

Online Supplement Tables A, B, & C

Online Table A: Allele distribution in the overall sample, in the Caucasians and African Americans, and Hardy Weinberg Equilibrium test

	Overall	Caucasians	African Americans	HWE p-value
ACEID, n	2974	1746	1228	
ACEID genotypes	D/D: 32%	31%	33%	<i>W=0.43</i>
	I/D: 49%	49%	49%	<i>AA=0.88</i>
	I/I: 19%	20%	18%	
AGT-M235T, n	2934	1719	1215	
AGT-M235T	C/C: 38%	18%	65%	<i>W=0.94</i>
	C/T: 41%	49%	31%	<i>AA=0.43</i>
	T/T: 21%	33%	4%	
AGT -6G/A, n	2943	1724	1214	
AGT -6G/A	A/A: 39%	18%	68%	<i>W=0.85</i>
	A/G: 41%	48%	29%	<i>AA=0.61</i>
	G/G: 20%	32%	3%	

HWE: Hardy Weinberg Equilibrium; ACEID: Angiotensin converting enzyme gene insertion deletion;

AGT: Angiotensinogen gene; A: Adenine; C: Cytosine; T: Thymine; G: Guanine; I: Insertion; D:

Deletion

Online Table-B: Characteristics of the overall sample and those on ACEINH and not on ACEINH

	Overall	Not on ACEINH	On ACEINH	p-value
<i>N</i>	3075	2600	465	
Age, mean±standard error (SE), years	73.63±0.05	73.66±0.06	73.45±0.14	0.1395
Gender, % women	1584 (52%)	1347 (52%)	231 (50%)	0.3972
Race, %African Americans	1273 (41%)	1053 (41%)	220 (47%)	0.006
Body Mass Index, mean±SE, kg/m ²	27.39±0.09	27.20±0.09	28.52±0.23	<0.0001
Education level, Mean±SE, years	13.04±0.07	13.06±0.08	12.97±0.15	<0.0001
Systolic Blood Pressure, mean±SE, mm Hg	135.86±0.38	135.07±0.40	140.41±1.08	<0.0001
Diastolic Blood Pressure, mean±SE, mm Hg	71.42±0.21	71.17±0.23	72.85±0.58	<0.0001
Current smoker, n (%)	318 (10%)	271 (10%)	46 (10%)	0.71
Alcohol, mean±SE drinks per day	2.12±0.03	2.15±0.03	1.97±0.07	0.0211
Energy expenditure, KCAL/KG/WEEK	7.68±0.32	7.76±0.35	7.21±0.81	0.54
Laboratory				
LDL, mean±SE, mg/dl	121.54±0.63	121.81±0.68	120.09±1.72	0.3319
HDL, mean±SE, mg/dl	54.09±0.31	54.51±0.34	51.67±0.75	0.001
Cholesterol, mean±SE, mg/dl	202.81±0.70	203.23±0.75	200.48±1.98	0.1587
Morbidities, n (%):				
Hypertension	1563 (51%)	1142 (44%)	416 (90%)	<0.0001

Diabetes	460 (15%)	335 (13%)	124 (27%)	<0.0001
Coronary Artery Disease	105 (3%)	80 (3%)	25 (5%)	0.0118
Congestive Heart Failure	95 (3%)	57 (2%)	38 (8%)	<0.0001
Cancer	4 (4%)	2 (2%)	2 (11%)	0.073
Stroke	223 (7%)	172 (7%)	51 (11%)	0.0011
Arthritis	1719 (57%)	1449 (57%)	265 (58%)	0.6987

Neuropsychological tests, score

mean±SE

CLOX1 (year 3)	10.61±0.05	10.63±0.05	10.47±0.12	0.175
3MSE	90.04±0.15	90.14±0.17	89.60±0.37	0.2018
DSST	35.24±0.27	35.45±0.29	34.09±0.70	0.0712
CES-D	4.72±0.10	4.73±0.10	4.73±0.27	0.9957

Medications

Receiving antihypertensives, n (%)	1673 (55%)	12.08 (47%)	465 (100%)	<0.0001
Angiotensin converting enzyme inhibitors, n (%)	465 (15%)	NA	NA	
Diuretics, n (%)	312 (10%)	271 (10%)	41 (9%)	0.2915
Beta Blockers, n (%)	410 (13%)	350 (14%)	60 (13%)	0.7446
Calcium channel blocker, n (%)	705 (23%)	582 (22%)	123 (27%)	0.0549
Angiotensin receptor blockers, n (%)	70 (2%)	70 (3%)	0	0.0003
Hormonal Supplement, n(%)	349 (11%)	298 (12%)	51 (11%)	0.7575

CLOX1: Executive clock draw test; DSST: Digit symbol substitution test; 3MSE:

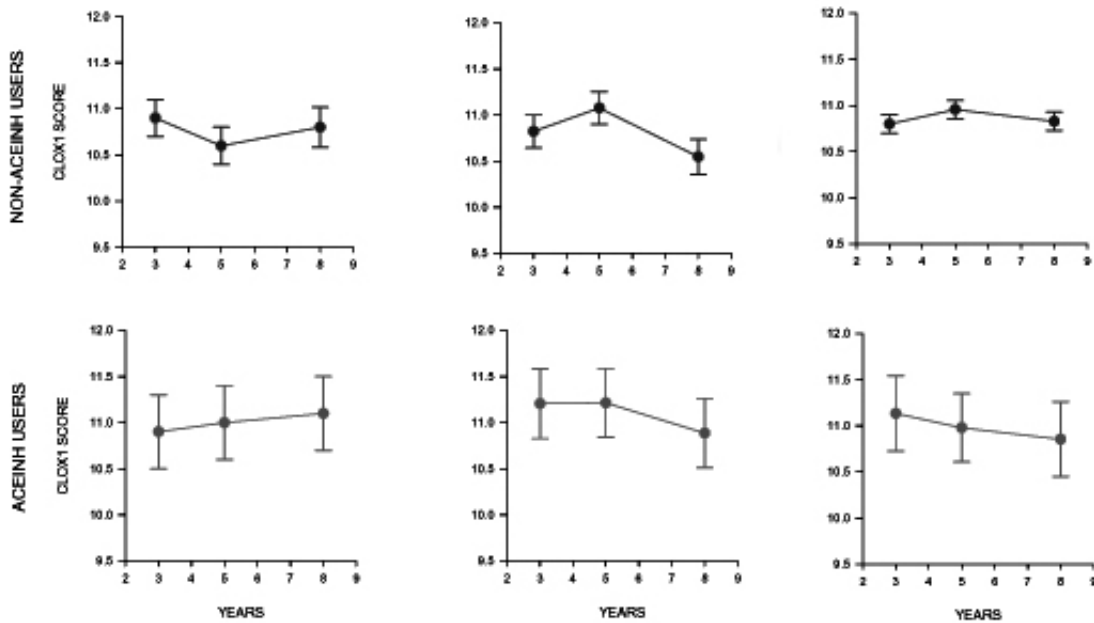
Modified mini mental status examination; CESD: Center for Epidemiologic Studies Depression Scale

Table C: longitudinal association between gene and cognitive function in Caucasians and African Americans (combined both ACEINH and NON-ACEINH exposure groups)

	<i>p</i>-value for association between gene and cognitive decline	
	Caucasians	African Americans
<i>ACE-ID</i>		
CLOX1	0.96	0.82
DSST	0.031	0.58
3MSE	0.67	0.79
<i>AGT6</i>		
CLOX1	0.007	0.60
DSST	0.50	0.04
3MSE	0.64	0.33
<i>AGTM235T</i>		
CLOX1	0.01	0.98
DSST	0.02	0.36
3MSE	0.64	0.53

Online Supplement Figures 1 & 2

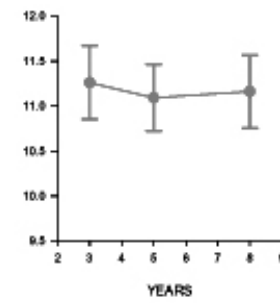
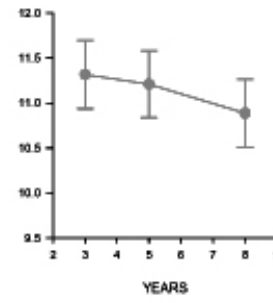
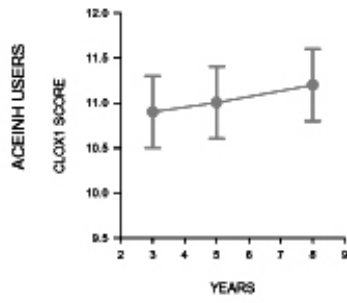
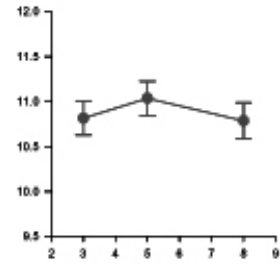
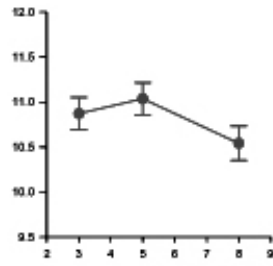
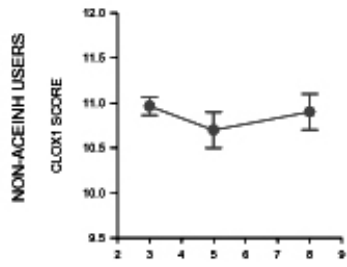
Figure1: Longitudinal change in CLOX1 score by AGT6 genotypes (AA, AG, GG) in the 2 ACEINH groups in whites (A) and African Americans (B)



Footnote: Values are the least square means of CLOX1 scores adjusted for baseline CLOX1, age, gender, BMI, education, systolic blood pressure, stroke, APOE, diabetes, and other antihypertensives.

Figure2: Longitudinal change in CLOX1 score by AGTM235T genotypes (CC, CT,TT) in the overall sample and in the 2 ACEINH groups in the whites (A) and African Americans (B)

Footnote: Values are the least square means of CLOX1 scores adjusted for baseline CLOX1, age, gender, BMI, education, systolic blood pressure, stroke, APOE, diabetes, and other antihypertensives.



B-African Americans

