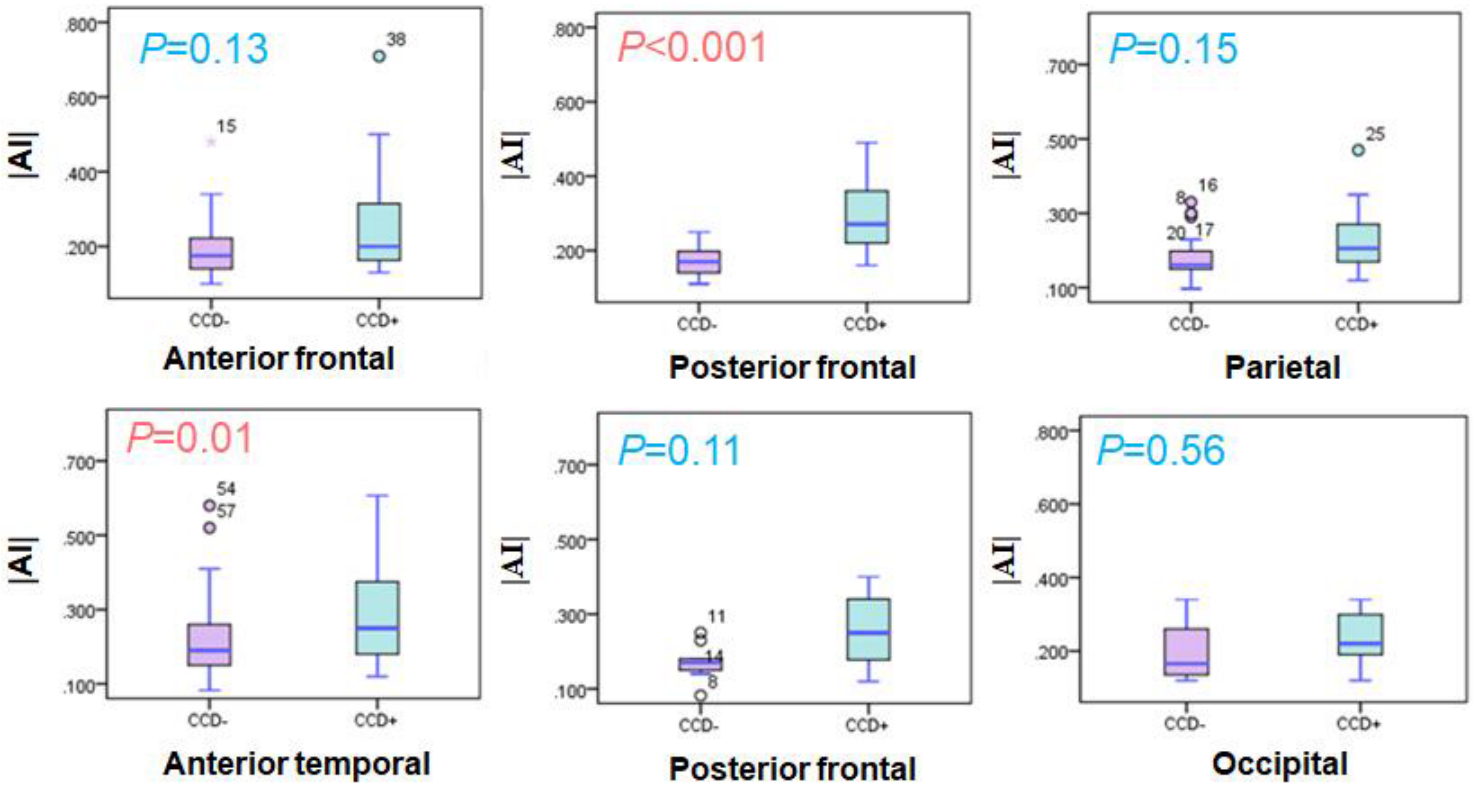

Figure 6

Comparison of the |AI| in different regions between CCD+ and CCD- patients. Significant differences in the posterior frontal and anterior temporal lobes were observed.

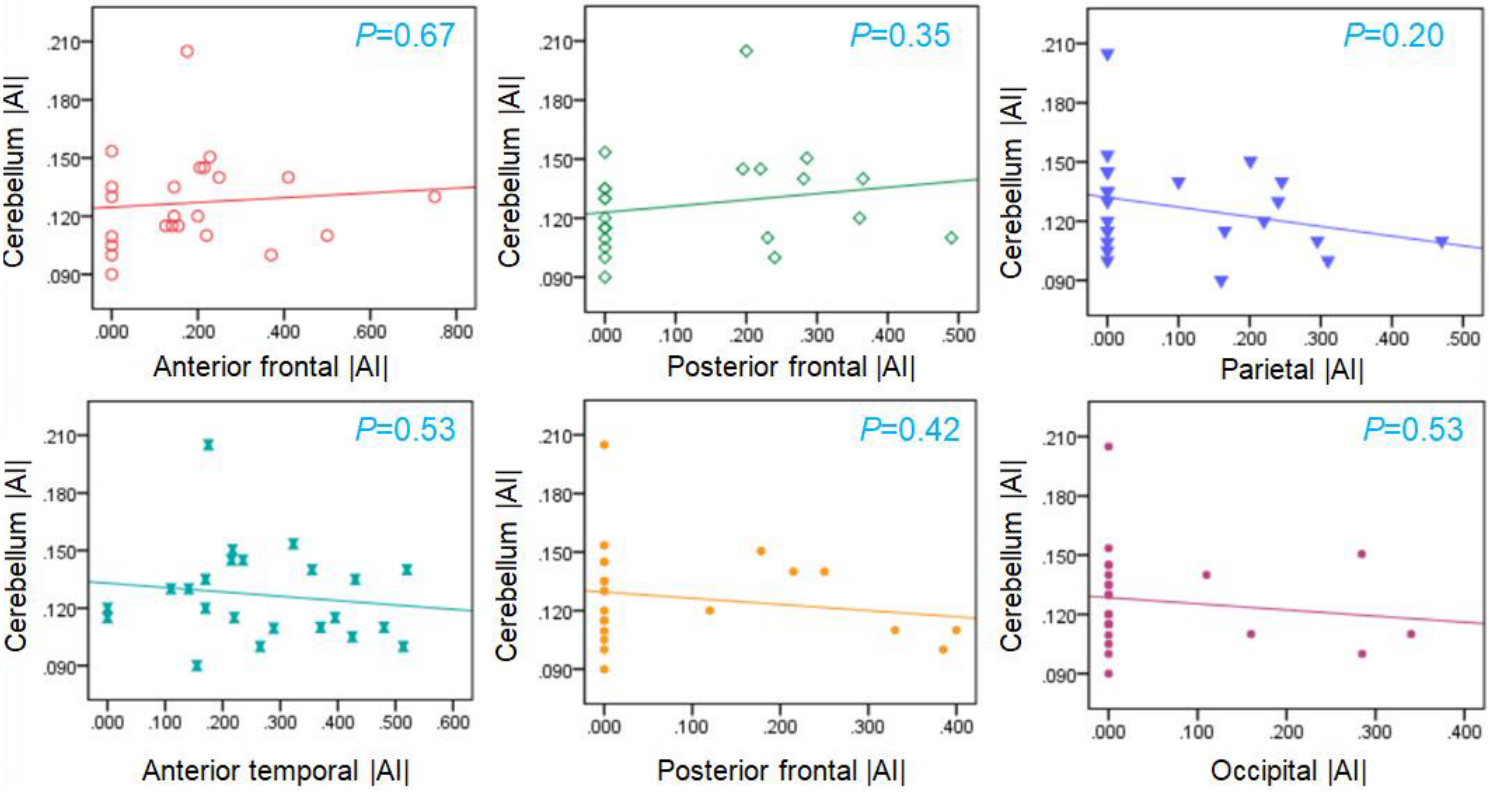

Figure 7

Analysis of the correlation of the |AI| between different supratentorial regions and the contralateral cerebellum in 23 CCD+ patients. No significant correlation of the |AI| between any supratentorial region and the contralateral cerebellum was identified.