Supplementary Data

Supplementary Table 1. Cognitive testing scores by gait phenotype and CKD status.

Supplementary Table 2. MNI coordinates of key brain regions (peak voxels in clusters) contributing to the gray matter volume covariance network associated with Chronic Kidney Disease.

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Supplementary Appendix 1. MRI pre-processing pipeline and multivariate analyses.

Supplementary Table 1. Cognitive Testing Scores by Gait Phenotype and CKD Status

	No CKD		CKD	
Cognitive Test	No Gait Phenotype (N=109)	+ Gait Phenotype (N=77)	No Gait Phenotype (N=38)	+ Gait Phenotype (N=88)
RBANS				
Total Scale	94.9 ± 12.5	93.9 ± 11.6	94.8 ± 13.3	89.3 ± 10.8
Subdomain Scores				
Immediate Memory	101.9 ± 12.4	101.9 ± 12.4	99.8 ± 11.6	95.7 ± 11.6
Visuospatial / Constructional	94.7 ± 11.7	91.6 ± 14.4	94.9 ± 12.7	88.8 ± 14.4
Language	92.5 ± 11.3	93.6 ± 10.5	92.8 ± 10.6	94.2 ± 9.0
Attention	101.9 ± 13.2	101.0 ± 13.5	100.8 ± 13.9	97.6 ± 14.4
Delayed Memory	95.8 ± 11.7	95.3 ± 11.1	96.6 ± 12.8	90.9 ± 10.0
Individual Cognitive Tests				
FCSRT (free recall) – n=307	32.6 ± 6.9	30.9 ± 6.8	30.8 ± 6.6	28.8 ± 6.3
FCSRT (total recall ≤ 44) – n(%), n=310	3 (3)	3 (4)	1 (3)	1 (1)
Letter Fluency (z score)	0.2 ± 1.0	0.2 ± 1.1	0.2 ± 1.2	- 0.1 ± 1.2
Category Fluency (z score)	0.6 ± 1.2	0.2 ± 1.3	0.3 ± 1.2	-0.1 ± 1.2
Trail Making Test A (z score)	0.66 (0.10-1.13)	0.64 (0.09-1.02)	0.90 (0.55-1.13)	0.50 (-0.35-0.77)
Trail Making Test B (z score) – n=307	0.54 (-0.05-1.05)	0.25 (-0.52-0.83)	0.53 (0.18-1.13)	0.00 (-0.97-0.63)
Trail Making Test Δ***** (sec) – n=307	55.4 (37.5-77.3)	67.2 (40.7-102.2)	51.1 (36.6-94.3)	77.4 (49.7-119.8)
Digit Symbol Substitution (scaled score)	11.5 ± 2.9	11.4 ± 3.3	11.9 ± 2.9	10.7 ± 3.1
Boston Naming Test (z score) – n= 308	0.5 (-0.4-1.0)	0.4 (-0.5-0.8)	0.7 (-0.1-1.0)	0.4 (-0.1-0.9)

Abbreviations: CKD, chronic kidney disease; RBANS, Repeatable Battery for the Assessment of Neuropsychological Status; FCSRT, The Free and Cued Selective Reminding Test. CKD defined as eGFR <60 mL/min/1.73m^2.

*Trail Making Test Δ = Trail Making Test Part B (sec) – Trail Making Test Part A (sec)

Continuous variables are represented as mean $\pm$ standard deviation if normally distributed and median (interquartile range) otherwise.

Supplementary Table 2. MNI coordinates of key brain regions (peak voxels in clusters) contributing to the gray matter volume covariance network associated with Chronic Kidney Disease. Threshold Z =1.96 , p <.05, 10 voxels (k).

Brain Region	X	Y	Z	k	Z-value
Positive (relatively less atrophy)					
Supplementary Motor Area	13	-13	60	192193	4.2964
Cerebellum (VIIIA)	1	-80	-46	68136	3.6607
Pallidum	-17	1	10	2013	2.9622
Inferior Occipital Gyrus	19	-105	-7	223	2.5542
Temporal Pole	-23	5	-50	193	2.2998
Inferior Occipital Gyrus	-32	-100	-10	164	2.4842
Calcarine Sulcus	4	-101	0	162	2.5967
Inferior Frontal Gyrus (orbital)	-55	38	-9	138	2.2726
Inferior Frontal Gyrus (orbital)	12	31	-8	93	2.5731
Cingulum (anterior)	1	30	4	82	2.2374
Middle Temporal Gyrus	-68	-21	-26	65	2.2568
Middle Frontal Gyrus (orbital)	51	52	-8	46	2.2939
Middle Occipital Gyrus	-8	-105	12	27	2.3724
Inferior Frontal Gyrus (orbital)	43	36	-21	20	2.2472
Inferior Frontal Gyrus (orbital)	36	39	0	16	2.2949
Inferior Frontal Gyrus (orbital)	58	36	-6	16	2.0873
Negative (relatively more atrophy)					
Calcarine Sulcus	15	-61	9	291958	-4.5668
Inferior Frontal Gyrus (orbital)	29	36	-14	1238	-3.8672
Middle Frontal Gyrus (orbital)	-26	37	-15	1544	-3.7436
Inferior Temporal Gyrus	49	0	-37	1195	-3.0773
Middle Occipital Gyrus	-46	-78	14	673	-2.9853
Cerebellum (Cruz II)	41	-57	-45	763	-2.8315
Cerebellum (IX)	-13	-43	-46	205	-2.5723
Superior Parietal	39	-43	58	112	-2.5312
Cerebellum (IX)	17	-42	-47	121	-2.4597
Precentral Gyrus	-47	2	44	24	-2.3520
Inferior Parietal	48	-52	48	30	-2.3302
Calcarine Sulcus	-8	-91	-3	187	-2.1947
Postcentral Gyrus	-55	-8	23	142	-2.1753
Cerebellum (VIIB)	-41	-54	-44	46	-2.1041
Middle Occipital Gyrus	-46	-77	-1	13	-2.0972
Inferior Parietal	-50	-54	42	37	-2.0902
Rectus	8	38	-25	19	-2.0821

Middle Temporal	-50	-68	19	15	-2.0428

Supplementary Table 3. MNI coordinates of key brain regions (peak voxels in clusters) contributing to the gray matter volume covariance network associated with the gait phenotype. Threshold Z =1.96 , p <.05, 10 voxels (k)

Brain Region	X	Y	Z	k	Z-value
Positive (relatively less atrophy)					
Superior Frontal Gyrus	33	51	39	602363	7.9227
Parahippocampal Gyrus	-28	-22	-21	26	2.1299
Parahippocampal Gyrus	22	-39	-5	42	2.3310
Caudate	-4	11	12	352	4.3203
Negative (relatively more atrophy)					
Rolandic Operculum	-40	-20	15	419685	-7.3831
Middle Frontal Gyrus (orbital)	-28	37	-14	1156	-4.7479
Superior Frontal Gyrus (orbital)	-12	18	-21	420	-4.1703
Inferior Frontal Gyrus (orbital)	29	36	-14	941	-3.9336
Inferior Temporal Gyrus	49	1	-37	1071	-3.9262
Cerebellum (VIII)	-5	-70	-40	2946	-3.4757
Cerebellum (IX)	-13	-44	-47	260	-3.2624
Cerebellum (Crus II)	-29	-79	-38	1047	-3.2508
Fusiform Gyrus	-27	-8	-39	131	-2.8090
Inferior Temporal Gyrus	-59	-50	-9	68	-2.6650
Superior Frontal Gyrus	25	24	46	171	-2.6241
Inferior Temporal Gyrus	63	-28	-19	48	-2.5278
Cerebellum (Crus II)	-42	-51	-43	62	-2.2085
Superior Parietal	-16	-69	47	42	-2.1997
Cerebellum (IX)	16	-43	-47	15	-2.1126
Precentral Gyrus	33	-3	51	20	-2.1088

Supplementary Appendix 1. MRI pre-processing pipeline and multivariate analyses.

MRI Acquisition and Pre-processing

Standard three-dimensional T1-weighted (structural) MRI images were obtained with a Philips 3T MRI scanner (Achieva Quasar TX; Philips Medical Systems, Best, Netherlands; TR/TE of 9.9/4.6 ms., 240 mm^2 FOV, 240 x 240 x 220 matrix and 1 mm voxel size) housed at the Gruss Magnetic Resonance Research Center at Albert Einstein College of Medicine (Bronx, NY, USA). T1-weighted images were first manually re-oriented to the anterior commissure – posterior commissure line and then pre-processed using SPM12 (Wellcome Department of Cognitive Neurology), which was implemented with MATLAB R2015a (Mathworks, Natick, MA). Each structural MRI image was analyzed using Voxel-Based Morphometry (VBM) and segmented into Gray Matter (GM), White Matter (WM), and Cerebrospinal Fluid (CSF), using a unified segmentation procedure and Diffeomorphic Anatomical Registration Through Exponentiated Line Algebra (DARTEL) (30). This VBM technique improves inter-subject alignment by modeling the shape of the brain using three parameters for each voxel. Gray matter and white matter is simultaneously aligned to produce a study-specific and increasingly crisp template to which the data are iteratively aligned. For each participant, a GM map, a WM map and a CSF map was created in the same space as the original T1-weighted image, where each voxel is assigned a probability value. These probability maps were manually examined to ensure proper segmentation, and then spatially normalized into Montreal Neurologic Institute (MNI) space. Finally, these

probability maps were spatially smoothed with an isotropic Gaussian kernel, full-width-at half-maximum = 8 mm.

Multivariate Analyses

Gray matter probability maps were first masked with a gray matter mask supplied by SPM12 to only include voxels with > 20% probability of being gray matter and linearly transformed. A PCA was then performed in order to generate a set of principal components, and their associated participant-specific (or pattern) expression scores. Participant-specific expression scores reflect the degree to which a participant displays a particular component or pattern. The expression scores of each PC were examined for potential outliers. The gray matter volume covariance patterns associated with CKD and gait phenotype/severity were then computed by regressing the participant-specific factor scores from the best linear combination of principal components (PCs) – selected using the Akaike information criteria (32) – against CKD and gait phenotype. The stability of the voxels in each GM volume covariance pattern were then tested using 1,000 bootstrap resamples (33). Voxels with bootstrap samples of $[Z] > 1.96$ and $p < 0.05$ were considered significant. These group-level covariance analyses allowed us to identify key ‘nodes’ in the gray matter volume covariance ‘networks’ associated with CKD and gait severity (34-38). This multivariate analysis assigns positive and negative weightings (or loadings) to each voxel (or variable) included in the analysis. In the current study, positively weighted regions will be interpreted as regions that have relatively more volume in individuals with CKD and gait severity, while negatively weighted regions will be interpreted as regions that have relatively less volume

(atrophy) in CKD and gait severity. It is important to note, however, that both positively and negatively weighted regions contribute to the derived gray matter covariance patterns that are associated with CKD and gait severity.