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The mean kurtosis (MK) is more sensitive diagnostic biomarker than fractional anisotropy (FA) for Parkinson's disease

A diagnostic performance study and meta-analysis

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Abstract

Background: The mean kurtosis (MK) and fractional anisotropy (FA) in patients of Parkinson's disease (PD) are usually measured by diffusion kurtosis imaging (DKI) and diffusion tensor imaging (DTI), separately.

Methods: In this study we perform a meta-analysis to discuss which noninvasive biomarker is more advantageous for PD, MK, or FA. Databases including Medline via PubMed, the Cochrane Central Register of Controlled Trials, Embase via OVID and China National Knowledge Infrastructure. Databases are searched up to December 31st, 2019. Four brain regions are identified for analysis based on data extracted from articles.

Results: The articles contain 5 trials with 274 total PD patients and 189 healthy controls (HCs). The results show not only significantly higher MK values of putamen, caudate, globus pallidus in PD compared to that of HCs (weighted mean difference [WMD] = 0.06, 95% CI = 0.02–0.09, $P = .002$, WMD = 0.03, 95% CI = 0.01–0.067, $P = .01$, WMD = 0.18, 95% CI = 0.11–0.24, $P < .00001$), but also a significantly higher FA in caudate of PD compared to HCs (WMD = 0.02, 95% CI = 0.00–0.03, $P = .006$).

Conclusion: This indicates that the sharp difference detected between PD patients and HCs can be detected by DKI and DTI. By further discussing results, we found that MK could be more sensitive diagnostic biomarker than FA toward PD diagnosis.

Abbreviations: DKI = diffusion kurtosis imaging, DTI = diffusion tensor imaging, FA = fractional anisotropy, HCs = healthy controls, MK = mean kurtosis, MR = magnetic resonance, PD = Parkinson's disease, ROI = region of Interesting, SN = substantia nigra, WMD = weighted mean difference.

Keywords: diffusion kurtosis imaging, diffusion tensor imaging, MRI, PD

1. Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disease worldwide. Major pathology change of PD is a progressive degeneration of dopaminergic neurons in the substantia nigra (SN), which results in a dopamine depletion in the striatum.[1] Moreover, due to the impairment in the dopaminergic neurotransmission, profound functional abnormity occur in the input and output structures of the basal ganglia.[2]

Owing to the close relationship between PD and the neurodegeneration in SN and basal ganglia,[3] magnetic resonance (MR) imaging can be used to measure structural alterations of PD patients, and may serve as sensitive and noninvasive biomarkers.[4] Current MR imaging technology has made possible the in vivo assessment of white matter integrity by means of diffusion tensor imaging (DTI).[5,6] This technique allows one to accurately and quantitatively measure fiber bundles Fractional anisotropy (FA). In recent years, a number of studies have shown that FA in the SN of early-stage PD patients is decreased.[7] However, DTI can result in several errors underestimating diffusion anisotropy in the DTI metrics of white matter when voxels include heterogeneous nerve tracts, such as crossing, diverging, and kissing fibers, which may reduce its accuracy in detecting pathological changes.[8] To overcome this issue, diffusion kurtosis imaging (DKI) has been applied recently.[9]

DKI is an improved DTI technique and is more capable of detecting microstructural changes of tissues compared with DTI technique. Mean kurtosis (MK) is a major parameter of DKI.[10] MK values are closely related to gray matter structure. When gray matter structures are more complex, MK values

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generated from DKI are higher.[11] Studies involving DTI and DKI for PD diagnosis in Taiwan have shown that the MK index has higher diagnostic efficiency than the FA index. However, it remains unknown whether or not the phenomenon is the same in the population of all over the world.[12] The objectives of this meta-analysis are to summarize all available evidence from studies on the application of MK and FA for the evaluation of neurodegeneration in SN and basal ganglia, to discuss which noninvasive biomarker is more advantageous for Parkinson's diagnosis.

2. Methods

2.1. Literature search strategy

Literature related to PD and DKI are searched in 4 databases including Medline via PubMed, the Cochrane Central Register of Controlled Trials, Embase via OVID and China National Knowledge Infrastructure, dated till December 31st, 2019. The keywords for PD and DKI are "Parkinson disease," "Parkinson's disease," "Parkinsons disease," "Parkinsonian" or "PD" and "diffusion kurtosis imaging," "DKI," "mean kurtosis," or "MK" respectively. The study is approved by the Ethics Committee of Qinhuangdao Municipal No. 1 Hospital (202101A141).

2.2. Study selection

Based on the keywords, titles and abstracts of the identified publications are screened. Following an exhaustive examination of the literature contents, articles are included according to our selection criteria: population (idiopathic PD patients), comparators (individuals free of neurological disorders), outcome measurement (MK and FA values of multiple brain regions), and language (articles written in English or Chinese). The study focused on the application of MK and FA to evaluate the degree of lesions in PD patients SN and basal ganglia. Therefore, all studies must be randomized controlled trial researches and provide the values of MK and FA, all subjects of papers must be person, SN and basal ganglia must be selected as region of interesting (ROIs), and the basal ganglia is subdivided into 3 groups (putamen, caudate, and globus pallidus).

2.3. Data extraction

The literature search and data extraction are conducted by 2 researchers independently. In the case of a dispute, a third investigator is included to discuss and reach an agreement. Apart from MK and FA measures the following data is extracted from the publications if available: sample size, age, sex, PD diagnosis, scanner make, MR field strength, MR method type, number of diffusion gradient directions, motion and eddy current correction and method of ROI placement. Assessment of the detailed information is listed in Table 1. As shown in this table, the disease severity (Hoehn and Yahr stage or unified PD rating scale) is not provided by all the included studies. Therefore, we don't include the disease severity as a source of variance in the analysis.

In case of visual identification and manual outlining of the SN, caudate, putamen and globus pallidus the method of ROI placement is classified as "manual." In case of manual identification and automated digital boundary detection by changes in gradients or manual identification by using connectivity measures the ROI placement was classified as "semi-manual."

Where available, mean and standard deviation measures of MK and FA are extracted. To allow comparability within the meta-analysis the mean MK and FA over all 4 regions is calculated. Also, for the purpose of the meta-analysis, the averaged results of subdivided ROI measures of this study are included.

Table 1

Characteristics of the 5 studies included for meta-analyses.

	PD patients			Healthy controls												
Article	n	Age	Gender (F/M)	n	Age	Gender (F/M)	PD diagnosis	Scanner make	MR field strength	MR method type	DKI/DTI dir	Deep brain nuclei studied	ROI placement	UPDRS score	UPDRS motor score	H-Y scale	Disease duration
Zhang et al	72	66.83 ± 5.41	46/26	72	66.08 ± 6.77	44/28	UK PD Brain Bank criteria	General electrics	3.0T	DKI/DTI	25/25	SN	Manual	14.94 ± 3.86	--	1.67 (1–2)	13.50 ± 6.79 (M)
Wang et al	30	64.5 ± 3.4	11/19	30	65.0 ± 5.1	12/18	National Institute of Neurological Disorders and Stroke (NINDS) criteria	Siemens	3.0T	DKI/DTI	64/64	SN, putamen, caudate, globus pallidus	Manual	--	33.6 ± 14.1	2 (1–3)	5.2 ± 2.0 (Y)
Surova et al	105	66 ± 11	61/44	44	66 ± 8	25/19	National Institute of Neurological Disorders and Stroke (NINDS) criteria	Siemens	3.0T	DKI/DTI	64/64	SN, putamen, caudate,	Manual	--	13 ± 10	2 ± 1	--
Sun et al	32	63 (57, 67)	11/21	20	58.550 ± 7.430	10/10	Chinese Parkinson's Disease & Movement Disorders Society, Neurology Branch of Chinese Medical Association	Philips	3.0T	DKI	32	SN, putamen, caudate, globus pallidus	Semi–manual	23(17.25,27.50)	--	1.5 (1.5, 2)	22 (19, 25.75) (M)
Gao et al	35	67.00 ± 8.76	17/18	23	66.48 ± 5.20	11/12	Chinese Parkinson's Disease & Movement Disorders Society, Neurology Branch of Chinese Medical Association	General Electrics	3.0T	DKI	15	SN, putamen, caudate, globus pallidus, red nucleus	Manual	--	--	--	3–10 (Y)

Age: Data in this column are presented as mean ± SD or Range or Median (Range) or Mean (Range); Data in this column are presented as mean ± SD or Range or Median (Range) or Mean (Range); The disease duration are presented as mean ± SD or Range or Median (Range) or Mean (Range), (Y) stands for yrs, and (M) stands for mo.

DKI = diffusion kurtosis imaging, DTI = diffusion tensor imaging, H-Y = Hoehn and Yahr, MK = mean kurtosis, PD = Parkinson's disease, ROI = region of interesting, SN = substantia nigra, SD = standard deviation, UPDRS = Unified Parkinson's Disease Rating Scale.

2.4. Quality assessment

The Newcastle-Ottawa Scale is employed to assess the quality of the chosen studies. This tool classified studies in 3 broad perspectives: selection of the study groups, comparability of the groups, and ascertainment of either exposure or outcome of interest for the studies. Semi-quantitative measurement using a star system assesses the quality of study. The highest quality studies can get a maximum of 9 stars. For further details see the supplementary material in Table 2.

2.5. Statistical analysis

Five MRI analysis articles are eventually selected for our meta-analysis. Means, standard deviations, and the number of samples are extracted in each study. Meta-analyses are conducted within the studies of the same brain region. All of the analyses are performed using Review Manager 5.2 for Windows. A 2-tailed P value < .05 is considered statistically significant. Weighted mean difference (WMD) is regarded as an effect size. Q-statistics and Chi^2 are used for assessing the heterogeneity. A random effects model is applied when heterogeneity is found by Q-statistics or when $P > .05$. A fixed effects model is applied otherwise. The diagnostic efficacy of MK and FA are evaluated by ROC curve analysis, and the area under the ROC curve is calculated. When the area under the curve is 0.5 to 0.7, the diagnostic accuracy is low, when the area is 0.7 to 0.9, the diagnostic accuracy is medium, and when the area is greater than 0.9, the diagnostic accuracy is high. Test level is $\alpha = 0.05$.

2.6. Patient and public involvement

No patients were involved in the design, recruitment or conduct of the study. The results of this review will not be disseminated to patients included in the trials of the review.

3. Results

3.1. Search results

The initial search using the keywords as described in the method section returns a total of 43 articles (See Flow Diagram for details). A subsequent screening of the titles and abstracts reduces the number to 42. Following an exhaustive examination of the contents, 12 articles are excluded according to the selection criteria detailed in the method section. Out of 12 reviewed articles are excluded for the following reasons: 4 publications because of the MK values are not measured, 2 publications because of the studies are reviews or meta-analysis, 2 publications because of the subjects are rats or mice, 2 publications because of white matter tracts are studied, 1 publication because of healthy control (HCs) is missed, 1 publication because of the values of MK is not normal distribution. Of the 5 articles being selected that report MK and FA value, 1 of them only studies the region of SN, 1 misses the region of globus pallidus. The disease comorbidity and diagnostic performance of the cohorts of these 23 studies are summarized in Table 1.

Table 2

Assessment of study quality: A = adequate definition of case, B = representativeness of cases, C = selection of control, D = definition of control, E = control for important factor or additional factor, F = exposure assessment, G = same method of ascertainment for cases and controls, H = nonresponse rate.

	Quality indications of Newcastle-Ottawa scale								
Article	A	B	C	D	E	F	G	H	Total
Zhang et al	0	1	0	1	2	1	1	1	7
Wang et al	0	1	0	1	1	1	1	1	6
Surova et al	0	1	0	1	2	1	1	1	7
Sun et al	0	1	1	1	2	1	1	1	8
Gao et al	0	1	1	1	1	1	1	1	7

3.2. Quality assessment

Quality assessment by Newcastle-Ottawa Scale suggests 4-stars or above out of a maximum of 9 for all of the 5 publications. The detailed quality assessment is listed in Table 2.

3.3. The comparison of MK and FA values in defined brain regions

Five articles are included in the MK subgroup of meta-analyses in 4 brain regions. The total subject numbers are 314 (SN), 319 (putamen), 319 (caudate), and 170 (globus pallidus). The numbers of subject in the FA subgroup are 467 (SN), 319 (putamen), 319 (caudate), and 170 (globus pallidus), respectively.

3.4. Substantia nigra

In the SN of PD subjects, the MK value is elevated (WMD = 0.11, 95% CI = 0.09–0.12, $P < .00001$), but the heterogeneity is quite obvious ($\chi^2 = 45.34$, $P < .00001$; Fig. 1A). Results of a sensitivity analysis ascribes the heterogeneity to the studies of Gao et al and Sun et al, as exclusion of them reduces the heterogeneity ($\chi^2 = 7.18$, $P = .007$; Fig. 1B) (WMD = 0.13, 95% CI = 0.11–0.14, $P < .00001$). Even if the above 2 groups of studies are excluded, there is a relatively high heterogeneity. Subsequent meta-analysis cannot demonstrate a significant MK changes in the SN.

In addition, 5 studies reported nigral FA changes induces by PD that show a significant FA reduction in SN of PD patients with an estimated WMD of –0.05 (95% CI = –0.06, –0.04, $P < .00001$; Fig. 1C). A high level of heterogeneity is recorded ($\chi^2 = 66.27$, $P < .00001$). When we remove the study of Wang et al and Zhang et al, the heterogeneity is acceptable ($\chi^2 = 3.16$, $P = .21$). Unfortunately, the nigral FA is no difference between the PD and control group ($P = .25$; Fig. 1D).

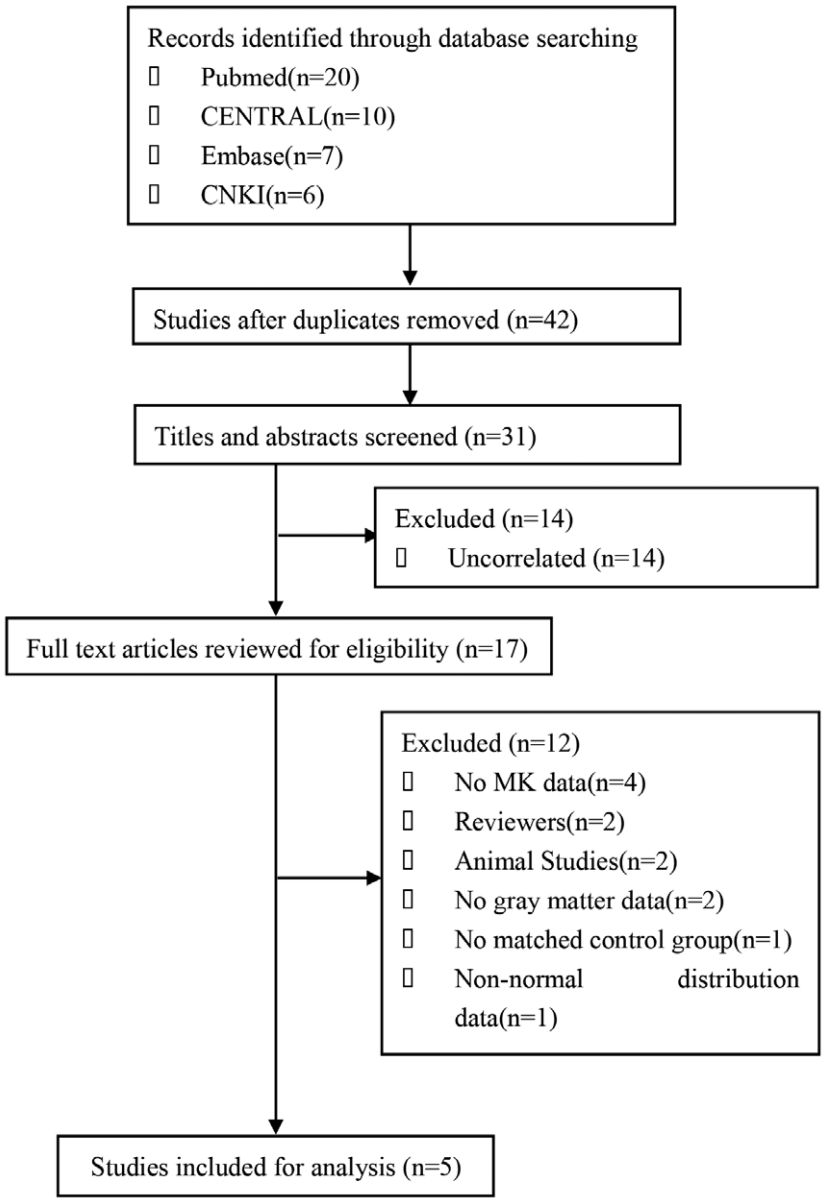
3.5. Putamen

For putamen, the MK values are also elevated (WMD = 0.06, 95% CI = 0.03–0.09, $P < .0001$), there is also a high degree of heterogeneity ($\chi^2 = 44.20$, $P < .00001$; Fig. 1E). When the article of Wang et al and Surova et al are removed based on sensitivity analysis, we still observed an increase of the values of MK in the putamen (WMD = 0.06, 95% CI = 0.02–0.09, $P = .002$) ($\chi^2 = 0.14$, $P = .71$; Fig. 1F).

There's a difference in the results of subgroup analysis for the FA in putamen, yet. Although the FA of PD is significantly lower than the control group (WMD = –0.01, 95% CI = –0.02 to –0.01, $P = .001$), but also there is significant heterogeneity ($\chi^2 = 18.99$ $P = .003$; Fig. 1G). On the one hand, Surova and Gao et al publications cover the obvious FA reduction in PD group (WMD = –0.03, 95% CI = –0.04 to –0.02, $P < .00001$; $\chi^2 = 0.47$, $P = .50$; Fig. 1H). On the other hand, the results no significant difference of FA changes is observed in the subgroup analysis for the studies of Wang et al and Sun et al (WMD = 0.01, 95% CI = 0.00–0.03, $P = .15$; $\chi^2 = 0.11$, $P = .73$; Fig. 1I). In a word, this meta-analysis document a no significant difference on FA changes in PD group.

3.6. Caudate

Similar to putamen, significant heterogeneity is detected in the caudate group, which are attributed to Gao et al and



Flow Diagram. Flow Diagram describing the selection process of articles retrieved from initial literature search. CENTRAL = Cochrane Central Register of Controlled Trials.

Wang et al as determined by a sensitivity analysis (χ^2 = 18.71, P = .0003; Fig. 1J). Although there is an increase of the MK values (WMD = 0.05, 95% CI = 0.03–0.07, P < .00001). Meta-analysis after exclusion of the above 2 papers shows a significant increase of MK (WMD = 0.03, 95% CI = 0.01–0.06, P = .01) (χ^2 = 0.02, P = .88; Fig. 1K).

Among the 4 studies that have reported FA changes, no changes of significant differences are documented on DTI measurements (FA) between the PD patients and HCs (WMD = 0.01, 95% CI = 0.00–0.01, P = .24) (χ^2 = 10.19, P = .02; Fig. 1L). When the value of χ^2 is reduced to 2.16 (P = .34), the meta-analysis of 3 studies also indicate significance with an estimated WMD of 0.02 (95% CI = 0.00–0.03, P = .006; Fig. 1M).

3.7. Globus pallidus

Results of analyses suggests an increase of the MK values in the globus pallidus (WMD = 0.07, 95% CI = 0.03–0.12, P = .001). Due to the removal of the article of Gao et al, the heterogeneity has dropped significantly from (χ^2 = 18.83, P < .0001; Fig. 1N) to (χ^2 = 2.29, P = .13; Fig. 1O). Despite of a high heterogeneity, there are studies that shows a significant increase in MK values in the globus pallidus (WMD = 0.18, 95% CI = 0.11–0.24, P < .00001).

The changes of FA are not significant difference between the PD patients and HCs (WMD = 0.01, 95% CI = –0.02 to 0.03, P = .62) (χ^2 = 8.31, P = .02; Fig. 1P). And in order to induce the heterogeneity, the article of the Gao et al is deleted (χ^2 = 0.01, P = .94). However, this meta-analysis also fail to certify that significant change of FA values in PD globus pallidus (WMD = –0.03, 95% CI = –0.06 to 0.00, P = .07; Fig. 1Q).

The above results are summarized in detail in Figure 1 and Table 3.

3.8. Comparison the efficiency of MK and FA in PD diagnosis

For the MK value, the results show that the area under ROC curve is 0.713 (P = .047), and diagnostic accuracy is

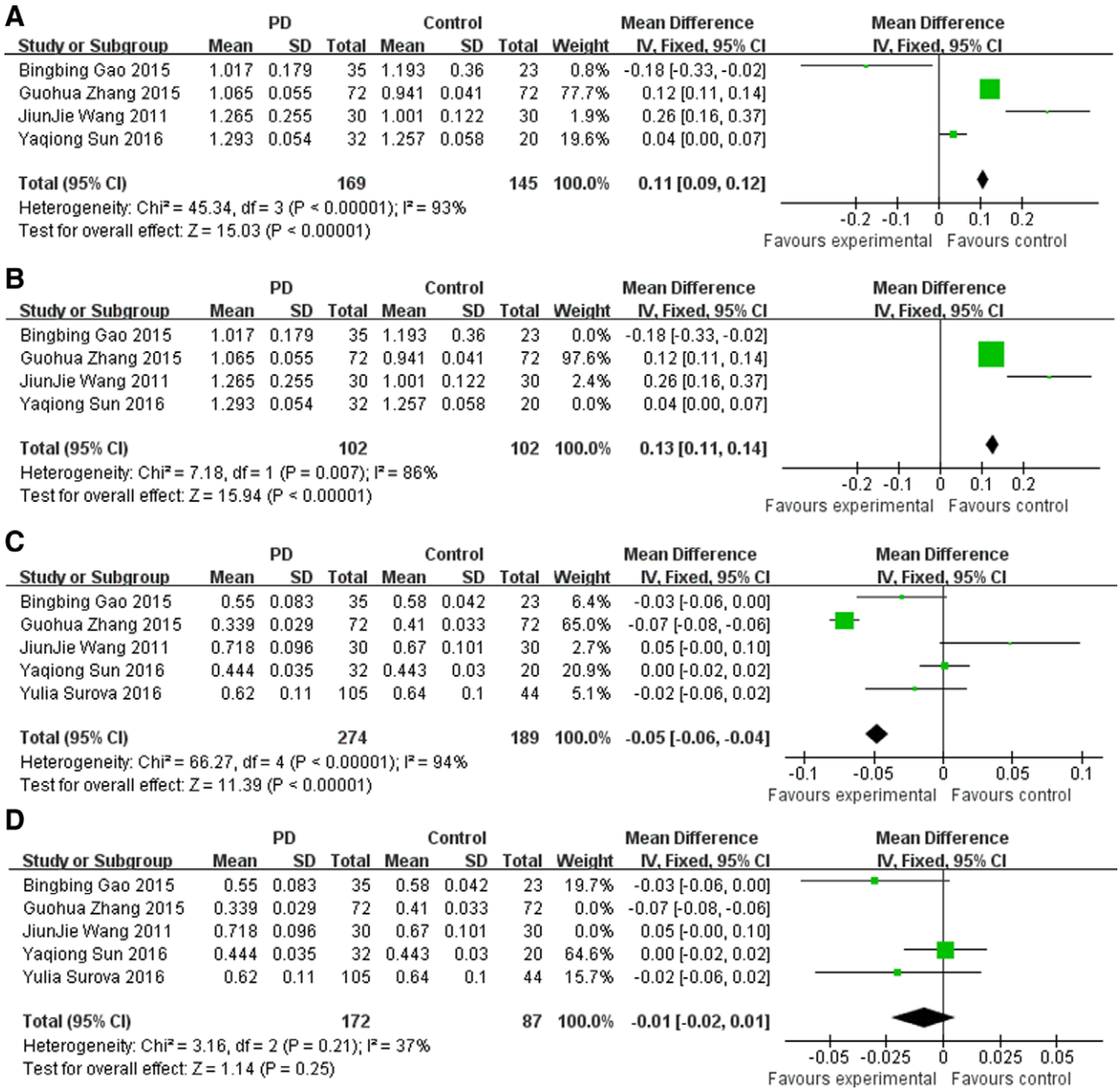


Figure 1. Forrest plot of subgroup analysis for MK and FA changes of PD. FA = fractional anisotropy, MK = mean kurtosis, PD = Parkinson's disease.

moderate. The value cutoff is 0.891, and the corresponding sensitivity and specificity are 46.7% and 100%, respectively. And for the FA value, the results show that the area under curve is 0.516 (P = .880), and diagnostic accuracy is low. The value cutoff is 0.311, and the corresponding sensitivity and specificity are 56.3% and 62.5%, respectively. See Figure 2 for details.

4. Discussion

DTI is widely used as an MRI technique in early diagnosis of PD, however, it is controversial that whether DTI is able to distinguish between patients and HCs. Cyril's research believed that DTI is a sensitive method to study PD pathophysiology and severity.[13] But some studies have found the opposite that the FA of SN is not a diagnostic biomarker of PD.[14] Although traditional DTI assumes that water molecules display Gaussian diffusion in a hindered and unrestricted environment, in biological structures, they are restricted by cell membranes or organelles and thus often display non-Gaussian diffusion.[10] Therefore, the sensitivity of DTI is limited by the diffusional and microstructural properties of biological structures.

Because kurtosis is a measure of the deviation of the diffusion profile from a Gaussian distribution, DKI quantifies the degree of diffusional non-Gaussian or tissue complexity. Therefore, DKI would appear adequate for analyzing the structure of the human brain.[15]

The MK value of DKI is more valuable for diagnosing pathologic changes of isotropic structures, such as gray matter, than the FA value because of the independence on the spatial direction of structures. Because the most significant pathologic changes in PD patients occur in the SN and basal ganglia, MK values in the gray matte applies to the diagnosis and evaluation of PD maybe more sensitive than FA values. This meta-analysis also find significantly higher MK values in the basal ganglia of PD patients over HCs, but the significant

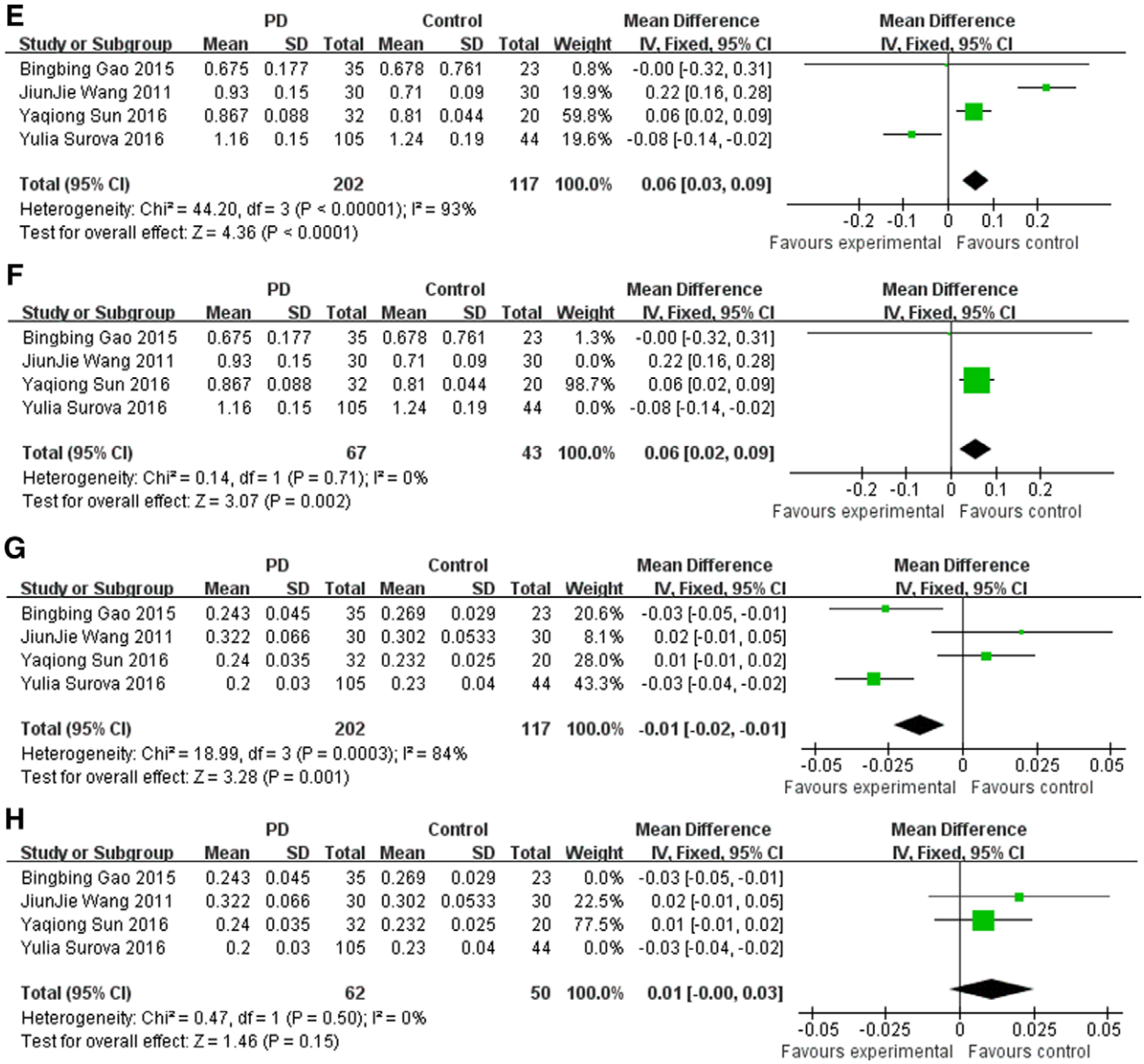


Figure 1. Continued

variables of FA values only appears in caudate, no statistical differences in other 3 brain regions. By means of analyses of heterogeneity, sensitivity, an obvious variation in results is found in the meta-analysis for PD-induced MK changes, so performed a measurement of MK in basal ganglia that could be a potential surrogate, noninvasive marker for precise diagnosis of PD. Combined with the results of comparative study of the accuracy of MK and FA, the accuracy of MK is higher than that of FA. So, the FA values may be slightly inferior to the MK in the diagnosis of PD.

The results show that the MK values of PD group were significantly higher than the control group, including putamen, caudate, globus pallidus. The observed increase in kurtosis and the absence of significant changes in mean diffusivity seem to suggest a distribution of water diffusion that peaks at the center and has heavier tails, even though the variance is maintained. This possibility can be related to neuronal loss and glial proliferation in the basal ganglia as a result of enlarged structural complexity.[16] Because the more complex the brain structure, the higher the MK value.[11] Therefore, the MK value is elevated in the lesion area. However, further studies are needed to shed more light on the mechanisms underlying the changes of MK in the basal ganglia of patients with PD.

Some studies have shown that MK values in the SN may reflect the severity of disease, the more serious the lesions, the higher the MK values.[17] This meta-analysis found that increase in MK values in SN is not significant due to the high heterogeneity. It can be caused by increased iron content in the SN, which can reduce the signal-to-noise ratio.[18] In addition, the volume of SN is much smaller than other nuclei. It can even be divided into pars compact and pars reticulate, and the lesions of PD are mainly in the SN pars compacta that the volume is smaller.[19] Therefore, there may be errors when researchers choose the ROI, and consequently induce an inaccurate in kurtosis value measurement.

Our study has a number of limitations. There is less research on the diagnosis of PD using DKI, this leads to greater heterogeneity of the studies and inaccurate results. Moreover, the sample size of each study is so small, these are where researchers will need to work in the future.

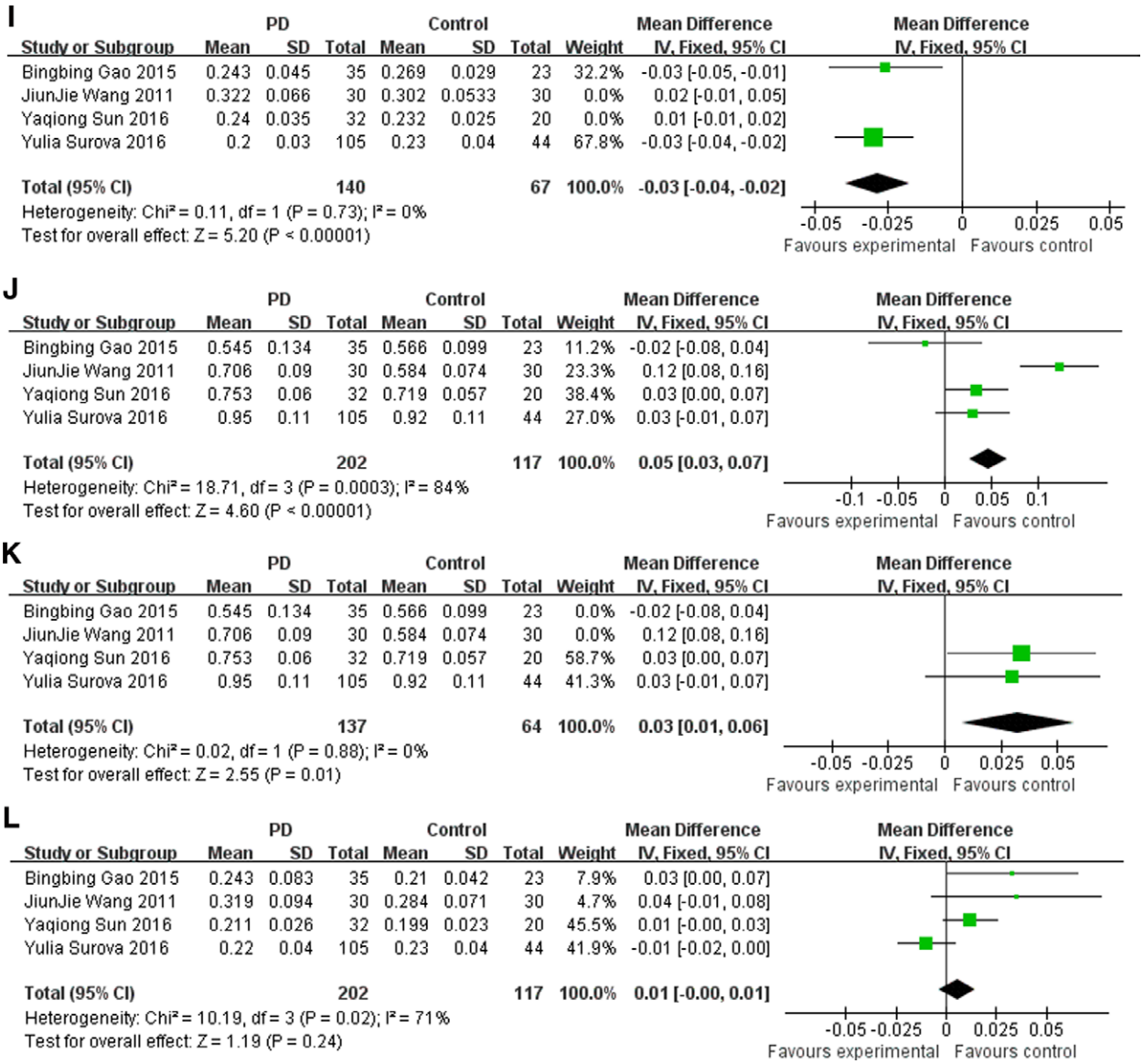


Figure 1. Continued

5. Conclusion

Our meta-analysis aims at providing a quantitative evaluation of structural brain changes associated with PD. We show that the value of MK is particularly relevant for subcortical areas (lesions in the putamen, caudate, globus pallidus). DKI evaluation of structural lesions remains difficult, due to the variability in PD pathophysiology and MRI acquisition parameters (e.g., artifacts and nature of the ROI). However, our meta-analysis and literature review contributes to significantly increasing our knowledge of PD pathophysiology. It also addresses the interesting possibility of follow-up of the disease severity and associated brain structural modulations using in vivo imaging. From our review and meta-analysis, we can summarize the following points: the MK value in putamen, caudate, globus pallidus could participate to the diagnosis of PD, it is a more sensitive diagnostic marker than the FA value; MK in SN maybe a good indicator to identify PD patients, but more research is needed to prove this point. Despite some limitations, DKI appears as a sensitive method to study PD pathophysiology and severity. The association of DKI with other MRI methods (VBM; generalized autocalibrating partially parallel acquisition; Diffusion Spectrum Imaging) should be considered to study brain alterations in PD.

Author contributions

YCD and STH conceived and designed the study. YCD, STH and JYZ extracted, cleaned, analyzed the data and revised the paper critically. YCD wrote the first draft of the paper, contributed to figures and paper preparation. All authors critically revised the paper and gave final approval for publication.

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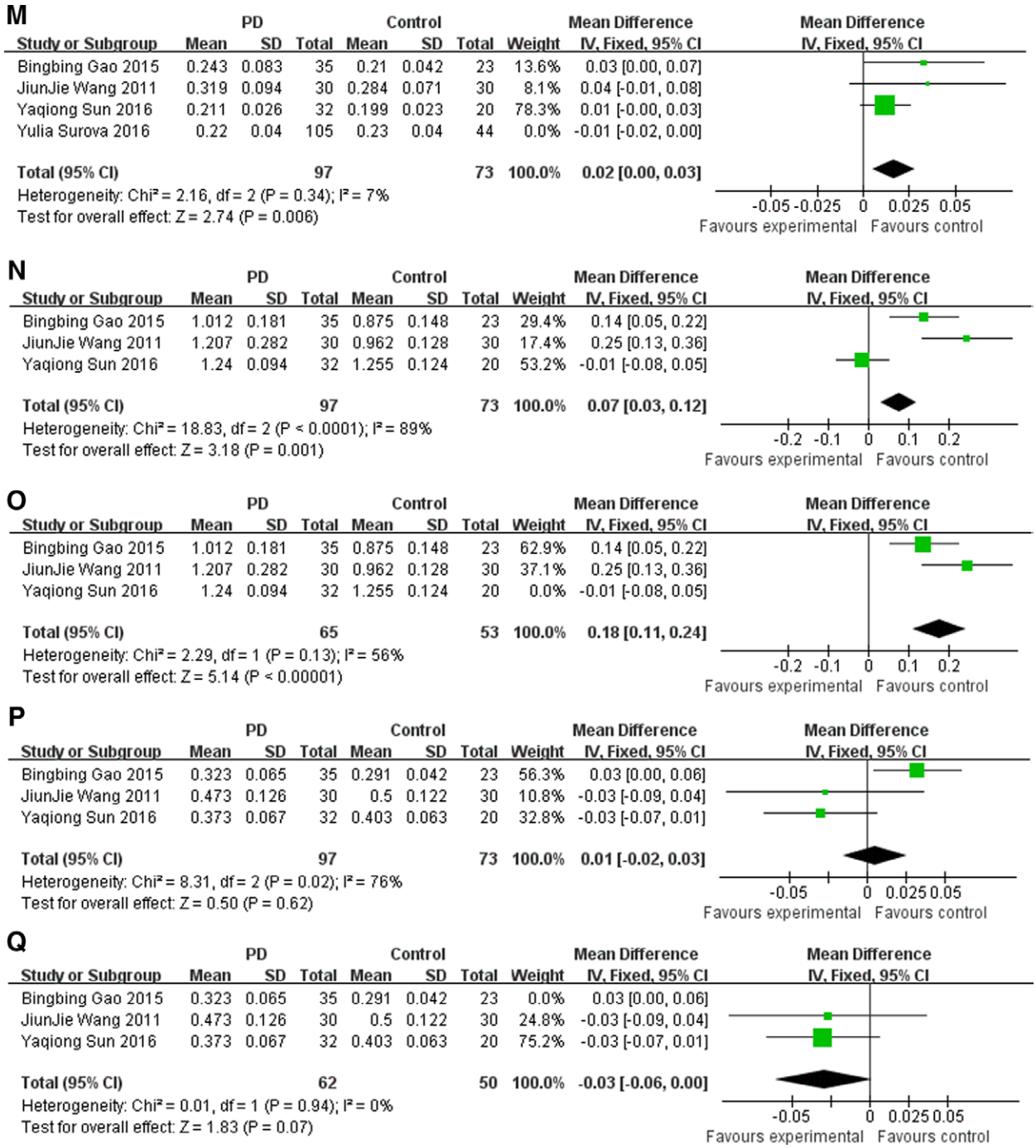

Figure 1. Continued

Table 3

× stands for no difference; √ stands for difference.

	MK				FA			
Subgroup	**WMD**	**95% CI**	***P***	**Results**	**WMD**	**95% CI**	***P***	**Results**
SN	0.13	0.11–0.14	<.00001	×	−0.01	−0.02 to 0.01	.25	×
Putamen	0.06	0.02–0.09	.002	√	0.01	0.00 to 0.03	.15	×
Caudate	0.03	0.01-0.06	.01	√	0.02	0.00 to 0.03	.006	√
Globus pallidus	0.18	0.11-0.24	<.00001	√	−0.03	−0.06 to 0.00	.07	×

CI = confidence interval, FA = fractional anisotropy, MK = mean kurtosis, SN = substantia nigra, WMD = weighted mean difference.

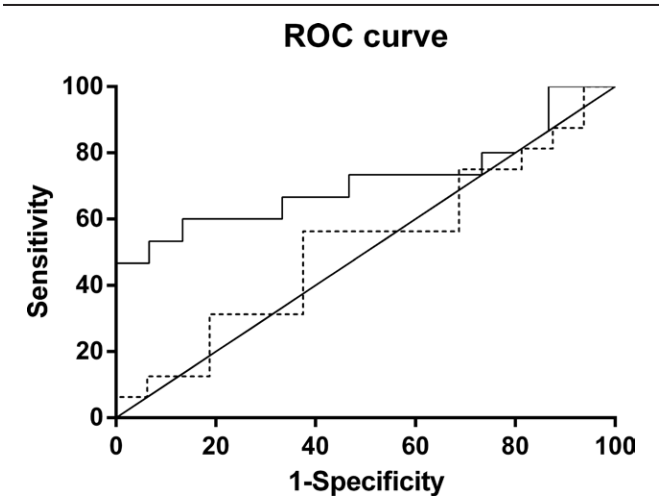

Figure 2. Solid line represents MK value and dotted line represents FA value. A = fractional anisotropy, MK = mean kurtosis.

References

[1] Schildt A, Walker MD, Dinelle K, et al. Single inflammatory trigger leads to neuroinflammation in LRRK2 rodent model without degeneration of dopaminergic neurons. J Parkinsons Dis. 2019;9:121–39.
[2] Wang Q, Chen J, Li M, et al. Eltoprazine prevents levodopa-induced dyskinesias by reducing causal interactions for theta oscillations in the dorsolateral striatum and substantia nigra pars reticulate. Neuropharmacology. 2019;148:1–10.
[3] Jia Q, Gao L, Zhang J, et al. Altered functional connectivity of the subthalamic nucleus during self-initiated movement in Parkinson's disease. J Neuroradiol. 2018;45:249–55.
[4] Surova Y, Nilsson M, Lampinen B, et al. Alteration of putaminal fractional anisotropy in Parkinson's disease: a longitudinal diffusion kurtosis imaging study. Neuroradiology. 2018;60:247–54.
[5] Li XR, Ren YD, Cao B, et al. Analysis of white matter characteristics with tract-based spatial statistics according to diffusion tensor imaging in early Parkinson's disease. Neurosci Lett. 2018;675:127–32.
[6] Guimaraes RP, Campos BM, de Rezende TJ, et al. Is diffusion tensor imaging a good biomarker for early Parkinson's disease? Front Neurol. 2018;9:626.
[7] Qiao PF, Shi F, Jiang MF, et al. Application of high-field magnetic resonance imaging in Parkinson's disease. Exp Ther Med. 2017;13:1665–70.
[8] Ye C, Prince JL. A Bayesian approach to fiber orientation estimation guided by volumetric tract segmentation. Comput Med Imaging Graph. 2016;54:35–47.
[9] Kamagata K, Tomiyama H, Hatano T, et al. A preliminary diffusional kurtosis imaging study of Parkinson disease: comparison with conventional diffusion tensor imaging. Neuroradiology. 2014;56:251–8.
[10] Arab A, Wojna-Pelczar A, Khairnar A, et al. Principles of diffusion kurtosis imaging and its role in early diagnosis of neurodegenerative disorders. Brain Res Bull. 2018;139:91–8.
[11] Zhang G, Zhang Y, Zhang C, et al. Diffusion kurtosis imaging of substantia nigra is a sensitive method for early diagnosis and disease evaluation in Parkinson's disease. Parkinsons Dis. 2015;2015:207624.
[12] Wang JJ, Lin WY, Lu CS, et al. Parkinson disease: diagnostic utility of diffusion kurtosis imaging. Radiology 2011;261:210–7.
[13] Atkinson-Clement C, Pinto S, Eusebio A, et al. Diffusion tensor imaging in Parkinson's disease: review and meta-analysis. Neuroimage Clin. 2017;16:98–110.
[14] Hirata FCC, Sato JR, Vieira G, et al. Substantia nigra fractional anisotropy is not a diagnostic biomarker of Parkinson's disease: a diagnostic performance study and meta-analysis. Eur Radiol. 2017;27:2640–8.
[15] Cheng JX, Zhang HY, Peng ZK, et al. Divergent topological networks in Alzheimer's disease: a diffusion kurtosis imaging analysis. Transl Neurodegener. 2018;7:10.
[16] Zhou Y, Zhu J, Lv Y, et al. Kir6.2 deficiency promotes mesencephalic neural precursor cell differentiation via regulating miR-133b/GDNF in a Parkinson's disease mouse model. Mol Neurobiol. 2018;55:8550–62.
[17] Zhang G, Zhang Y, Zhang C, et al. Striatal silent lacunar infarction is associated with changes to the substantia nigra in patients with early-stage Parkinson's disease: a diffusion kurtosis imaging study. J Clin Neurosci. 2016;33:138–41.
[18] Wang JY, Zhuang QQ, Zhu LB, et al. Meta-analysis of brain iron levels of Parkinson's disease patients determined by postmortem and MRI measurements. Sci Rep. 2016;6:36669.
[19] Wang H, Chen Y, Chen J, et al. Cell cycle regulation of DNA polymerase beta in rotenone-based Parkinson's disease models. PLoS One. 2014;9:e109697.