Neurological Sciences (2019) 40:2097–2103
https://doi.org/10.1007/s10072-019-03947-8

ORIGINAL ARTICLE

Altered white matter microstructure in patients with post-stroke depression detected by diffusion kurtosis imaging

Xue-Yong Shen[1] · Ze-Xin Fan[1] · Li Wang[1] · Sha Cui[2] · Jin-Liang Niu[2]

Received: 25 October 2018 / Accepted: 22 May 2019 / Published online: 30 May 2019

Abstract

The aim of our study is to determine the pathological changes of white matter microstructure in patients with early post-stroke depression (PSD), and to investigate the association between white matter integrity examined by diffusion kurtosis imaging (DKI) and early PSD. Thirty-eight patients with acute cerebral infarction were selected, including 17 patients with depression (PSD group), and 21 patients without depression (N-PSD group). In addition, 20 normal healthy controls (NORM group) were selected. All were taken DKI scans. The white matter of the frontal lobe, temporal lobe, parietal lobe, occipital lobe, anterior limb of internal capsule, and posterior limb of internal capsule, in addition to the genu of corpus callosum and splenium of corpus callosum was selected as a region of interest (ROI). Selected parameters include fractional anisotropy (FA) and mean kurtosis (MK). Compared with N-PSD group and NORM group, FA value of the left frontal lobe and MK value of the bilateral frontal lobe, bilateral temporal lobe, and genu of corpus callosum in PSD group were decreased ($P < 0.05$). Our results indicated that the early PSD patients had white matter microstructure abnormalities in the frontal lobe, temporal lobe, and genu of corpus callosum. DKI provides a comprehensive brain imaging reference for detecting early microstructural damage of white matter in PSD patients, which can be used as an imaging biomarker to detect early PSD and its progression potentially.

Keywords Post-stroke depression · Diffusion kurtosis imaging · Magnetic resonance imaging · Biomarker

Introduction

Post-stroke depression (PSD) patients demonstrated mood swings, sluggishness, irritability or indifference, lack of pleasure, pessimism, suicidal ideation, etc. [1, 2]. PSD affects approximately one-third of stroke survivors and can occur at any stage after stroke. PSD patients generally have poor prognosis, poor quality of life, high recurrent rate of vascular events, and high mortality compared with patients without depression [3]. Accordingly, defining the risk factors associated with PSD is extraordinarily important. Too many risk factors like insomnia, serum levels of homocysteine, the severity of stroke, and so on may be associated with PSD [4, 5]. However, the pathogenesis of PSD is more remarkable [6]. As a special type of depression, the theory of the emotional ring damage of PSD has been extensively studied recently. The limbic-cortical-striatal-pallidal-thalamic (LCSPT) circuit [7] is considered to be closely associated with the negative emotions. The proper function of this circuit is based on the integrity of the white matter fibers of the brain. When stroke occurs in a patient, it may directly or indirectly interrupt the above-mentioned neurological circuits associated with emotion control. The abnormality of fiber bundles in white matter may be the underlying basis leading to the neuronal network dysfunction [8].

At present, the main imaging technique to study white matter fiber integrity is diffusion tensor imaging (DTI); this imaging technique is based on the standard distribution of normal tissues distributed by water molecules in a given tissue. However, there are restrictions on diffusion barriers such as cell membranes in the human body, and the diffusion of water molecules in the tissues does not obey the Gaussian

Xue-Yong Shen and Ze-Xin Fan contributed equally to this work.

✉ Li Wang
wangli19891992@163.com

[1] Department of Neurology, The Second Hospital Affiliated to Shanxi Medical University, Taiyuan 030001, Shanxi, People's Republic of China

[2] Department of Medical Imaging, The Second Hospital Affiliated to Shanxi Medical University, Taiyuan 030001, Shanxi, People's Republic of China

distribution [9]. As an extension of DTI, diffusion kurtosis imaging (DKI) used in this study is a method to explore the diffusion characteristics of non-Gaussian distribution of water molecules. It can overcome the limitations of DTI and observe changes in brain microstructure within multiple *b* values. It can more accurately describe diffusion signals and provide richer organizational microstructure information [10, 11]. This study aimed to use DKI to study possible changes in the white matter microstructure of patients with acute PSD.

Material and methods

Patients and control subjects

The Ethics Review Board of our institution examined and approved this research protocol in accordance with the Declaration of Helsinki before the study. Thirty-eight patients with acute cerebral infarction who were hospitalized at the Second Hospital of Shanxi Medical University from May 2017 to December 2017 were selected, including 17 patients with post-stroke depression (PSD group), and 21 patients without post-stroke depression (N-PSD group). Enrollment criteria are as follows: all subjects were confirmed by cranial CT or MRI examinations and were first-episode patients. Exclusion criteria are as follows: patients with disturbance of consciousness, aphasia, hearing impairment, and severe cognitive impairment who cannot cope with the examiner; patients with cerebral infarction, cerebral hemorrhage, and subarachnoid hemorrhage; patients with heart and lung failure, liver and renal insufficiency, and end-stage disease; people who have had depression or mental illness previously, have taken or are taking antidepressants or other psychoactive drugs, and those who have metal materials or other artificial implants in their bodies cannot perform magnetic resonance imaging. In addition, 20 normal healthy control subjects (NORM group) were selected. All subjects were right-handed and all subjects had informed consent.

At the time of admission, demographic data and stroke characteristics were collected. Stroke severity was evaluated by the National Institutes of Health and Stroke Scale (NIHSS) and modified Rankin Scale (MRS). The infarction area was divided into groups according to the Adams [12] classification method. The infarct area < 1.5 cm was the lacunar infarction group. The infarct area between 1.5 and 3.0 cm, with the occlusion of small vessels involving 1 anatomical site, was the small infarction group. The infarct area > 3.0 cm, with the occlusion of large brain arteries involving more than 2 anatomical sites, was the large infarction group. Fasting blood was collected via venipuncture in BD Vacutainer® (New Jersey, USA) tubes at 7:00 am on the morning after the admission. Serum levels of homocysteine (HCY) were measured using standard laboratory methods.

Two weeks after the onset of stroke, two well-trained neurologists used 24 items of the Hamilton Depression Scale (HAMD-24 item) to assess the depression status. The diagnosis of PSD meets the diagnostic criteria for depression in the American Diagnostic and Statistical Manual for Mental Disorders (DSM-V). All subjects were divided into three groups according to Hamilton scale scores and the exclusion and diagnostic criteria mentioned above, including 17 patients with post-stroke depression (PSD group), 21 patients without post-stroke depression (N-PSD group), and 20 healthy controls (NORM group).

DKI scan

At the time of admission, demographic data and stroke characteristics were collected. Two weeks after the onset of stroke, the Hamilton Depression Scale was evaluated. MRI scans were performed using a GE MR750W 3.0T magnetic resonance scanner, including T1 weighted images, T2 weighted images, DWI sequences, and DKI sequences. The DKI scan uses axial scanning parameters: repetition time (TR) 6500 ms, echo time (TE) 95.80 ms, FOV 24 cm, matrix 128 × 128, number of layers 25, layer thickness 3.6 mm, layer Pitch 0.4 mm, *b* value (0, 1250, 2500 s/mm^2), 25 diffusive magnetically sensitive directions, and scan time 11′10″. Data were analyzed by using function tool 9.4.05 post-processing software of GE AW 4.6 post-processing workstation. Selected parameters include fractional anisotropy (FA) and mean kurtosis (MK). The white matter of the frontal lobe, temporal lobe, parietal lobe, occipital lobe, the anterior limb of internal capsule, and the posterior limb of internal capsule, in addition to the genu of corpus callosum and the splenium of corpus callosum were selected, totaling to 14 regions of interest (ROI). The diameter is about 10 mm, and the corresponding FA and MK values were determined. Each ROI was measured three times and averaged. When selecting the ROI, try to avoid the infarct zone, brain gray matter, cerebral sulcus, and vascular space, and try to satisfy all patients with the same level, bilateral symmetry, and the same area. All imaging technicians were blind to the group distribution of research subjects.

Statistics

The statistical analyses were performed with SPSS 20.0. The study data conforms to normal distribution, and quantitative data are expressed as mean ± standard deviation. One-way analysis of variance (ANOVA) was used to compare quantitative differences among three different groups. For the factors that meet the homogeneity of variance data, the LSD method was used for comparison between groups; for those data that did not meet the

homogeneity of variance, the Dunnett T3 test was used to compare the groups. Chi-square test was used to compare the differences between the groups in the classification data. $P < 0.05$ was considered statistically significant.

Results

Demographic data of the study subjects

The demographic data of the three groups of subjects including gender, age, marriage, education level, family history of psychiatric disorders, and HCY are comparable. There was no significant difference among three groups ($P > 0.05$) (Table 1). Stroke severity was evaluated by NIHSS, MRS, and infarct area. There was no significant difference among PSD group and N-PSD group ($P > 0.05$) (Table 1). Shi Y et al. [13] found that female gender, age, family history, severity of stroke, and level of handicap were risk factors for PSD. Among them, main risk factors for PSD were neurological severity, while we have the different result. Maybe it is because the sample size was not large enough to elucidate the moderate size of difference between groups. Compared with N-PSD group and NORM group, percentage of insomnia patients in PSD group was increased ($P < 0.01$) (Table 1). The reason could be that insomnia is likely to lead to various psychological problems, and depression is one of the most common mental disorders.

FA value in the three groups

Compared with the N-PSD group and NORM group, FA value of the left frontal lobe of the PSD group was decreased ($P < 0.05$) (Table 2) (Fig.1). The occurrence of PSD may be associated with the decreased FA value in the frontal lobe, especially the left frontal lobe. The frontal lobe is extensively connected with other cerebral cortices, limbic systems, and subcortical regions and is an important component of the LCSPT loop [7].

MK value in the three groups

MK value of the bilateral frontal lobe, bilateral temporal lobe, and genu of corpus callosum in the PSD group was smaller than those in the N-PSD group and NORM group ($P < 0.05$) (Table 3). The structure of temporal lobe is complex, and its inner side is a component of the limbic system, especially the hippocampal formation, which is associated with advanced neurological functions such as mentality and emotion [14]. Therefore, it can be speculated that the occurrence of early PSD may be associated with the white matter injury in the temporal lobe. In addition, corpus callosum is a commissural fiber that connects the cerebral hemispheres on both sides and widely connects intracranial frontal lobes, parietal lobes, temporal lobes, and occipital lobes, and plays an important role in information integration and transmission in the human brain [15]. The white matter microstructure injury in the corpus callosum may also contribute to early PSD.

Table 1 Character of the study subjects

		PSD	N-PSD	NORM	χ^2/F	P
Gender	Male	10 (58.82%)	11 (52.38%)	9 (45%)	0.709	0.712
	Female	7 (41.18%)	10 (47.62%)	11 (55%)		
Age (years)		64 ± 10.95	64.71 ± 10.42	64.9 ± 9.72	0.038	0.963
Marital status	No spouse	2 (11.76%)	3 (14.29%)	1 (5%)	1.100	0.577
	Married	15 (88.24%)	18 (85.71%)	19 (95%)		
Education	≥ 9 years	4 (23.53%)	8 (38.1%)	4 (20%)	1.848	0.432
	≤ 9 years	13 (76.47%)	13 (61.9%)	16 (80%)		
Insomnia	Have	12 (70.6%)	2 (9.5%)	4 (20%)	18.104	< 0.01
	No	5 (29.4%)	19 (90.5%)	16 (80%)		
Family history of psychiatric disorders	Have	16 (94.1%)	20 (95.2%)	20 (100%)	1.381	0.746
	No	1 (5.9%)	1 (4.8%)	0 (0%)		
NIHSS		6.41 ± 4.32	6.14 ± 4.05	–	0.001	0.846
MRS		2.65 ± 1.46	2.67 ± 1.39	–	0.182	0.967
HCY		21.35 ± 7.26	18.86 ± 6.39	21.00 ± 5.22	0.913	0.407
Infarct size	Lacunar infarction	4 (23.5%)	7 (33.3%)	–	0.560	0.915
	Small infarction	8 (47.1%)	8 (38.1%)	–		
	Large infarction	5 (29.4%)	6 (28.6%)	–		

NIHSS, National Institutes of Health Stroke Scale; *MRS*, Modified Rankin Scale; *HCY*, homocysteine

Table 2 FA value in the three groups

Location	FA			*F*	*P*	*P*1	*P*2	*P*3
	PSD	N-PSD	NORM					
L-F	0.239 ± 0.076	0.286 ± 0.053	0.291 ± 0.072	3.353	0.042	0.034	0.022	0.826
R-F	0.248 ± 0.139	0.252 ± 0.122	0.243 ± 0.101	0.027	0.973	0.913	0.911	0.816
L-T	0.209 ± 0.082	0.221 ± 0.109	0.227 ± 0.106	0.151	0.860	0.706	0.591	0.862
R-T	0.242 ± 0.102	0.257 ± 0.119	0.263 ± 0.103	0.178	0.837	0.673	0.562	0.863
L-P	0.256 ± 0.111	0.25 ± 0.102	0.265 ± 0.099	0.104	0.901	0.867	0.793	0.652
R-P	0.242 ± 0.087	0.236 ± 0.081	0.251 ± 0.09	0.160	0.852	0.837	0.744	0.576
L-O	0.135 ± 0.04	0.143 ± 0.076	0.139 ± 0.048	0.086	0.918	0.680	0.819	0.849
R-O	0.123 ± 0.054	0.13 ± 0.069	0.131 ± 0.068	0.076	0.927	0.754	0.716	0.955
L-ALIC	0.221 ± 0.032	0.215 ± 0.092	0.227 ± 0.072	0.102	0.903	0.991	0.983	0.958
R-ALIC	0.252 ± 0.041	0.255 ± 0.063	0.258 ± 0.063	0.055	0.947	0.998	0.982	0.998
L-PLIC	0.247 ± 0.042	0.249 ± 0.053	0.243 ± 0.059	0.062	0.940	0.913	0.827	0.730
R-PLIC	0.241 ± 0.053	0.238 ± 0.059	0.249 ± 0.061	0.213	0.809	0.880	0.655	0.530
G-CC	0.262 ± 0.071	0.268 ± 0.077	0.253 ± 0.079	0.224	0.800	0.795	0.711	0.508
S-CC	0.271 ± 0.059	0.275 ± 0.08	0.282 ± 0.084	0.110	0.896	0.876	0.650	0.752

L-F, the left frontal lobe; *R-F*, the right frontal lobe; *L-T*, the left temporal lobe; *R-T*, the right temporal lobe; *L-P*, the left parietal lobe; *R-P*, the right parietal lobe; *L-O*, the left occipital lobe; *R-O*, the right occipital lobe; *L-ALIC*, the anterior limb of left internal capsule; *R-ALIC*, the anterior limb of right internal capsule; *L-PLIC*, the posterior limb of left internal capsule; *R-PLIC*, the posterior limb of right internal capsule; *G-CC*, the genu of corpus callosum; *S-CC*, the splenium of corpus callosum

P value is the comparison result between the three groups; *P*1 is the comparison result between the PSD group and the N-PSD group; *P*2 value is the comparison result between the PSD group and the NORM group; *P*3 is the comparison result between the N-PSD group and the NORM group

Discussion

DKI is a new technique proposed by Jensen et al. in 2005 to study the non-Gaussian diffusion behavior of water molecules. It provides more complete information on water distribution and organization structure [9]. Compared with DTI, DKI can provide a more comprehensive description of the in vivo diffusion process of water molecules. By quantifying mean and orientation kurtosis values and diffusion coefficients, DKI can provide higher sensitivity and specificity for the diffusion characteristics of neural tissue. DKI is a further development of DTI technology. The scan can obtain multiple parameters such as FA and MK. FA is a parameter for the anisotropic response of water molecules in brain tissue. FA value is positively correlated with the thickness and integrity of myelin sheath and the compactness of fibers. MK is the average value of the diffuse kurtosis of the organization along each direction of the space. It is the most characteristic DKI parameter and is a dimensionless parameter. MK value is considered to be an indicator of the complexity of the microstructure of tissue. The more complex and precise the structure is, the greater the degree of non-Gaussian diffusion of water molecules is, and the larger MK value is [16, 17].

In our current study, we found that FA values of the left frontal lobe and MK values of the bilateral frontal lobes of the PSD group were smaller than those of the N-PSD group and

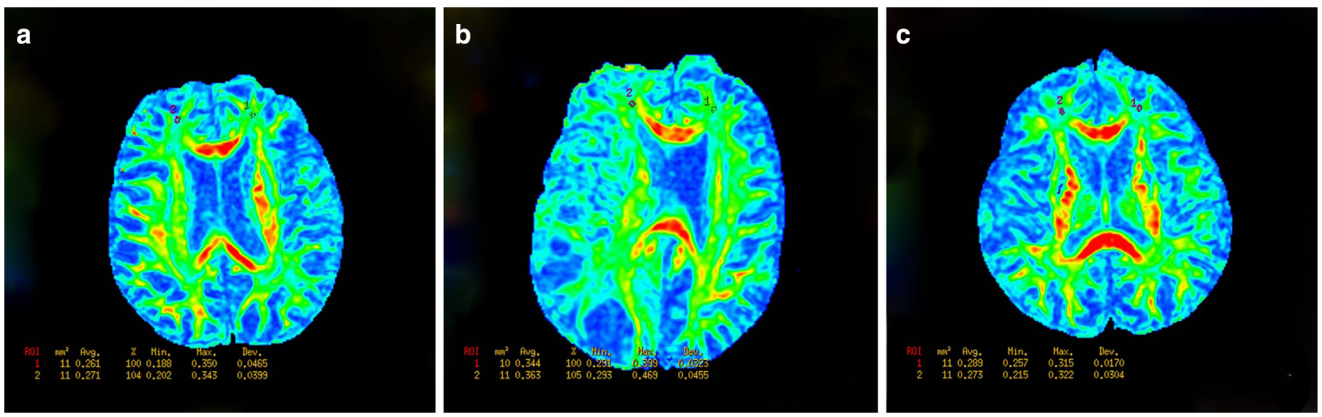

Fig. 1 FA value in a PSD patient (**a**), a non-PSD patient (**b**), and a healthy control (**c**). Tables 1, 2 stand for the frontal lobe. Our results showed that the FA value in the left frontal lobe of PSD group was decreased than those in N-PSD group and NORM group ($P < 0.05$)

Table 3 MK value in the three groups

Location	MK			F	P	P1	P2	P3
	PSD	N-PSD	NORM					
L-F	0.868 ± 0.122	0.982 ± 0.097	1.016 ± 0.119	8.565	0.001	0.003	<0.001	0.338
R-F	0.904 ± 0.067	1.018 ± 0.074	1.055 ± 0.122	17.007	< 0.001	< 0.001	< 0.001	0.585
L-T	0.748 ± 0.065	0.851 ± 0.057	0.874 ± 0.071	19.544	< 0.001	< 0.001	< 0.001	0.252
R-T	0.739 ± 0.079	0.865 ± 0.069	0.881 ± 0.076	19.686	< 0.001	< 0.001	< 0.001	0.494
L-P	0.863 ± 0.11	0.844 ± 0.102	0.877 ± 0.094	0.527	0.593	0.578	0.680	0.311
R-P	0.908 ± 0.039	0.889 ± 0.063	0.852 ± 0.097	2.916	0.068	0.591	0.075	0.405
L-O	0.947 ± 0.136	0.968 ± 0.125	0.983 ± 0.106	0.399	0.673	0.609	0.376	0.687
R-O	0.927 ± 0.101	0.938 ± 0.107	0.906 ± 0.095	0.511	0.603	0.734	0.544	0.321
L-ALIC	0.851 ± 0.037	0.832 ± 0.043	0.844 ± 0.047	0.948	0.394	0.185	0.635	0.374
R-ALIC	0.849 ± 0.042	0.868 ± 0.063	0.855 ± 0.066	0.540	0.586	0.318	0.734	0.492
L-PLIC	0.882 ± 0.065	0.871 ± 0.077	0.903 ± 0.079	0.959	0.390	0.644	0.405	0.176
R-PLIC	0.891 ± 0.079	0.906 ± 0.082	0.909 ± 0.091	0.243	0.785	0.592	0.508	0.889
G-CC	0.9 ± 0.041	1.011 ± 0.055	1.019 ± 0.068	25.098	< 0.001	< 0.001	< 0.001	0.666
S-CC	0.964 ± 0.04	0.952 ± 0.066	0.938 ± 0.065	1.134	0.333	0.875	0.363	0.856

the NORM group. Bae et al. [18] found that in the elderly patients with depression compared with the normal control group, the FA value of the white matter of the bilateral frontal gyrus and left middle frontal lobe decreased significantly. In conclusion, the frontal lobe contains active metabolites such as monoamines and acetylcholine that regulate emotions. The occurrence of PSD may be related to the frontal lobe.

In this study, the ROI of the temporal lobe was chosen to be on the inner side of the temporal lobe. Because of its proximity to the limbic system, it has abundant fiber connections with the surrounding tissue and it is relatively easy to detect changes in the white matter fiber microstructure. This study found that MK value of bilateral temporal lobe of PSD patients was smaller than that of the N-PSD group and NORM group. In a study, Nobuhara K et al. [19] conducted a DTI imaging study of 13 elderly patients with depression and a matched control group. It was also found that FA value of the temporal lobe white matter in the depression group was significantly reduced, which is consistent with the results of this study. The temporal lobe is similar to the frontal lobe, and is also an important brain region with enriched monoamine and acetylcholine. The white matter microstructure change in the temporal lobe may contribute to occurrence of early PSD.

The fiber of the parietal lobe is very extensive, and the efferent fibers can be added to various fiber structures such as cone system and extrapyramidal system, cortical network structure, and so on. This complex fiber connection in the parietal lobe may be associated with cognition function and emotional control. Williamson J et al. [14] analyzed the correlation between DTI-FA values and cognition and emotion in 108 ischemic stroke patients at 3 to 6 months after stroke, and found that compared with temporal and occipital lobes, the correlation between FA values and cognition and emotion scores in the parietal lobe was stronger and more consistent. This study found no statistically significant differences between the three parameters in the parietal lobe. The discrepancy between our study and the previous study may be due to the subjects selected for the previous study which were patients with PSD in the middle or later stages of stroke. However, in our study, only patients with early PSD were selected.

The function of the occipital lobe is mainly related to vision. In a study of 120 patients with depression, Friberg TR et al. [20] found that patients with severe symptoms of clinical depression have an effect on the perception of light in the surrounding environment as compared with those with mild depression. The visual pathways of depression patients may have neurophysiological changes. This suggests that the occipital lobe may be associated with depressive symptoms. Our study found no statistically significant differences between the three parameters of the occipital lobe. The reasons for this differentiated result may because of age of subjects (the average age of the study subjects in this study was 41.8 ± 17.7 years, and the average age of the PSD group in our study was 64 ± 10.95 years) or the relatively small number of cases in this study, A separate group study of severe PSD patients was not conducted.

Yasuno F et al. [21] found that the injury of the microstructure of anterior limb of internal capsule may cause negative emotional changes. We found no statistically significant differences between the three parameters of internal capsule. Another study by Yasuno F et al. [22] found that FA values

of the white matter in the anterior limb of bilateral internal capsule in PSD patients were significantly lower at 10–28 days after stroke, and FA value of these regions increased significantly after 6 months, suggesting that the white matter damage in PSD patients may be reversible. In previous study, both HAMD-17 and Zung's self-rating scales were used, and the early scale assessment time was 10–28 days after onset.

Our study found that MK values of the genu of corpus callosum in PSD patients were smaller than those in the N-PSD group and NORM group. A study by Choi S et al. [15] found that the FA value of the genu of corpus callosum in patients with depression was significantly lower than in healthy controls. However, a study of elderly patients with depression by Nobuhara K et al. [19] found that there was no significant difference in the FA value of the corpus callosum area between the depressive group and the normal control group. Although the above two studies are all related to the study of depression, PSD is a special type of depressive disorder caused by stroke. Whether there is a common pathogenesis of depressive disorder induced in different situations remains an open question.

In the current study, we explored a new technology to study white matter microstructure in PSD patients. DKI represents accurate information on the diffusion of water molecules and has a unique advantage in responding to the microstructural damage of white matter in brain tissue. The disadvantages of DKI include long scanning time and challenge in coordinating with some patients. It is believed that with the continuous improvement of magnetic resonance apparatus, scanning technology and post-processing technology, this imaging technology will be more widely used in clinical not only for monitoring white matter microstructure change, but also for understanding the underlying pathogenesis of the structure changes. The limitations of the current study include small sample numbers and no grading of PSD, which will be improved in future follow-up studies.

Conclusion

Our results indicated that the pathological changes in the white matter microstructure in the frontal lobe, temporal lobe, and genu of corpus callosum may be underlying mechanism of post-stroke depression. DKI provides a comprehensive brain imaging reference for detecting early microstructural damage of white matter in PSD patients, which can be undertaken as a potential brain structure imaging biomarker to predict the progression of PSD.

Funding information This study was supported by Doctor Wenzhen Duan of Johns Hopkins University School of Medicine.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Zhao FY, Yue YY, Li L, Lang SY, Wang MW, du XD, Deng YL, Wu AQ, Yuan YG (2018) Clinical practice guidelines for post-stroke depression in China. Rev Bras Psiquiatr 40(3):325–334
2. Zhang N, Wang CX, Wang AX, Bai Y, Zhou Y, Wang YL, Zhang T, Zhou J, Yu X, Sun XY, Liu ZR, Zhao XQ, Wang YJ, on behalf of the Prospective Cohort study on Incidence and Outcome of Patients with Poststroke Depression in China (PRIOD) Investigators (2012) Time course of depression and one-year prognosis of patients with stroke in mainland China. CNS Neurosci Ther 18(6):475–481
3. Towfighi A, Ovbiagele B, El HN, Hackett ML, Jorge RE, Kissela BM, Mitchell PH, Skolarus LE, Whooley MA, Williams LS (2017) Poststroke depression: a scientific statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 48(2):e30–e43
4. Li Y, Cao LL, Liu L, Qi QD (2017) Serum levels of homocysteine at admission are associated with post-stroke depression in acute ischemic stroke. Neurol Sci 38(5):811–817
5. Wang L, Tao Y, Chen Y, Wang H, Zhou H, Fu X (2016) Association of post stroke depression with social factors, insomnia, and neurological status in Chinese elderly population. Neurol Sci 37(8):1305–1310
6. Robinson RG, Jorge RE (2016) Post-stroke depression: a review. Am J Psychiatry 173(3):221–231
7. Sheline YI (2003) Neuroimaging studies of mood disorder effects on the brain. Biol Psychiatry 54(3):338–352
8. Liao Y, Huang X, Wu Q, Yang C, Kuang W, du M, Lui S, Yue Q, Chan R, Kemp G, Gong Q (2013) Is depression a disconnection syndrome? Meta-analysis of diffusion tensor imaging studies in patients with MDD. J Psychiatry Neurosci 38(1):49–56
9. Jensen JH, Helpern JA, Ramani A, Lu H, Kaczynski K (2005) Diffusional kurtosis imaging: the quantification of non-gaussian water diffusion by means of magnetic resonance imaging. Magn Reson Med 53(6):1432–1440
10. Grinberg F, Maximov II, Farrher E, Neuner I, Amort L, Thönneßen H, Oberwelland E, Konrad K, Shah NJ (2017) Diffusion kurtosis metrics as biomarkers of microstructural development: a comparative study of a group of children and a group of adults. Neuroimage 144(Pt A):12–22
11. Kamiya K, Kamagata K, Miyajima M, Nakajima M, Hori M, Tsuruta K, Mori H, Kunimatsu A, Arai H, AokiS OK (2016) Diffusional kurtosis imaging in idiopathic normal pressure hydrocephalus: correlation with severity of cognitive impairment. Magn Reson Med Sci 15(3):316–323
12. Adams HP, Bendixen BH, Kappelle LJ et al (1993) Classification of subtype of acute ischemic stroke definitions for use in a multicenter clinical trial, TOAST. Trial of org 10172 in acute stroke treatment. Stroke 24(1):35–39
13. Shi Y, Yang D, Zeng Y, Wu W (2017) Risk factors for post-stroke depression: a meta-analysis. Front Aging Neurosci 9:218
14. Williamson J, Nyenhuis D, Stebbins GT, Lamb D, Simkus V, Sripathirathan K, Wang C, de Toledo-Morrell L, Gorelick P (2010) Regional differences in relationships between apparent white matter integrity, cognition and mood in patients with ischemic stroke. J Clin Exp Neuropsychol 32(7):673–681
15. Choi S, Han KM, Won E, Yoon BJ, Lee MS, Ham BJ (2015) Association of brain-derived neurotrophic factor DNA methylation

and reduced white matter integrity in the anterior corona radiata in major depression. J Affect Disord 172:74–80
16. Lätt J, Nilsson M, Wirestam R, Ståhlberg F, Karlsson N, Johansson M, Sundgren PC, van Westen D (2013) Regional values of diffusional kurtosis estimates in the healthy brain. J Magn Reson Imaging 37(3):610–618
17. Das SK, Wang JL, Bing L, Bhetuwal A, Yang HF (2017) Regional values of diffusional kurtosis estimates in the healthy brain during normal aging. Clin Neuroradiol 27(3):283–298
18. Bae JN, MacFall JR, Krishnan KR, Payne ME, Steffens DC, Taylor WD (2006) Dorsolateral prefrontal cortex and anterior cingulate cortex white matter alterations in late-life depression. Biol Psychiatry 60(12):1356–1363
19. Nobuhara K, Okugawa G, Sugimoto T, Minami T, Tamagaki C, Takase K, Saito Y, Sawada S, Kinoshita T (2006) Frontal white matter anisotropy and symptom severity of late-life depression: a magnetic resonance diffusion tensor imaging study. J Neurol Neurosurg Psychiatry 77(1):120–122
20. Friberg TR, Borrero G (2000) Diminished perception of ambient light: a symptom of clinical depression. J Affect Disord 61(1–2): 113–118
21. Yasuno F, Taguchi A, Yamamoto A, Kajimoto K, Kazui H, Kudo T, Kikuchi-Taura A, Sekiyama A, Kishimoto T, Iida H, Nagatsuka K (2014) Microstructural abnormality in white matter, regulatory T lymphocytes, and depressive symptoms after stroke. Psychogeriatrics 14(4):213–221
22. Yasuno F, Taguchi A, Yamamoto A, Kajimoto K, Kazui H, Sekiyama A, Matsuoka K, Kitamura S, Kiuchi K, Kosaka J, Kishimoto T, Iida H, Nagatsuka K (2014) Microstructural abnormalities in white matter and their effect on depressive symptoms after stroke. Psychiatry Res 223(1):9–14