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Supplementary Data 1: MRI data acquisition

CBF: CBF was measured using a pulsed arterial spin labeling (ASL) sequence optimized to measure blood flow in gray matter (repetition time/echo time (TR/TE) = 2500/12 ms, field of view (FOV) = 256 x 256 mm², flip angle = 90 deg, matrix = 64 x 64, slice thickness/gap = 8.0/2.0 mm, voxel in-plane resolution = 4 x 4 mm², 9 axial slices) acquiring 115 pairs of alternating labeled and unlabeled images.^{1,2} The label offset was set to the distance between magnet isocenter and the junction of the cavernous and cerebral portions of the internal carotid arteries. However, in a subset of sessions, images were acquired so that the superior slice was at the vertex of the brain. We accounted for this variance by including slice position (upper or lower) as a covariate in the statistical analysis.

Cerebral neurochemicals: Neurochemical concentrations were measured with magnetic resonance spectroscopic imaging (MRSI) using a multi-voxel point resolved spectroscopy (PRESS) localized sequence (TR/TE = 1500/30 ms, FOV = 160 x 160 mm², area of interest = 80 x 80 mm², matrix = 16 x 16, final matrix size after 2x zero padding = 32 x 32, elliptical sampling, slice thickness = 10 mm, voxel in-plane resolution = 10 x 10 mm²).^{3,4} MRSI data were acquired from a fronto-parietal slab placed superior to the corpus callosum and parallel to the anterior commissure-posterior commissure plane, which was positioned to cover the largest two-dimensional area of brain possible. The MRSI slab was carefully placed based on anatomical features in the mid-sagittal T₁-weighted anatomic image to ensure that data were collected from the same anatomic location across participants at repeated time points. B₀ shimming was performed using a vendor-provided field mapping technique.

White matter integrity: White matter integrity was measured by diffusion tensor imaging (DTI).^{5,6} Data from the whole brain were collected using a double-refocused spin echo sequence optimized to capture major white matter tracts (TR/TE = 10,000/90 ms, FOV 300 × 300 mm, flip

angle = 90 deg, matrix = 128 × 128, slice thickness = 2 mm, voxel in-plane resolution = 2.34 x 2.34 mm, 75 axial slices). The diffusion gradients were applied along 64 directions (diffusion gradient pulse δ = 14 ms, diffusion application time Δ = 53 ms, b value = 1,000 s/mm²).

*T*₁ and *T*₂*: *T*₁- and *T*₂*-weighted anatomic images were also collected and used to align the CBF, MRSI, and DTI data, and for normalization of the regional atlas masks. *T*₁-weighted images were acquired with a 3D magnetization-prepared rapid acquisition gradient echo (MPRAGE) sequence (TR/TE = 2300/2.98 ms, FOV = 240 x 256 mm, flip angle = 9 deg, matrix = 240 x 256, slice thickness = 1.2 mm, voxel in-plane resolution = 1.0 x 1.0 mm, 176 sagittal slices).⁷ *T*₂*-weighted images were utilized as the primary anatomic dataset for DTI alignment procedures. These images were acquired with a 2D fast low-angle shot (FLASH) sequence (TR/TE = 650/20 ms, FOV = 220 X 220 mm, flip angle = 20 deg, matrix = 256 x 256, slice thickness = 4.0 mm, voxel in-plane resolution = 0.86 x 0.86 mm, 44 axial slices).⁸

MR Data Analysis

CBF: Arterial spin labeling (ASL) data were processed using the ASLtbx⁹ with SPM12,¹⁰ modified for pulsed ASL. For each session, labeled and unlabeled ASL images were independently motion corrected and then a combined mean image was computed. The mean image was co-registered to match the *T*₁-weighted anatomical image. The ASL images were then temporally filtered and spatially smoothed with a 6 mm full-width half-maximum Gaussian kernel. CBF was then estimated by subtraction of labeled and unlabeled mean images, resulting in a mean CBF image (units = ml/min/100g tissue). The structural correlation based outlier rejection (SCORE) algorithm was used to remove outlier voxels.¹¹ The *T*₁-weighted scan was then normalized using unified segmentation-normalization (SPM12). In addition to whole gray matter CBF, we also assessed regional CBF. These regions were selected *a priori* based on atlas-based regional parcellations of the whole gray matter area distributed across the entire

brain. For regional CBF, we used 14 gray matter regions from the Automated Anatomical Labeling atlas; anterior cingulate cortex, middle frontal gyrus, hippocampus, primary motor cortex, posterior cingulate cortex, precuneus, superior parietal cortex, temporal cortex, thalamus, pallidum, putamen, caudate, frontal cortex, and parietal cortex.¹² Mean CBF was computed in regions of interest created from the intersection of the individual gray matter segmentation (probability > 0.5) performed under the SPM unified segmentation algorithm and regional masks from the Automated Anatomical Labeling atlas. Since calculation of CBF includes the MRI longitudinal relaxation time (T1) of blood as a variable, and T1 of blood varies with hematocrit, the calculation was corrected for hematocrit.¹³

Neurochemicals: Magnetic resonance spectroscopic imaging (MRSI) data were analyzed using LCModel¹⁴ with a numerically simulated basis set for concentrations of N-acetylaspartate (NAA), Cho, glutamate and glutamine (Glx), ml and total creatine (Cr). Metabolite concentrations were extracted from gray matter within the MRSI acquisition slab. Voxels were selected for analysis based on the tissue fraction (gray/white matter) in each voxel using the segmented T₁-weighted images and slice selection profiles of radiofrequency pulses corresponding to the spectroscopic voxels. Voxels were included in the analysis if the tissue fraction was greater than 50% gray matter. Analysis was further limited to the center of the region to capture the best quality data and reduce off-resonance effects from the skull and fat surrounding the head. Final concentrations of neurochemicals were therefore obtained from the central 50 x 50 mm² region of the acquisition slab by averaging concentration values using weighting factors derived from the goodness of LCModel fit.¹⁵ To correct for the differences in levels of different neurochemicals, we normalized the values within each individual by reporting concentrations for NAA, Cho, ml and Glx as ratios to Cr.¹⁶

White matter integrity: Diffusion tensor imaging (DTI) data were processed using Analysis of Functional NeuroImages (AFNI)¹⁷ software, and TORTOISE version 3.1.4 DIFF_PREP and DIFF_CALC processing modules. Processing steps included eddy current correction modeled with quadratic functions; motion distortion correction; echo planar imaging distortion correction; Gibbs ringing correction;¹⁸ and denoising. TORTOISE DIFF_CALC EstimateTensorNLLS was used to fit the tensors. DIFFCALC GUI version 2.5 running under IDL Virtual Machine was used to compute the eigenvectors, derive the tensors, and save the output metrics.

DTI output metrics included fractional anisotropy (FA), a measurement of whether diffusion is constrained along any axis, indicating the presence of white matter fiber tracts (range 0-1, with 0 indicating equal diffusion in all directions and 1 indicating unidirectional diffusion), and mean diffusivity (MD), which is calculated by dividing the total diffusion for all three eigenvectors at each voxel by three (for the three eigenvectors, units = 10^{-3} mm²/sec). Diffusivity is reduced in constrained areas like dense white matter fiber tract bundles. High MD may indicate more free water or edema in the brain.¹⁹ Mean FA and MD were exported for each participant and session from regional white matter tract masks. We used 11 white matter tracts from the Johns Hopkins University DTI-based white matter atlases; anterior thalamic radiation, cingulum in the cingulated cortex areas, cingulum in the hippocampal area, corticospinal tract, forceps major, forceps minor, inferior fronto-occipital fasciculus, inferior longitudinal fasciculus, superior longitudinal fasciculus, temporal projection of the superior longitudinal fasciculus, and uncinata fasciculus.²⁰⁻²² A combined All-tract mask was created as the overlap of all regional masks.

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Supplementary Table 1. Characteristics of patients with and without a post-KT MRI

	ESKD patients with baseline MRI only (n=7)	ESKD patients with follow-up MRI (n=22)
Age years, mean ± SD	57.61 ± 12.10	51.23 ± 10.90
Race, n (%)		
White	4 (57.1)	21 (95.4)
Black	1 (14.3)	1 (4.6)
Other	2 (28.6)	0
Sex n (%)		
Males	5 (71.4)	15 (68.2)
Females	2 (28.6)	7 (31.8)
Education, n (%)		
High school diploma	1 (14.3)	5 (22.7)
Some college	3 (42.9)	6 (27.3)
4-year college degree	1 (14.3)	6 (27.3)
Graduate school	2 (28.6)	5 (22.7)
Comorbid conditions, n (%)		
Coronary artery disease	2 (28.6)	5 (22.7)
Diabetes	2 (28.6)	5 (22.7)
Hypertension	6 (85.7)	19 (86.4)
Stroke	0 (0)	1 (4.6)
Depression	2 (28.57)	5 (22.7)
Smoking	4 (57.14)	6 (27.3)
On anticoagulants, n (%)	0	2 (9.1)
Atrial fibrillation, n (%)	1 (14.3)	1 (4.6)
Cause of ESKD, n (%)		
Diabetes	2 (28.6)	4 (18.2)
Hypertension	2 (28.6)	1 (4.5)
ADPKD	2 (28.6)	6 (27.3)
Other	1 (14.3)	11 (50)
Dialysis modality, n (%)		
In center hemodialysis	1 (14.3)	10 (45.5)
Home hemodialysis	1 (14.3)	2 (9.1)
Peritoneal dialysis	5 (71.4)	4 (18.2)
Not on dialysis	0 (0)	6 (27.3)

ESKD: end-stage kidney disease, ADPKD: autosomal dominant polycystic kidney disease. Continuous values are presented as mean + standard deviation (SD), p values represent unadjusted two sample t test. Categorical variables are presented as frequency (percentage), p value represents unadjusted nonparametric Fisher exact test.

Supplementary Table 2: Transplantation related clinical characteristics of 22 end stage kidney disease (ESKD) patients who received kidney transplantation (KT).

Clinical Characteristics	
ESKD patients transplanted, <i>n</i> (% of ESRD patients on the study)	22 (75.0)
Living donor KT, <i>n</i> (%)	16 (72.7)
Pre-emptive KTs, <i>n</i> (%)	6 (27.3)
Pre-KT kidney function of pre-emptive KTs, <i>mean</i> ± <i>SD</i>	
Serum creatinine (mg/dl)	4.4 ± 0.1
eGFR (ml/min/1.73m²)	12.3 ± 1.6
Time on dialysis before transplant (months), <i>mean</i> ± <i>SD</i>	20.5 ± 19.2
Induction, <i>n</i> (%)	
Basiliximab	5 (22.7)
Thymoglobulin	17 (77.3)
PRA >20, <i>n</i> (%)	8 (36.4)
DGF, <i>n</i> (%)	1 (4.5)
Acute rejection, <i>n</i> (%)	1 (4.5)
ESKD: end stage kidney disease, KTs: kidney transplantation, eGFR: estimated glomerular filtration rate, PRA: panel reactive antibody, DGF: delayed graft function.	

Supplementary Table 3: Unadjusted MRI measurements in controls and ESKD patients.

	Controls (n=19) (mean ± SD)	1-year pre-KT (n=4) (mean ± SD)	Pre-KT (n=29) (mean ± SD)	3 mos. post-KT (n=22) (mean ± SD)	12 mos. post-KT (n=18) (mean ± SD)
CBF					
Total gray matter	33.72 ± 4.83	37.74 ± 4.87	36.34 ± 10.17	29.52 ± 6.59	31.93 ± 5.58
Regions analyzed					
ACC	33.37 ± 7.16	35.94 ± 6.78	30.49 ± 15.98	26.59 ± 10.48	30.58 ± 7.74
Frontal Mid	29.09 ± 8.03	34.90 ± 11.15	28.81 ± 12.43	22.30 ± 9.95	25.24 ± 7.77
Hippocampus	34.93 ± 7.66	38.89 ± 12.63	37.41 ± 11.27	28.83 ± 8.22	35.00 ± 9.39
M1	28.08 ± 7.14	26.94 ± 8.08	31.90 ± 11.34	25.92 ± 8.78	25.55 ± 5.82
PCC	51.45 ± 7.92	47.31 ± 13.86	51.74 ± 18.04	40.84 ± 13.41	41.59 ± 13.37
Precuneus	39.13 ± 6.45	35.20 ± 9.84	43.46 ± 15.12	35.27 ± 10.69	31.71 ± 8.20
Superior Parietal	26.91 ± 9.47	15.28 ± 8.26	30.03 ± 14.45	23.40 ± 11.67	20.25 ± 9.02
Temporal	37.12 ± 6.98	37.46 ± 5.19	36.14 ± 9.82	29.93 ± 6.47	35.54 ± 8.61
Thalamus	43.08 ± 8.6	48.34 ± 19.47	48.56 ± 17.67	37.06 ± 12.95	38.74 ± 10.33
Pallidum	33.85 ± 9.33	34.67 ± 17.34	36.53 ± 13.94	28.81 ± 10.29	33.75 ± 10.76
Putamen	31.16 ± 7.53	35.73 ± 14.77	33.58 ± 12.07	26.28 ± 7.20	30.38 ± 7.83
Caudate	25.08 ± 5.6	40.40 ± 30.86	28.11 ± 9.21	21.31 ± 4.75	24.67 ± 6.82
Frontal	28.57 ± 6.3	35.62 ± 9.33	30.48 ± 10.11	24.76 ± 7.51	27.46 ± 5.54
Parietal	33.21 ± 6.09	31.11 ± 8.51	38.60 ± 12.47	30.82 ± 8.02	29.54 ± 7.01
Neurochemicals analyzed					
NAA/Cr	1.5 ± 0.08	1.47 ± 0.18	1.53 ± 0.15	1.53 ± 0.13	1.55 ± 0.15
Cho/Cr	0.31 ± 0.04	0.34 ± 0.03	0.35 ± 0.04	0.31 ± 0.04	0.31 ± 0.03
Glx/Cr	1.27 ± 0.23	1.07 ± 0.08	1.22 ± 0.16	1.17 ± 0.12	1.36 ± 0.18
ml/Cr	0.82 ± 0.07	0.98 ± 0.10	0.95 ± 0.11	0.87 ± 0.07	0.91 ± 0.07
DTI Regions and metrics analyzed					
All tracts FA	0.4 ± 0.03	0.38 ± 0.02	0.38 ± 0.03	0.39 ± 0.03	0.39 ± 0.03
All tracts MD	0.84 ± 0.04	0.91 ± 0.09	0.90 ± 0.09	0.86 ± 0.09	0.87 ± 0.09
Regional FA					
ATR	0.32 ± 0.04	0.28 ± 0.04	0.29 ± 0.05	0.30 ± 0.05	0.30 ± 0.05
CG	0.39 ± 0.12	0.41 ± 0.10	0.37 ± 0.10	0.39 ± 0.09	0.40 ± 0.09
CH	0.33 ± 0.08	0.31 ± 0.10	0.33 ± 0.08	0.37 ± 0.07	0.32 ± 0.09
CST	0.53 ± 0.04	0.54 ± 0.04	0.52 ± 0.03	0.53 ± 0.03	0.54 ± 0.03
FMAJ	0.54 ± 0.06	0.49 ± 0.05	0.51 ± 0.05	0.52 ± 0.06	0.51 ± 0.06
FMIN	0.36 ± 0.04	0.36 ± 0.02	0.36 ± 0.04	0.37 ± 0.03	0.37 ± 0.04
IFOF	0.42 ± 0.03	0.39 ± 0.03	0.39 ± 0.04	0.41 ± 0.04	0.40 ± 0.04
ILF	0.42 ± 0.03	0.39 ± 0.02	0.39 ± 0.03	0.41 ± 0.04	0.40 ± 0.03
SLF	0.39 ± 0.03	0.37 ± 0.03	0.37 ± 0.03	0.38 ± 0.03	0.38 ± 0.03
SLFT	0.48 ± 0.03	0.46 ± 0.04	0.46 ± 0.04	0.47 ± 0.04	0.47 ± 0.04
UF	0.34 ± 0.05	0.35 ± 0.02	0.32 ± 0.05	0.33 ± 0.05	0.34 ± 0.05
Regional MD					
ATR	0.94 ± 0.13	1.12 ± 0.21	1.08 ± 0.27	1.02 ± 0.28	1.04 ± 0.26
CG	0.78 ± 0.05	0.78 ± 0.06	0.80 ± 0.05	0.77 ± 0.04	0.77 ± 0.05
CH	0.92 ± 0.2	0.93 ± 0.24	0.91 ± 0.20	0.83 ± 0.13	0.89 ± 0.19
CST	0.77 ± 0.07	0.75 ± 0.04	0.76 ± 0.05	0.75 ± 0.03	0.75 ± 0.04

FMAJ	0.88 ± 0.09	1.02 ± 0.06	0.97 ± 0.12	0.94 ± 0.14	0.96 ± 0.12
FMIN	0.87 ± 0.06	0.92 ± 0.08	0.91 ± 0.08	0.87 ± 0.07	0.88 ± 0.10
IFO	0.81 ± 0.04	0.89 ± 0.11	0.86 ± 0.07	0.84 ± 0.07	0.84 ± 0.08
ILF	0.83 ± 0.07	0.90 ± 0.12	0.88 ± 0.11	0.84 ± 0.08	0.85 ± 0.09
SLF	0.77 ± 0.04	0.81 ± 0.07	0.81 ± 0.05	0.79 ± 0.04	0.79 ± 0.05
SLFT	0.73 ± 0.03	0.75 ± 0.05	0.75 ± 0.03	0.74 ± 0.03	0.74 ± 0.03
UF	0.91 ± 0.1	0.86 ± 0.05	0.94 ± 0.14	0.90 ± 0.12	0.90 ± 0.14

KT: kidney transplantation, CBF: cerebral blood flow, ACC: anterior cingulate cortex, Frontal Mid: middle frontal gyrus, M1: primary motor cortex, PCC: posterior cingulate cortex, NAA: N-acetylaspartate, Cr: total creatine, Cho: choline, Glx: glutamate and glutamine, ml: myo-inositol, FA: fractional anisotropy, MD: mean diffusivity. Units are ml/min/100g tissue for CBF, ratios to creatine for neurochemicals, scalar (0-1) for FA, and 10^{-3} mm²/sec for MD.

Supplementary Table 4: Estimated effect of covariates for primary MRI variables in the mixed model analysis.

Parameters	CBF	NAA/Cr	Cho/Cr	Glx/Cr	ml/Cr	FA	MD
Age	-0.09 ± 0.08	-0.005 ± 0.002*	-0.0002 ± 0.0005	-0.002 ± 0.002	0.00006 ± 0.001	-0.001 ± 0.0003*	0.004 ± 0.0008*
Sex (F)	3.78 ± 1.82*	0.023 ± 0.03	0.01 ± 0.01	-0.15 ± 0.04*	-0.03 ± 0.02	0.005 ± 0.007	-0.035 ± 0.018
Race							
Other than White	5.76 ± 5.71	0.07 ± 0.11	-0.06± 0.03	-0.06 ± 0.13	0.18 ± 0.07*	-0.02 ± 0.02	0.029 ± 0.054
White	4.88 ± 3.90	-0.09 ± 0.07	-0.03± 0.02	-0.004 ± 0.09	0.02 ± 0.05	-0.008 ± 0.02	-0.005 ± 0.036
Education (E)	-5.35 ± 3.12	-0.12 ± 0.06	0.014± 0.02	-0.004 ± 0.07	-0.011 ± 0.04	-0.003 ± 0.013	0.0034 ± 0.032
Slice (L)	-4.05 ± 2.16	---	---	---	---	---	---
<p>*p-value <0.05 for that covariate, CBF: cerebral blood flow in total grey matter, NAA: N-acetylaspartate, Cr: total creatine, Cho: choline, Glx: glutamate and glutamine, ml: myo-inositol, FA: all tracts fractional anisotropy, MD: all tracts mean diffusivity, F: Female, E: lower education, L: lower slice. All values are in mean ± standard error. Slice was adjusted only for cerebral blood flow.</p>							

Supplementary Table 5: Comparison of repeated MRI measurements in pre-KT patients. No changes were observed in one year.

Imaging measure	1-year pre-KT (n=4) (mean ± SD)	Pre-KT (n=4) (mean ± SD)	p-value ^a
CBF	30.95 ± 8.28	37.74 ± 4.87	0.13
NAA/Cr	1.47 ± 0.17	1.47 ± 0.17	>0.99
Cho/Cr	0.37 ± 0.03	0.34 ± 0.03	0.25
Glx/Cr	1.21 ± 0.11	1.07 ± 0.08	0.13
ml/Cr	0.97 ± 0.12	0.98 ± 0.09	0.63
All tracts FA	0.37 ± 0.03	0.38 ± 0.02	0.63
All tracts MD	0.93 ± 0.11	0.91 ± 0.08	0.63

KT: kidney transplantation, CBF: cerebral blood flow, NAA: N-acetylaspartate, Cr: total creatine, Cho: choline, Glx: glutamate and glutamine, ml: myo-inositol, FA: fractional anisotropy, MD: mean diffusivity. ^a p-value for Wilcoxon signed rank nonparametric test. Units are ml/min/100g tissue for CBF, ratios to creatine for neurochemicals, scalar (0-1) for FA, and 10⁻³ mm²/sec for MD.

Supplementary Figure 1: Flowchart of end stage kidney disease patients undergoing MRI assessment at baseline, 3 months post- transplant and 12 months post-transplant.

