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Original Article

ORIGINAL ARTICLE

Abnormal neurovascular coupling exists in patients with peritoneal dialysis and hemodialysis: evidence from a multi-mode MRI study

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ABSTRACT

Background. Neurovascular coupling (NVC), as indicated by a comprehensive analysis of the amplitude of low-frequency fluctuation (ALFF) and cerebral blood flow (CBF), provides mechanistic insights into neurological disorders. Patients undergoing peritoneal dialysis (PD) and hemodialysis (HD) often face cognitive impairment, the causes of which are not fully understood.

Methods. ALFF was derived from functional magnetic resonance imaging, and CBF was quantified using arterial spin labeling in a cohort comprising 58 patients with PD, 60 patients with HD and 62 healthy controls. Voxel-based global analysis for both ALFF and CBF, alongside region-based analyses of ALFF-CBF coupling coefficients, were conducted. Additionally, the study explored the correlation between clinical laboratory indices and imaging metrics.

Results. Compared with HC, NVC was reduced in the bilateral medial superior frontal gyrus (SFGmed), insula, posterior cingulate cortex (PCC) and caudate (CAU) among dialysis patients. Furthermore, the PD group exhibited lower NVC in the bilateral SFGmed, bilateral PCC and left CAU compared with the HD group. Within the PD group, sodium level was negatively correlated with the ALFF-CBF coupling coefficient in the right insula. Additionally, a positive correlation emerged between the ALFF-CBF coupling coefficient in bilateral SFGmed and the dialysis adequacy.

Conclusion. While Montreal Cognitive Assessment scores did not significantly differ between patients with PD and HD, PD group demonstrated poorer NVC in the bilateral SFGmed, bilateral PCC and left CAU. Sodium level and dialysis adequacy may affect NVC in patients with PD.

Keywords: cognitive impairment, hemodialysis, neurovascular coupling, peritoneal dialysis

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KEY LEARNING POINTS

What was known:

- Previous studies have noted abnormalities in neural activities and CBF in ESRD patients undergoing HD and PD, with our research indicating a significant decoupling in neurovascular function compared with healthy controls (HC).

This study adds:

- Compares ALFF and CBF among patients with PD, HD and HC to identify regions of interest (ROIs).
- Assesses differences in NVC at these ROIs across the three groups.
- Explores correlations between imaging metrics and clinical laboratory indices, as well as neuropsychiatric scores.

Potential impact:

- This research will identify potential biological markers of cognitive impairment in dialysis patients.

INTRODUCTION

End-stage renal disease (ESRD) represents the final, irreversible phase of chronic kidney disease (CKD), affecting approximately 2%–3% of all CKD patients [1]. The global incidence and prevalence of ESRD are on the rise. Common treatments include hemodialysis (HD), peritoneal dialysis (PD) and kidney transplantation [2]. Despite some improvements in cognitive functions, such as working memory [3], ESRD patients are prone to cognitive impairments (CI), with severe CI observed in 8%–37% of those on HD [4–8] and 4%–33% on PD [5, 8]. These impairments [9] may be exacerbated by hemodynamic challenges linked to dialysis-induced hypoperfusion [10]. Thus, there is an urgent imperative to explore the underlying neuropathological mechanisms of cognitive decline in patients with HD and PD.

Resting-state functional magnetic resonance imaging (fMRI) uses blood oxygen level-dependent signals [11] to assess brain activity, with the amplitude of low-frequency fluctuation (ALFF) indicating the strength of local neuronal activity [12]. Cerebral blood flow (CBF), measured non-invasively through arterial spin labeling (ASL), reflects nutrient and toxin transport [3] in the brain and their impact on neuronal health and cognition. Neurovascular coupling (NVC) is critical for understanding the coordination of blood perfusion and neural function, with dysfunction in this area linked to neuropsychiatric disorders.

Previous studies have noted abnormalities in neural activities and CBF in ESRD patients undergoing HD and PD [13], with our research indicating a significant decoupling in neurovascular function compared with healthy controls (HC) [14]. Despite these findings, research into the differences in NVC between HD and PD treatments remains limited.

This study aims to: (i) compare ALFF and CBF among patients with PD, HD and HC to identify regions of interest (ROIs); (ii) assess differences in NVC at these ROIs across the three groups; and (iii) explore correlations between imaging metrics and clinical laboratory indices, as well as neuropsychiatric scores, to identify potential biological markers of cognitive impairment in dialysis patients.

MATERIALS AND METHODS

Study population

Patients were recruited from the Nephrology Department of Beijing Friendship Hospital, Capital Medical University. The study included right-handed individuals diagnosed with ESRD due to glomerulonephritis or primary hypertensive nephropathy, who had been undergoing PD or HD for over 6 months. Exclusion criteria were as follows: under 18 years of age, previous kidney transplantation, diabetic nephropathy, brain lesions (e.g. stroke, head trauma, hemorrhage, infarction, tumors), a medical history of or current use of immunosuppression or psychiatric drugs, psychiatric disorders, substance abuse and claustrophobia. HC were recruited through advertisements posted within the local community. Our criteria required participants to be right-handed and aged between 18 and 65 years, without a history of chronic kidney disease, diabetes, brain lesions (e.g. stroke, head trauma, hemorrhage, infarction, tumors), medical history and current medical of immunosuppression or psychiatric drugs, psychiatric disorders, substance abuse or claustrophobia. The study was approved by the Medical Ethics Committee of Beijing Friendship Hospital and adhered to the Declaration of Helsinki. All participants provided informed consent.

In this study, information regarding previous cerebrovascular events in patients was initially obtained through patient self-report and a review of medical records. To ensure the accuracy of this information, we assessed MRI images of all participants to exclude individuals with brain lesions, such as infarction. A total of 127 patients (62 patients with PD and 65 patients with HD) underwent comprehensive assessments, including MRI scans, the Montreal Cognitive Assessment (MoCA) and laboratory tests. Exclusions from the final analysis were due to chronic infarction or head motion artifacts, affecting four patients with PD and five patients with HD. Additionally, 64 age- and gender-matched HCs were recruited from the community; 2 were excluded for similar reasons. The final analysis included 58 patients with PD, 60 with HD and 62 HC. The details of participant inclusion and exclusion are presented in Fig. 1.

Clinical and biochemical assessments

Before the patients underwent MRI examination, we conducted MoCA scores, a useful tool that has been proven to be suitable for healthy individuals and dialysis patients in China [15, 16], and a series of laboratory tests [e.g. Kt/V, residual renal function (RRF), hemoglobin, white blood cell, platelet, albumin, cholesterol, triglycerides, ferritin, creatinine, calcium, phosphorus, sodium and parathyroid hormone]. Regarding the calculation of the RRF, we used the urea clearance rate to represent the RRF according to the Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines [17]. According to the calculation formula: CLUREA (mL/min) = [urine urea (mL/dL) × urine volume (mL)]/[urine volume collection time (min) × 0.9 × serum urea (mg/dL)], we collected and measured the urinary nitrogen

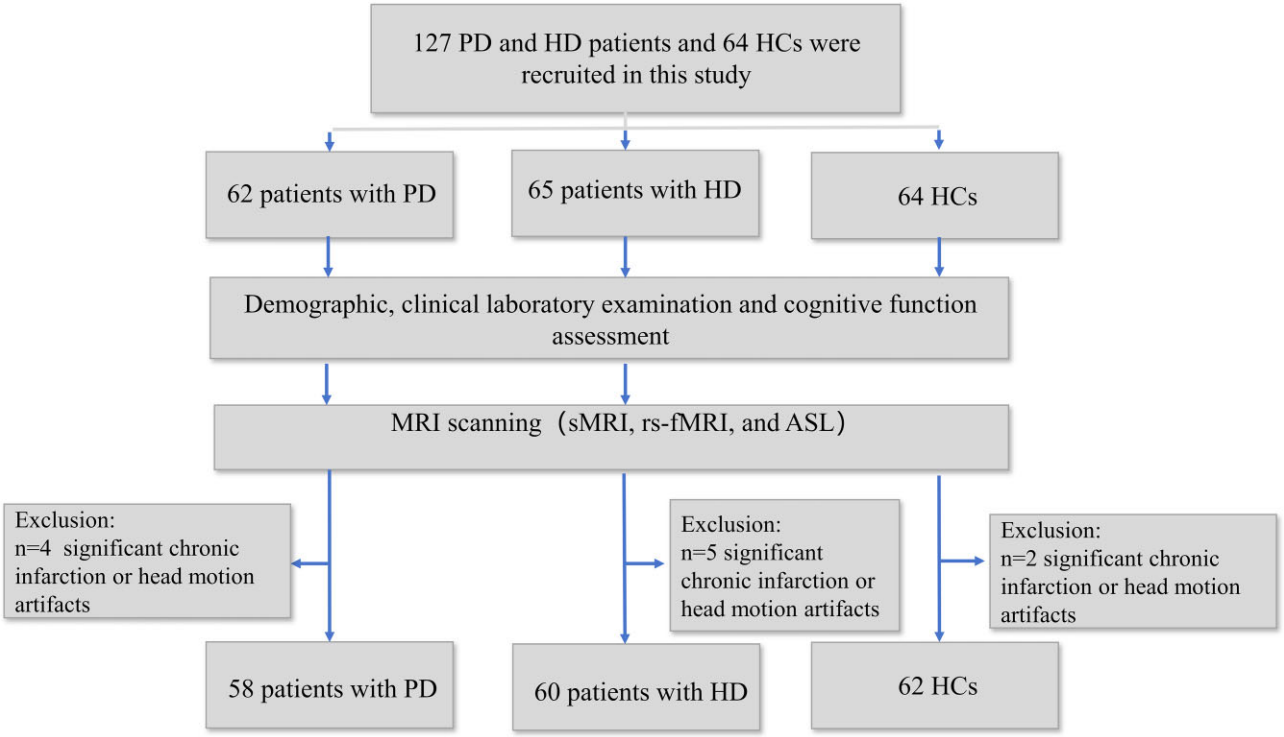

Figure 1: Summary of patients with PD, patients with HD and HC, recruitment and exclusions. sMRI, structural MRI; rs-fMRI, resting state MRI; ASL, arterial spin labeling.

content in 24-h urine, after clarifying the volume of 24-h urine, finally obtain the outcomes of RRF of PD and HD patients.

MRI data acquisition

All MRI examinations were performed using a 3.0 Tesla MRI scanner (Discovery MR750W, General Electric, Milwaukee, WI, USA) with an 8-channel head coil. To avoid head movements, subjects were told to close their eyes, stay awake and remain relaxed. In addition, to avoid the impact of changes of hemodynamics, we have taken the MRI during their dialysis interval for HD patients who dialysis three times a week regularly.

T1-weighted structural MRI data were collected from subjects using the high-resolution 3D brain volume imaging sequence (parameters: TR 8.8 ms, TE 3.5 s, flip angle 15°, field of view 240 mm × 240 mm, matrix 256 × 256, number of layers 196, thickness 1 mm).

Resting-state fMRI data were acquired with a gradient echo-single shot echo planar imaging sequence (parameters: TR 2000 ms, TE 35 ms, flip angle 90°, field of view 240 mm × 240 mm, matrix 256 × 256, number of layers 28, thickness 5 mm, time points 200).

CBF maps were obtained using a 3D pseudo-continuous ASL sequence (parameters: TR 4844 ms, TE 10.5 ms, flip angle 111°, field of view 240 mm × 240 mm, matrix 128 × 128, number of layers 36, slice thickness = 4 mm).

Resting state fMRI data preprocessing and ALFF calculating

Utilizing the DPARSF package (http://rfmri.org/DPARSF) based on Matlab2018b (The MathWorks, Inc., Natick, MA, USA), the preprocessing of fMRI data followed a series of steps [18]. Initially, the first 10 volumes were discarded from each time series, followed by slice-timing and head motion corrections. Strict exclusion criteria were applied, removing data instances where head motion exceeded 3 mm or angular rotation exceeded 3°. Subsequently, spatial normalization to the Montreal Neurological Institute (MNI) space was conducted using the Diffeomorphic Anatomical Registration Through Exponentiated Lie (DARTEL) algorithm. Nuisance signals (Friston 24 head motion parameters, white matter, and cerebrospinal fluid signals) were regressed out using linear trends [19]. Bandpass filtering within the 0.01–0.1 Hz frequency range was then applied.

The calculation of ALFF involved transforming the time series of each voxel into the frequency domain using Fast Fourier Transform. The energy value was computed by integrating the area beneath the peak of the functional spectrum. The square root of the functional spectrum was then calculated to obtain the average signal amplitudes within the frequency range of 0.01–0.1 Hz, representing the ALFF value for each voxel. Furthermore, ALFF values were standardized by dividing them by the mean ALFF value of the entire brain, facilitating subsequent analysis. Finally, Gaussian kernel spatial smoothing was applied with a full width at half maximum (FWHM) of 6 mm. Details of ALFF processing are outlined in Step 1 of Fig. 2.

ASL data preprocessing

Initially, ASL difference images are generated by subtracting label images from control images. Combined with proton density-weighted reference images, CBF maps are calculated by averaging the three types of images. Subsequently, these CBF images are then normalized to the MNI space using a PET-perfusion

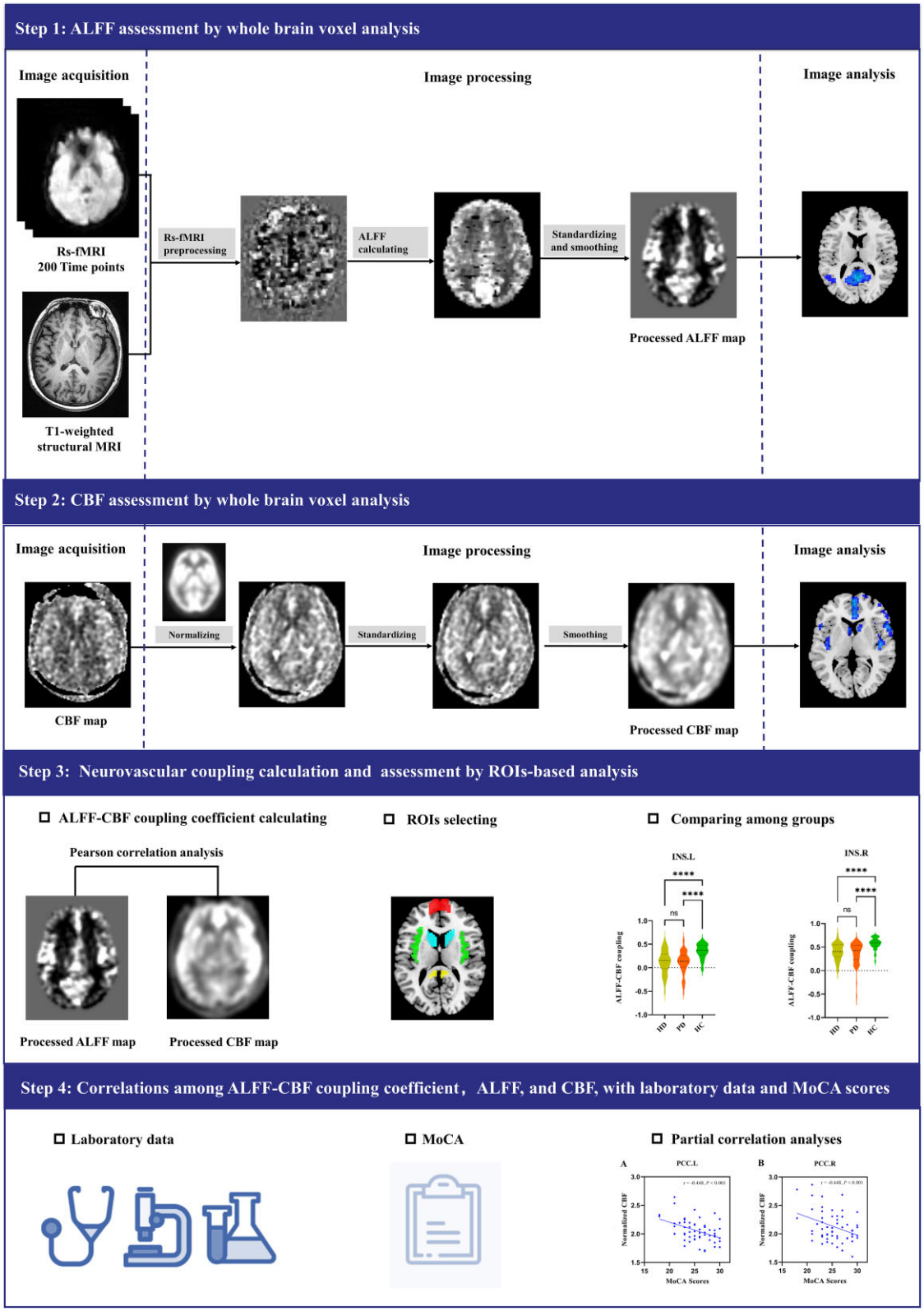

Figure 2: Diagram illustrating the workflow of the experimental procedures. rs-fMRI, resting state MRI.

Table 1: Demographics and neuropsychologic tests of the PD, HD and HC groups.

	PD ($n = 58$)	HD ($n = 60$)	HC ($n = 62$)	*P*-value
Age (years)	53.9 ± 1.3	51.9 ± 1.4	52.2 ± 1.5	.431[a]
Sex (male/female)	23/35	32/28	29/32	.328[b]
Dialysis duration (months)	36 (12, 60)	69 (21, 124)	NA	.013[c]
Kt/V	1.5 ± 0.5	1.5 ± 0.4	NA	.740[d]
Type 2 diabetes (yes/no)	18/39	28/32	NA	.095[b]
Hypertenison (yes/no)	39/18	50/10	NA	.059[b]
RRF (mL/min)	4.1 (3.8, 4.6)	3.8 (3.2, 4.9)	NA	.064[c]
Hemoglobin (g/L)	116.6 ± 13.5	115.5 ± 11.4	NA	.627[d]
WBC ($\times 10^9$/L)	7.8 ± 2.1	6.2 ± 1.5	NA	.007[d]
Platelet ($\times 10^9$/L)	233.0 (197.5, 264.0)	191.5 (154.5, 220.3)	NA	<.001[c]
Albumin (g/L)	36.8 ± 4.4	42.0 ± 3.0	NA	.006[d]
Cholesterol (mmol/L)	4.5 (3.8, 5.0)	4.2 (3.7, 4.8)	NA	.324[c]
Triglyceride (mmol/L)	2.1 (1.5, 3.1)	1.6 (1.1, 2.8)	NA	.053[c]
Ferritin (ng/mL)	159.3 (72.7, 359.3)	118.1 (65.7, 237.6)	NA	.074[c]
Creatinine (μmol/L)	988.6 ± 277.9	967.9 ± 201.9	NA	.017[d]
Calcium (mmol/L)	2.4 ± 0.2	2.2 ± 0.2	NA	<.001[d]
Phosphorus (mmol/L)	1.8 ± 0.5	2.0 ± 0.6	NA	.031[d]
Sodium (mmol/L)	139.3 ± 2.6	139.7 ± 2.6	NA	.770[d]
PTH (pg/mL)	144.6 (65.3, 247.2)	189.4 (93.1, 341.5)	NA	.100[c]
MoCA scores	25 (23, 28)	25 (23, 27)	NA	.568[c]

Data are presented as mean ± standard deviation, *n* or median (interquartile range).
[a]ANOVA.
[b]Chi-square test.
[c]Mann–Whitney U test.
[d]Two independent samples t-test.
NA, not applicable; WBC, white blood cell; PTH, parathyroid hormone.

template in the SPM12 software (https://www.fil.ion.ucl.ac.uk/spm/software/spm12/). After non-brain tissue removal, each individualized CBF map is standardized by dividing it by the group-level average CBF value of the gray matter. Finally, the standardized CBF maps are further spatially smoothed using a Gaussian kernel with dimensions of 6 mm × 6 mm × 6 mm FWHM. Details of CBF processing are showed in Step 2 of Fig. 2.

NVC coefficient calculating

The NVC was calculated using custom MATLAB 2018b code. We identified eight ROIs based on ALFF and CBF results. These included the bilateral medial superior frontal gyrus (SFGmed), insula (INS), posterior cingulate cortex (PCC) and caudate nucleus (CAU), following the automated anatomical labeling template. For each ROI, voxel values from the ALFF and CBF maps were extracted and transformed into two large vectors specific to each modality. The ALFF-CBF coupling coefficients were then determined by computing Pearson correlation coefficients between these vectors for all participants.

Statistical analysis

The statistical analysis was performed using SPSS 26.0 software (version 26.0, SPSS Inc., Chicago, IL, USA) and SPM12 software. Age differences among the three groups were compared using one-way analysis of variance (ANOVA). The chi-square test was employed to examine gender differences among the three groups. Two independent sample *t*-tests were utilized to compare normally distributed data between the PD and HD groups. Mann–Whitney U tests were used to compare non-normally distributed data between the PD and HD groups. Controlling for dialysis duration as covariates, two independent sample *t*-tests were conducted to compare ALFF and CBF between each pair of groups [false discovery rate (FDR) corrected]. Partial correlation analyses were conducted to explore the relationship between clinical laboratory parameters or neuropsychological test scores and imaging metrics in the patients, adjusting for dialysis duration. A significance level of $P < .05$ was applied for statistical significance.

RESULTS

Demographic and clinical data

The demographic and clinical characteristics of the study participants are detailed in Table 1. Analysis of the three groups revealed no significant disparities in terms of age and sex. The dialysis duration and levels of white blood cells, platelets, albumin, creatinine, calcium and phosphorus in the PD group differed from those of the HD group. No significant differences were observed in Kt/V, RRF, the history of type 2 diabetes and hypertension, hemoglobin, cholesterol, triglycerides, ferritin, sodium, parathyroid hormone, and the MoCA score between the PD and HD groups. For the excluded patients due to chronic infarction, the dialysis vintage had no significant difference between the included patients.

Comparison of ALFF among groups

Compared with the HD group, the ALFF of the bilateral PCC was significantly decreased in the PD group ($P < .001$, FDR corrected) (Fig. 3). Compared with the HC group, the ALFF of the bilateral PCC and left middle temporal gyrus was significantly decreased in the PD group ($P < .001$, FDR corrected) (Fig. 3). Compared with the HC group, the ALFF of the bilateral PCC was significantly

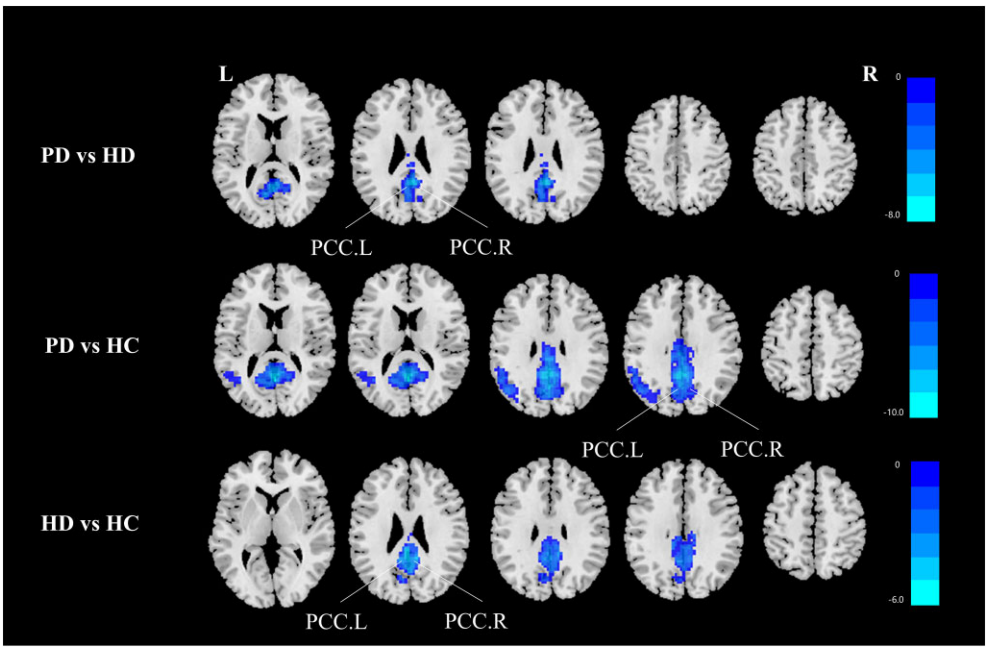

Figure 3: Comparison of ALFF among the PD, HD and HC groups. The cold color indicates a significant decrease in ALFF between groups ($P < .05$, FDR-corrected). PCC.L, left posterior cingulate gyrus; PCC.R, right posterior cingulate gyrus.

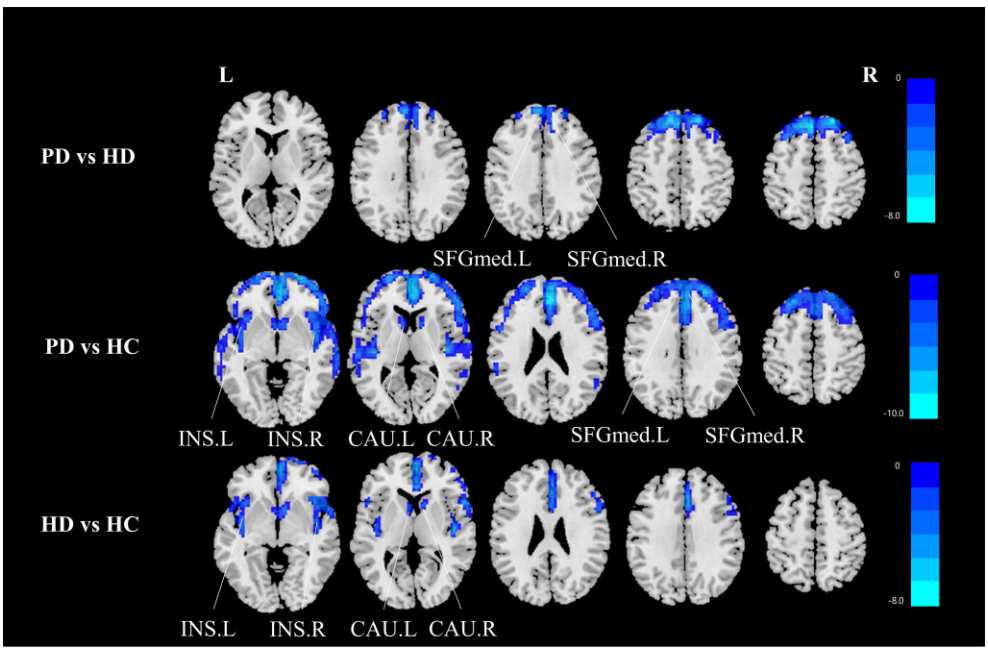

Figure 4: Comparison of CBF among the PD, HD and HC groups. The cold color indicates a significant decrease in CBF between groups ($P < .05$, FDR-corrected). SFGmed.L, left medial superior frontal gyrus; SFGmed.R, right medial superior frontal gyrus; INS.L, left insula; INS.R, right insula; CAU.L, left caudate nucleus; CAU.R, right caudate nucleus.

decreased in the HD group ($P < .001$, FDR corrected) (Fig. 3). The peak intensity of each brain region listed above is shown in Supplementary data, Table S1.

Comparison of CBF among groups

Compared with the HD group, the CBF of the bilateral SFGmed was significantly decreased in the PD group ($P < .001$, FDR corrected) (Fig. 4). Compared with the HC group, the CBF of the bilateral SFGmed, bilateral CAU and bilateral INS was significantly decreased in the PD group ($P < .001$, FDR corrected) (Fig. 4). Compared with the HC group, the CBF of the bilateral SFGmed, bilateral CAU and bilateral INS was significantly decreased in the HD group ($P < .001$, FDR corrected) (Fig. 4). The peak intensity of each brain region listed above is shown in Supplementary data, Table S2.

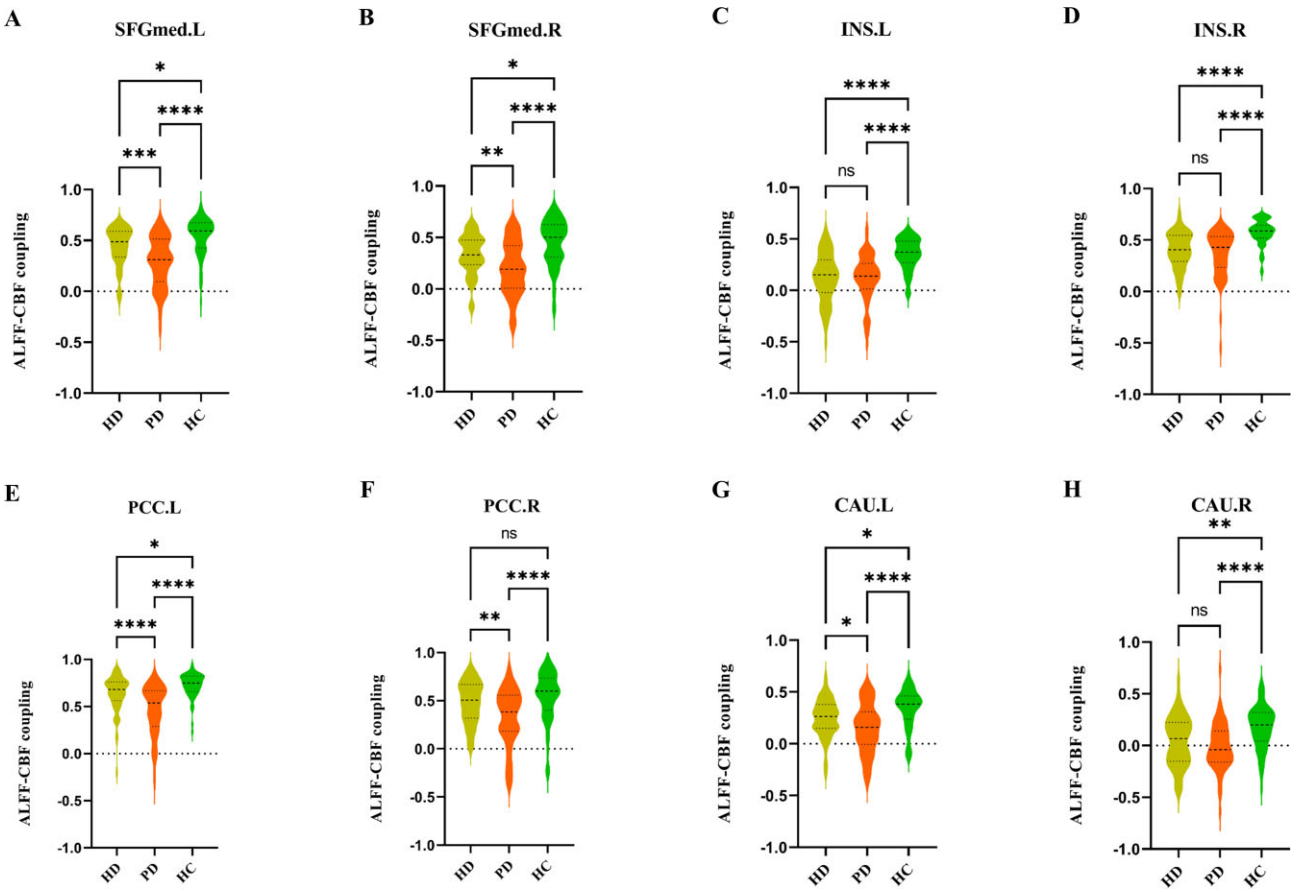

Figure 5: (**A–H**) Comparison of ALFF-CBF coupling coefficient among the PD, HD and HC groups. **** Significant group differences with Duncan's test correction, $P < .0001$; *** significant group differences with Duncan's test correction, $P < .001$; ** significant group differences with Duncan's test correction, $P < .01$; * significant group differences with Duncan's test correction, $P < .05$. SFGmed.L, left medial superior frontal gyrus; SFGmed.R, right medial superior frontal gyrus; INS.L, left insula; INS.R, right insula; PCC.L, left posterior cingulate gyrus; PCC.R, right posterior cingulate gyrus; CAU.L, left caudate nucleus; CAU.R, right caudate nucleus.

Comparison of ALFF-CBF coupling coefficient among groups

Compared with the HD group, the PD group had significantly lower ALFF-CBF coupling coefficient in the left SFGmed ($P < .001$), right SFGmed ($P < .01$), left PCC ($P < .0001$), right PCC ($P < .001$) and left CAU ($P < .05$) (Fig. 5). Compared with the HC group, the PD group had significantly lower ALFF-CBF coupling coefficient in the bilateral SFGmed ($P < .0001$), bilateral INS ($P < .0001$), bilateral PCC ($P < .0001$) and bilateral CAU ($P < .0001$) (Fig. 5). Compared with the HC group, the HD group had significantly lower ALFF-CBF coupling coefficient in the bilateral SFGmed ($P < .05$), bilateral INS ($P < .0001$), left PCC ($P < .05$), left CAU ($P < .05$) and right CAU ($P < .01$) (Fig. 5). The Dunn multiple comparison test was used in the *post hoc* test of intergroup comparison.

Correlation analysis

Partial correlation analyses, controlling for dialysis duration, were conducted (Fig. 6).

Within the PD group, MoCA scores were found to negatively correlate with the CBF of the left PCC ($r = –0.448$, $P < .001$) and the right PCC ($r = –0.372$, $P = .004$). Conversely, a positive correlation was observed between MoCA scores and the ALFF-CBF coupling coefficient of the right INS ($r = 0.299$, $P = .024$).

Hemoglobin level in the PD group was positively associated with CBF of the right INS ($r = 0.283$, $P = .033$). In the HD group, hemoglobin level positively correlated with CBF of the left SFGmed ($r = 0.336$, $P = .009$) and the left INS ($r = 0.311$, $P = .016$).

Sodium level within the PD group negatively correlated with the ALFF-CBF coupling coefficient of the right INS ($r = –0.328$, $P = .013$). In the PD group, a positive correlation was observed between Kt/V and the ALFF-CBF coupling coefficient of the left SFGmed ($r = 0.407$, $P = .002$), as well as the right SFGmed ($r = 0.337$, $P < .010$).

DISCUSSION

This investigation marks the first comparative study of NVC differences between patients undergoing PD and HD. We observed that, compared with HC, the dialysis group exhibited a decrease in ALFF in the bilateral PCC, with a similar reduction observed between the PD and HD group within the PCC. Compared with HC, CBF was reduced in the bilateral INS, CAU and SFGmed between the dialysis groups, with a further decrease in CBF noted in the bilateral SFGmed when comparing the PD with the HD group. Compared with HC, NVC was diminished in the bilateral SFGmed, INS, PCC and CAU within the dialysis groups. when compared with HD, the PD group demonstrated lower NVC in the bilateral SFGmed, bilateral PCC and left CAU. Moreover, in

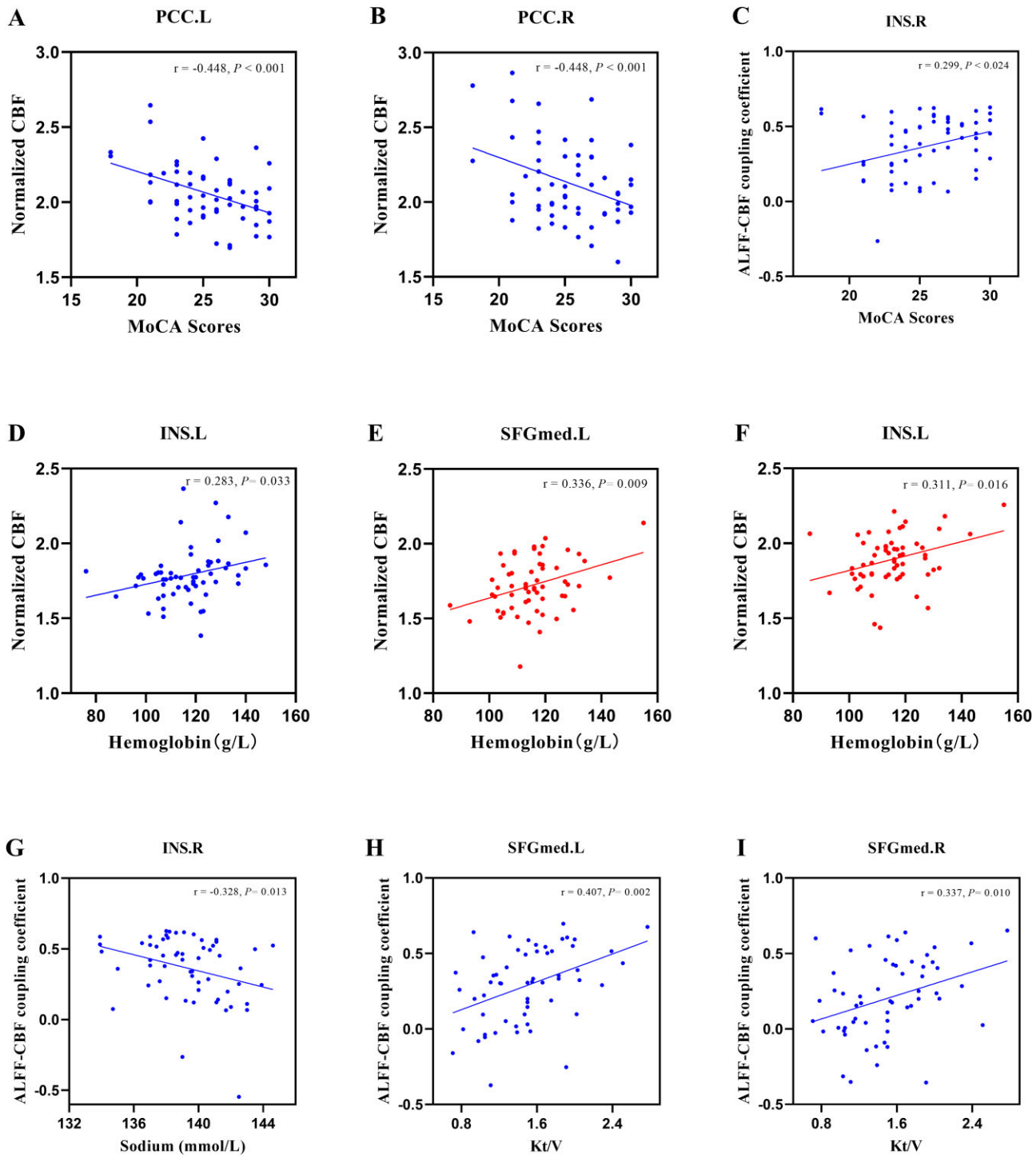

Figure 6: (A–I) Partial correlation analyses in the PD and HD groups were adjusted for dialysis duration. Blue represents the PD group, while red indicates the HD group. PCC.L, left posterior cingulate gyrus; PCC.R, right posterior cingulate gyrus; INS.R, right insula; INS.L, left insula; SFGmed.L, left medial superior frontal gyrus; SFGmed.R, right medial superior frontal gyrus.

the PD group, sodium level was negatively correlated with the ALFF-CBF coupling coefficient in the right INS. Additionally, the ALFF-CBF coupling coefficient of the bilateral SFGmed was positively correlated with Kt/V.

In our study, it was found that the ALFF in the PCC region was reduced in patients with PD and HD compared with HC. Notably, this reduction was more pronounced in patients with PD than in those with HD. The PCC, located in the medial parietal cortex and spanning Brodmann areas 23 and 31 [20], is implicated in several neurodegenerative and psychiatric diseases [21]. It plays a key role in the default mode network (DMN) [22–24] of brain, which is essential for a range of cognitive functions

including learning, memory, orientation, decision-making, emotion, creativity and executive control [25]. Luo *et al*. reported that patients with ESRD displayed lower ALFF values in the DMN compared with HC. This decline was especially significant in patients with PD, primarily affecting the left upper parietal, left inferior parietal, and left precuneus regions [26]. While Luo *et al*. did not specifically compare ALFF between patients with PD and HD, their findings align closely with ours. These observations suggest that variations in ALFF in the PCC may be linked to different dialysis treatments and contribute to the pathophysiological mechanisms underlying cognitive CI, with PD potentially exerting more detrimental effects.

Our study revealed significant reductions in CBF in the bilateral SFGmed of patients with PD compared with those with HD. Furthermore, patients with PD showed decreased CBF in the bilateral INS, CAU and SFGmed relative to HC, while CBF was also reduced in the bilateral INS and CAU in patients with HD compared with HC. The SFGmed, located in the upper prefrontal cortex, is crucial for regulating motor activity [27, 28], working memory [29], resting state and cognitive control [30]. The INS, deeply situated within the lateral sulcus, is well vascularized and supplied by the middle cerebral artery [31]. It is involved in neural activities such as attention, salience processing [32] and speech [33]. The CAU, part of the basal ganglia, also receives blood supply from the middle cerebral artery and participates in diverse cognitive functions like goal-directed action [34], memory [35], learning [36], sleep [37], emotion [38], language and threshold control. Jiang *et al*. [39] compared whole-brain CBF in patients with PD and HD, and those not undergoing dialysis, finding widespread regional declines primarily in the bilateral frontal and anterior cingulate cortices for both patients with PD and HD compared with non-dialysis ESRD patients. This finding corroborates our results and underscores similar trends in CBF reductions, indirectly supporting our conclusions. Previous studies suggest that post-dialysis, ESRD patients exhibit reduced CBF across various brain regions including the left frontal, parietal and temporal lobes, and specific areas like the left putamen and right INS [3]. Our research further indicates that PD may lead to more extensive CBF reductions across brain regions compared with HD. Continuous CBF is essential for neural function [38] as it meets metabolic demands, and there is growing evidence linking decreased CBF with CI in degenerative disorders [40, 41]. However, existing research on the relationship between CI and CBF in dialysis patients suggests that lower CBF could paradoxically ameliorate CI by reducing the delivery of uremic toxins to the brain [39]. This hypothesis, along with our findings, necessitates further investigation to validate these relationships.

The brain requires high-volume blood flow and has low vascular resistance [42] to support its functions. A crucial aspect of this is the NVC mechanism [43], which ensures that blood supply matches oxygen demands. Dysfunctional NVC is linked to pathological brain changes and neurological disorders [44, 45]. In this study, we used the ALFF-CBF pattern to assess NVC function, focusing on regions such as the bilateral SFGmed, INS, CAU and PCC. Our findings indicate significant differences in these regions between dialysis patients and HC, with generally poorer NVC in patients with PD and HD compared with HC. Specifically, patients with PD showed better performance in the SFGmed and PCC but similar results to HD patients in the INS and CAU. This suggests more extensive neurovascular dysfunction in PD than in HD [43]. This may relate to the observed significant decreases in ALFF in the SFG and CBF in the PCC of patients with PD compared with those with HD. Li *et al*. identified NVC dysfunction primarily in the PCC, fusiform gyrus and middle frontal gyrus [43] of ESRD patients, linking it to CI. Our results support the hypothesis that more severe NVC dysfunction could contribute to greater cognitive deficits in patients with PD.

In our study, MoCA scores showed no significant differences between patients with PD and HD, yet distinct imaging markers were identified for each group. For patients with PD, a negative correlation was found between CBF in bilateral PCC and MoCA scores, aligning with previous findings that reduced CBF may improve cognitive function [39]. Furthermore, ALFF-CBF coupling coefficient in the right INS positively correlated with MoCA scores, suggesting that NVC could be early markers of CI and play a role in the pathophysiology of brain diseases. In a prior study [39], the result illustrated that CBF was negatively correlated with hemoglobin levels. The authors explain the phenomenon as anemia causing vasodilatation to increase the blood volume, the result was similar to the other study focused on changes in the CBF of patients with PD [3]. Furthermore, the two studies discovered that decreased CBF may improve the cognitive function of dialysis patients. A prospective cohort study [46] found that there is a significant nonlinear correlation between hemoglobin and dementia, additionally, for every one standard deviation increase in hemoglobin levels, the risk of dementia decreased by 11%. However, our study found that lower hemoglobin levels correlated with greater reductions in CBF in both patients with PD and HD. This trend may be attributed to the body has not yet had time to make corresponding compensatory responses. The different results may suggest that in future research, we could categorize patients based on their scores on the MoCA. Then, we can investigate the relationship between the hemoglobin level and CBF for each group of patients. This approach will help us better understand the connection between these two indicators at different cognitive levels and confirm the underlying mechanism.

In patients with PD, we found a negative correlation between sodium level and ALFF-CBF coupling coefficient in the right INS. Previous study had discovered a new phenomenon called inverse neurovascular coupling [47]. This occurs when hypertonic saline is injected into rats, leading to an increase in hypothalamic vasopressin neuron discharge, followed by local cerebral vasoconstriction and reduced CBF. It may be possible that this mechanism can explain why higher sodium levels lead to poorer NVC in our research. However, since this experiment was only conducted on rodents, further validation is required to determine whether it can serve as a people-relevant pathophysiological mechanism. Additionally, in patients with PD, peritoneal Kt/V—a measure of dialysis adequacy—is positively correlated with ALFF-CBF coupling coefficient in the bilateral SFGmed. This supports previous findings that better dialysis adequacy correlates with improved cognitive function [48], suggesting that Kt/V may influence cognitive outcomes by modulating NVC. Overall, our analysis reveals that several laboratory indicators are linked with imaging markers in dialysis patients, and these markers correlate with cognitive function. These associations might represent underlying pathophysiological mechanisms of cognitive dysfunction. By further exploring these correlations, imaging indicators could serve as early markers for cognitive impairment, aiding in the prompt diagnosis and treatment of affected individuals. Except for these imaging markers, white matter lesions (WMLs) have been proven to be related to CI in patients with CKD [49] and will increase the burden of stroke [50]. In future research, it is necessary that explore the relationship between WMLs and stroke burden in dialysis patients with CI.

There are several limitations in this study. First, our study results were limited to a relatively small sample size, which may have impacted the comprehensive analyses of the contents of imaging markers in CI of patients with PD and HD. Second, we have not yet completed the arteriopathy screen in the final included procedure to exclude the effect on NVC in this study. Third, we only conducted a cross-sectional study on PD and HD patients, and have not yet carried out the longitude trace. In future research, in addition to improving the above deficiencies, we will consider taking dialysis vintage as a common grouping criterion to explore the overall cognitive function level of patients with different dialysis durations and conduct an in-depth exploration.

CONCLUSION

While MoCA scores did not significantly differ between patients with PD and HD, the PD group demonstrated poorer NVC in the bilateral SFGmed, bilateral PCC and left CAU. Sodium level and dialysis adequacy may affect NVC in patients with PD. Thus, it may provide new insights into the neural mechanisms that may underlie cognitive decline in patients with PD.

SUPPLEMENTARY DATA

Supplementary data are available at *Clinical Kidney Journal* online.

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AUTHORS' CONTRIBUTIONS

For this article, X.Y. and W.Y. designed and conducted the study, contributed to the data analysis and drafted the manuscript. W.L., L.S., J.L., M.L., Z.Y., Z.W. collected the data. H.W. and W.G. contributed to the design of the study, provided advice on the data analysis and revised the manuscript.

DATA AVAILABILITY STATEMENT

The data underlying this article are available in the article and in its online supplementary material.

CONFLICT OF INTEREST STATEMENT

All authors declare no conflicts of interest.

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