Supplementary materials for:

Parasympathetic and sympathetic nervous systems interactively predict change in cognitive functioning in midlife adults

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Table S1: Association of resting baseline PNS activity with change in cognitive functioning

	BTACT			Episodic Memory			Executive Functioning		
	Estimates	*CI*	*p*	*Estimates*	*CI*	*p*	*Estimates*	*CI*	*p*
Intercept (M2)	1.959	1.420 – 2.498	**<0.001**	0.827	0.251 – 1.403	**0.005**	2.159	1.631 – 2.687	**<0.001**
MIDUS Wave	-0.185	-0.224 – -0.146	**<0.001**	-0.117	-0.179 – -0.056	**<0.001**	-0.326	-0.363 – -0.289	**<0.001**
HF HRV (baseline)	-0.053	-0.094 – -0.012	**0.012**	-0.032	-0.080 – 0.016	0.189	-0.055	-0.095 – -0.014	**0.008**
MIDUS Wave x HF HRV	0.030	-0.001 – 0.061	0.057	0.027	-0.021 – 0.076	0.273	0.035	0.005 – 0.064	**0.020**
Covariates									
EPI	-0.014	-0.097 – 0.070	0.747	0.004	-0.085 – 0.093	0.938	-0.010	-0.092 – 0.072	0.808
Gender	0.039	-0.056 – 0.133	0.423	0.571	0.470 – 0.673	**<0.001**	-0.147	-0.240 – -0.054	**0.002**
Age	-0.026	-0.031 – -0.021	**<0.001**	-0.021	-0.026 – -0.016	**<0.001**	-0.025	-0.030 – -0.021	**<0.001**
Years between Waves	-0.170	-0.227 – -0.112	**<0.001**	-0.092	-0.154 – -0.031	**0.003**	-0.177	-0.233 – -0.121	**<0.001**
Circulatory	-0.184	-0.350 – -0.017	**0.031**	-0.200	-0.378 – -0.023	**0.027**	-0.178	-0.341 – -0.015	**0.033**
Heart Disease	-0.082	-0.260 – 0.097	0.369	-0.040	-0.230 – 0.150	0.682	-0.070	-0.244 – 0.104	0.431
High BP	-0.123	-0.238 – -0.007	**0.037**	0.008	-0.116 – 0.131	0.904	-0.115	-0.229 – -0.002	**0.045**
Heart Murmur	0.071	-0.069 – 0.210	0.320	-0.010	-0.160 – 0.139	0.891	0.084	-0.053 – 0.221	0.229
TIA/Stroke	-0.095	-0.372 – 0.182	0.503	-0.243	-0.533 – 0.048	0.102	-0.124	-0.391 – 0.143	0.363
Emphysema/COPD	-0.078	-0.379 – 0.222	0.609	0.243	-0.075 – 0.562	0.135	-0.207	-0.500 – 0.086	0.166
Major Depressive Disorder	-0.028	-0.145 – 0.089	0.641	-0.091	-0.216 – 0.034	0.155	-0.049	-0.164 – 0.066	0.404
Medication	-0.060	-0.122 – 0.002	0.056	-0.065	-0.131 – 0.002	0.056	-0.048	-0.109 – 0.012	0.117
Random Effects									
σ^2		0.16			0.43			0.16	
τ_{00}		0.39			0.33			0.38	

	BTACT	Episodic Memory	Executive Functioning
ICC	0.71	0.43	0.71
N	867	869	869
Observations	1666	1733	1738
Marginal R^2 / Conditional R^2	0.187 / 0.764	0.166 / 0.527	0.222 / 0.773

Table S2: Association of EPI concentration with change in cognitive functioning

	BTACT			Episodic Memory			Executive Functioning		
	Estimates	*CI*	*p*	*Estimates*	*CI*	*p*	*Estimates*	*CI*	*p*
Intercept (M2)	1.955	1.416 – 2.493	**<0.001**	0.827	0.251 – 1.402	**0.005**	2.159	1.631 – 2.687	**<0.001**
Midus Wave	-0.184	-0.223 – -0.145	**<0.001**	-0.117	-0.179 – -0.056	**<0.001**	-0.326	-0.363 – -0.289	**<0.001**
EPI	-0.043	-0.133 – 0.048	0.354	0.003	-0.101 – 0.108	0.950	-0.019	-0.107 – 0.069	0.677
MIDUS Wave x EPI	0.059	-0.011 – 0.129	0.097	0.000	-0.109 – 0.110	0.994	0.017	-0.049 – 0.083	0.611
Covariates									
HF HRV (baseline)	-0.039	-0.077 – -0.000	**0.049**	-0.018	-0.059 – 0.023	0.380	-0.037	-0.075 – 0.000	0.053
Age	-0.026	-0.031 – -0.021	**<0.001**	-0.021	-0.026 – -0.016	**<0.001**	-0.025	-0.030 – -0.021	**<0.001**
Gender	0.039	-0.056 – 0.134	0.421	0.571	0.470 – 0.672	**<0.001**	-0.147	-0.240 – -0.054	**0.002**
Years between Waves	-0.169	-0.227 – -0.112	**<0.001**	-0.092	-0.154 – -0.031	**0.003**	-0.177	-0.233 – -0.121	**<0.001**
Circulatory	-0.186	-0.353 – -0.020	**0.028**	-0.200	-0.378 – -0.023	**0.027**	-0.178	-0.341 – -0.015	**0.033**
Heart Disease	-0.082	-0.260 – 0.096	0.368	-0.040	-0.230 – 0.150	0.680	-0.070	-0.244 – 0.104	0.431
High BP	-0.122	-0.237 – -0.006	**0.039**	0.008	-0.116 – 0.131	0.904	-0.115	-0.229 – -0.002	**0.045**
Heart Murmur	0.072	-0.068 – 0.211	0.313	-0.010	-0.159 – 0.139	0.891	0.084	-0.053 – 0.221	0.229
TIA/Stroke	-0.095	-0.372 – 0.182	0.501	-0.243	-0.533 – 0.048	0.102	-0.124	-0.391 – 0.143	0.363
Emphysema/COPD	-0.077	-0.377 – 0.223	0.615	0.243	-0.075 – 0.562	0.134	-0.207	-0.500 – 0.086	0.166
Major Depressive Disorder	-0.027	-0.144 – 0.090	0.648	-0.091	-0.216 – 0.034	0.155	-0.049	-0.164 – 0.066	0.404
Medication	-0.061	-0.122 – 0.001	0.055	-0.065	-0.131 – 0.002	0.056	-0.048	-0.109 – 0.012	0.117
Random Effects									
σ^2		0.16			0.43			0.16	
τ_{00}		0.39			0.33			0.38	

	BTACT	Episodic Memory	Executive Functioning
ICC	0.71	0.43	0.71
N	867	869	869
Observations	1666	1733	1738
Marginal R^2 / Conditional R^2	0.187 / 0.763	0.165 / 0.527	0.221 / 0.772

Table S3: Association of HF HRV recovery with change in cognitive functioning

	BTACT			Episodic Memory			Executive Functioning		
	Estimates	*CI*	*p*	*Estimates*	*CI*	*p*	*Estimates*	*CI*	*p*
Intercept (M2)	1.960	1.416 – 2.503	**<0.001**	0.793	0.216 – 1.369	**0.007**	2.170	1.635 – 2.705	**<0.001**
MIDUS Wave	-0.184	-0.223 – -0.145	**<0.001**	-0.119	-0.182 – -0.057	**<0.001**	-0.326	-0.364 – -0.289	**<0.001**
HF HRV (recovery)	-0.073	-0.154 – 0.009	0.082	-0.072	-0.166 – 0.023	0.137	-0.030	-0.110 – 0.051	0.470
MIDUS Wave x HF HRV	0.071	0.007 – 0.135	**0.030**	0.013	-0.086 – 0.113	0.792	0.039	-0.021 – 0.099	0.204
Covariates									
EPI	-0.007	-0.091 – 0.078	0.878	0.017	-0.073 – 0.107	0.712	-0.010	-0.093 – 0.073	0.814
Age	-0.025	-0.029 – -0.020	**<0.001**	-0.020	-0.025 – -0.015	**<0.001**	-0.024	-0.028 – -0.019	**<0.001**
Gender	0.026	-0.070 – 0.122	0.590	0.564	0.463 – 0.666	**<0.001**	-0.158	-0.252 – -0.064	**0.001**
Years between Waves	-0.171	-0.228 – -0.113	**<0.001**	-0.090	-0.151 – -0.029	**0.004**	-0.179	-0.236 – -0.122	**<0.001**
Circulatory	-0.198	-0.365 – -0.032	**0.020**	-0.210	-0.386 – -0.033	**0.020**	-0.187	-0.351 – -0.024	**0.025**
Heart Disease	-0.101	-0.280 – 0.079	0.272	-0.051	-0.241 – 0.140	0.602	-0.094	-0.270 – 0.082	0.296
High BP	-0.130	-0.247 – -0.014	**0.029**	0.001	-0.123 – 0.124	0.992	-0.124	-0.238 – -0.009	**0.035**
Heart Murmur	0.081	-0.059 – 0.221	0.256	-0.007	-0.156 – 0.142	0.931	0.095	-0.043 – 0.233	0.177
TIA/Stroke	-0.095	-0.373 – 0.182	0.502	-0.204	-0.498 – 0.091	0.175	-0.132	-0.405 – 0.142	0.345
Emphysema/COPD	-0.079	-0.379 – 0.222	0.608	0.248	-0.069 – 0.564	0.126	-0.208	-0.502 – 0.086	0.166
Depression	-0.023	-0.141 – 0.095	0.698	-0.080	-0.205 – 0.045	0.210	-0.044	-0.160 – 0.072	0.456
Medication	-0.048	-0.110 – 0.014	0.130	-0.053	-0.119 – 0.013	0.119	-0.041	-0.103 – 0.020	0.185

Random Effects

σ^2		0.16			0.42			0.15	
τ_{00}		0.39			0.32			0.38	

	BTACT	Episodic Memory	Executive Functioning
ICC	0.71	0.43	0.71
N	843	844	844
Observations	1622	1683	1688
Marginal R^2 / Conditional R^2	0.181 / 0.764	0.162 / 0.523	0.215 / 0.774

Table S4: HF HRV recovery and EPI interactively predict change in cognitive functioning

	BTACT			Episodic Memory			Executive Functioning		
	Estimates	*CI*	*p*	*Estimates*	*CI*	*p*	*Estimates*	*CI*	*p*
Intercept (M2)	1.958	1.415 – 2.501	**<0.001**	0.793	0.215 – 1.370	**0.007**	2.169	1.634 – 2.704	**<0.001**
MIDUS Wave	-0.182	-0.221 – -0.143	**<0.001**	-0.118	-0.180 – -0.055	**<0.001**	-0.323	-0.360 – -0.286	**<0.001**
HF HRV (recovery)	-0.080	-0.162 – 0.002	0.056	-0.076	-0.171 – 0.019	0.115	-0.036	-0.117 – 0.044	0.378
EPI	-0.033	-0.125 – 0.058	0.475	0.021	-0.085 – 0.126	0.703	-0.018	-0.108 – 0.072	0.695
HF HRV x EPI	0.150	-0.011 – 0.311	0.067	0.088	-0.099 – 0.275	0.357	0.137	-0.021 – 0.296	0.090
Wave x EPI	0.053	-0.017 – 0.123	0.135	-0.007	-0.117 – 0.104	0.903	0.016	-0.050 – 0.082	0.633
Wave x HF HRV	0.075	0.011 – 0.139	**0.021**	0.021	-0.079 – 0.121	0.679	0.051	-0.009 – 0.111	0.095
Wave x HF HRV x EPI	-0.176	-0.305 – -0.048	**0.007**	-0.149	-0.347 – 0.049	0.141	-0.248	-0.367 – -0.130	**<0.001**
Covariates									
Age	-0.025	-0.029 – -0.020	**<0.001**	-0.020	-0.025 – -0.015	**<0.001**	-0.024	-0.028 – -0.019	**<0.001**
Gender	0.028	-0.068 – 0.124	0.564	0.565	0.463 – 0.666	**<0.001**	-0.158	-0.252 – -0.063	**0.001**
Years between Waves	-0.171	-0.228 – -0.113	**<0.001**	-0.090	-0.152 – -0.029	**0.004**	-0.179	-0.236 – -0.122	**<0.001**
Circulatory	-0.202	-0.368 – -0.035	**0.018**	-0.210	-0.387 – -0.034	**0.020**	-0.188	-0.352 – -0.024	**0.025**
Heart Disease	-0.099	-0.278 – 0.081	0.281	-0.051	-0.241 – 0.140	0.603	-0.094	-0.270 – 0.082	0.296
High BP	-0.129	-0.246 – -0.013	**0.030**	0.001	-0.123 – 0.124	0.991	-0.124	-0.238 – -0.009	**0.035**
Heart Murmur	0.083	-0.057 – 0.223	0.247	-0.007	-0.156 – 0.142	0.932	0.095	-0.043 – 0.233	0.177
TIA/Stroke	-0.106	-0.384 – 0.172	0.456	-0.206	-0.501 – 0.090	0.172	-0.134	-0.408 – 0.141	0.340
Emphysema/COPD	-0.080	-0.380 – 0.221	0.602	0.248	-0.069 – 0.565	0.125	-0.207	-0.502 – 0.087	0.168
Major Depressive Disorder	-0.021	-0.139 – 0.097	0.725	-0.080	-0.205 – 0.046	0.212	-0.044	-0.160 – 0.072	0.460

	BTACT			Episodic Memory			Executive Functioning		
	Estimates	*CI*	*p*	*Estimates*	*CI*	*p*	*Estimates*	*CI*	*p*
Medication	-0.051	-0.113 – 0.012	0.111	-0.053	-0.119 – 0.013	0.117	-0.042	-0.103 – 0.020	0.182
Random Effects									
σ^2		0.16			0.42			0.15	
τ_{00}		0.39			0.32			0.38	
ICC		0.71			0.43			0.72	
N		843			844			844	
Observations		1622			1683			1688	
Marginal R^2 / Conditional R^2		0.184 / 0.766			0.163 / 0.523			0.217 / 0.778	

Table S5: HF HRV reactivity and EPI interactively predict change in cognitive functioning

	BTACT			Episodic Memory			Executive Functioning		
	Estimates	*CI*	*p*	*Estimates*	*CI*	*p*	*Estimates*	*CI*	*p*
Intercept (M2)	1.948	1.405 – 2.491	**<0.001**	0.797	0.220 – 1.375	**0.007**	2.160	1.626 – 2.695	**<0.001**
MIDUS Wave	-0.185	-0.223 – -0.146	**<0.001**	-0.114	-0.176 – -0.053	**<0.001**	-0.327	-0.364 – -0.290	**<0.001**
HF HRV (reactivity)	0.065	-0.022 – 0.153	0.143	0.044	-0.058 – 0.145	0.399	0.034	-0.053 – 0.120	0.445
EPI	-0.028	-0.119 – 0.063	0.549	0.019	-0.087 – 0.124	0.728	-0.009	-0.099 – 0.080	0.837
HF HRV x EPI	-0.202	-0.370 – -0.034	**0.018**	-0.131	-0.326 – 0.064	0.187	-0.200	-0.365 – -0.035	**0.018**
Wave x EPI	0.050	-0.019 – 0.120	0.152	-0.008	-0.118 – 0.102	0.883	0.012	-0.053 – 0.078	0.714
Wave x HF HRV	-0.051	-0.119 – 0.017	0.142	0.027	-0.079 – 0.134	0.615	-0.038	-0.102 – 0.026	0.241
Wave x HF HRV x EPI	0.192	0.054 – 0.330	**0.006**	0.234	0.029 – 0.439	**0.025**	0.263	0.140 – 0.385	**<0.001**
Covariates									
Age	-0.025	-0.030 – -0.020	**<0.001**	-0.021	-0.026 – -0.016	**<0.001**	-0.024	-0.029 – -0.020	**<0.001**
Gender	0.035	-0.061 – 0.130	0.480	0.570	0.469 – 0.672	**<0.001**	-0.153	-0.247 – -0.058	**0.002**
Years between Waves	-0.169	-0.227 – -0.111	**<0.001**	-0.091	-0.152 – -0.029	**0.004**	-0.177	-0.234 – -0.121	**<0.001**
Circulatory	-0.200	-0.367 – -0.033	**0.019**	-0.212	-0.389 – -0.035	**0.019**	-0.189	-0.353 – -0.024	**0.024**
Heart Disease	-0.101	-0.280 – 0.078	0.267	-0.057	-0.247 – 0.133	0.554	-0.088	-0.263 – 0.088	0.329
High BP	-0.124	-0.240 – -0.007	**0.038**	0.007	-0.117 – 0.131	0.913	-0.119	-0.234 – -0.004	**0.042**
Heart Murmur	0.074	-0.066 – 0.214	0.299	-0.009	-0.158 – 0.140	0.909	0.085	-0.053 – 0.222	0.229
TIA/Stroke	-0.093	-0.376 – 0.191	0.522	-0.180	-0.481 – 0.122	0.242	-0.125	-0.404 – 0.155	0.382
Emphysema/COPD	-0.088	-0.389 – 0.214	0.569	0.242	-0.076 – 0.561	0.136	-0.211	-0.507 – 0.085	0.162
Major Depressive Disorder	-0.025	-0.143 – 0.094	0.685	-0.082	-0.208 – 0.044	0.202	-0.046	-0.163 – 0.070	0.436

	BTACT			Episodic Memory			Executive Functioning		
	Estimates	*CI*	*p*	*Estimates*	*CI*	*p*	*Estimates*	*CI*	*p*
Medication	-0.053	-0.116 – 0.009	0.094	-0.055	-0.122 – 0.011	0.104	-0.042	-0.104 – 0.019	0.176
Random Effects									
σ^2		0.16			0.42			0.15	
τ_{00}		0.39			0.33			0.39	
ICC		0.72			0.44			0.72	
N		854			855			855	
Observations		1642			1705			1710	
Marginal R^2 / Conditional R^2		0.186 / 0.770			0.164 / 0.528			0.219 / 0.781	

Table S6. Follow-up analyses of PNS x SNS on change in BTACT scores using quadratic index of PNS responsivity

	BTACT		
	Estimates	*CI*	*p*
Intercept (M2)	1.990	1.451 – 2.529	**<0.001**
MIDUS Wave	-0.183	-0.222 – -0.144	**<0.001**
HF HRV (quadratic index)	-0.052	-0.109 – 0.005	0.072
EPI	-0.037	-0.127 – 0.054	0.427
HF HRV x EPI*	0.119	0.005 – 0.233	**0.041**
Wave x HF HRV	0.044	0.000 – 0.089	**0.049**
Wave x EPI	0.054	-0.016 – 0.123	0.129
Wave x HF HRV x EPI	-0.128	-0.218 – -0.037	**0.006**
Covariates			
Age	-0.025	-0.030 – -0.021	**<0.001**
Gender	0.036	-0.059 – 0.131	0.456
Years between Waves	-0.174	-0.231 – -0.116	**<0.001**
Circulatory	-0.200	-0.367 – -0.034	**0.019**
Heart Disease	-0.095	-0.274 – 0.083	0.296
High BP	-0.125	-0.241 – -0.009	**0.034**
Heart Murmur	0.074	-0.066 – 0.214	0.298
TIA/Stroke	-0.093	-0.371 – 0.185	0.510
Emphysema/COPD	-0.070	-0.372 – 0.231	0.647
Major Depressive Disorder	-0.023	-0.141 – 0.095	0.699
Medication	-0.057	-0.119 – 0.005	0.073
Random Effects			
σ^2		0.16	
τ_{00}		0.39	
ICC		0.71	
N		865	
Observations		1662	
Marginal R^2 / Conditional R^2		0.188 / 0.766	

*Although significant in the MLM, these effects are not evident in cross-sectional models focused on MIDUS 2.

Table S7: Age weakly and inconsistently moderates the interaction between HRV and EPI on changes in cognitive functioning (BTACT scores)

	Baseline HRV			HRV Reactivity			HRV Recovery		
	Estimates	*CI*	*p*	*Estimates*	*CI*	*p*	*Estimates*	*CI*	*p*
Intercept	1.875	1.336 – 2.414	**<0.001**	1.911	1.367 – 2.455	**<0.001**	1.941	1.397 – 2.484	**<0.001**
MIDUS Wave	-0.207	-0.250 – -0.164	**<0.001**	-0.197	-0.238 – -0.156	**<0.001**	-0.194	-0.236 – -0.153	**<0.001**
HF HRV	-0.066	-0.110 – -0.021	**0.004**	0.088	-0.007 – 0.183	0.069	-0.105	-0.196 – -0.015	**0.023**
EPI	-0.032	-0.132 – 0.069	0.537	0.010	-0.090 – 0.109	0.848	0.002	-0.098 – 0.102	0.969
Age	-0.027	-0.032 – -0.022	**<0.001**	-0.025	-0.030 – -0.020	**<0.001**	-0.025	-0.030 – -0.020	**<0.001**
Wave x HF HRV	0.041	0.007 – 0.075	**0.019**	-0.048	-0.121 – 0.024	0.193	0.070	0.000 – 0.140	**0.049**
Wave x EPI	0.042	-0.036 – 0.120	0.292	0.019	-0.056 – 0.095	0.616	0.026	-0.050 – 0.102	0.508
Wave x Age	0.002	-0.002 – 0.006	0.244	0.001	-0.002 – 0.005	0.441	0.001	-0.002 – 0.005	0.470
HF HRV x EPI	0.085	-0.000 – 0.169	0.051	-0.226	-0.429 – -0.023	**0.029**	0.144	-0.046 – 0.334	0.138
HF HRV x Age	0.005	0.001 – 0.009	**0.010**	-0.008	-0.016 – -0.000	**0.045**	0.007	-0.001 – 0.015	0.071
EPI x Age	-0.007	-0.015 – 0.002	0.109	-0.009	-0.018 – -0.000	**0.048**	-0.008	-0.016 – 0.001	0.085
Wave x HF HRV x EPI	-0.047	-0.114 – 0.020	0.165	0.238	0.085 – 0.392	**0.002**	-0.225	-0.369 – -0.081	**0.002**
Wave x HF HRV x Age	-0.002	-0.005 – 0.001	0.225	0.001	-0.006 – 0.007	0.818	-0.001	-0.008 – 0.005	0.652
Wave x EPI x Age	0.006	-0.001 – 0.013	0.086	0.007	-0.000 – 0.013	0.056	0.006	-0.001 – 0.013	0.097
HF HRV x EPI x Age	-0.010	-0.016 – -0.003	**0.002**	0.009	-0.006 – 0.023	0.234	-0.006	-0.020 – 0.009	0.437
Wave x HF HRV x EPI x Age	0.004	-0.001 – 0.009	0.102	-0.011	-0.023 – 0.002	0.103	0.011	-0.001 – 0.023	0.062
Covariates									
Gender	0.042	-0.052 – 0.137	0.381	0.042	-0.053 – 0.138	0.385	0.037	-0.059 – 0.134	0.445

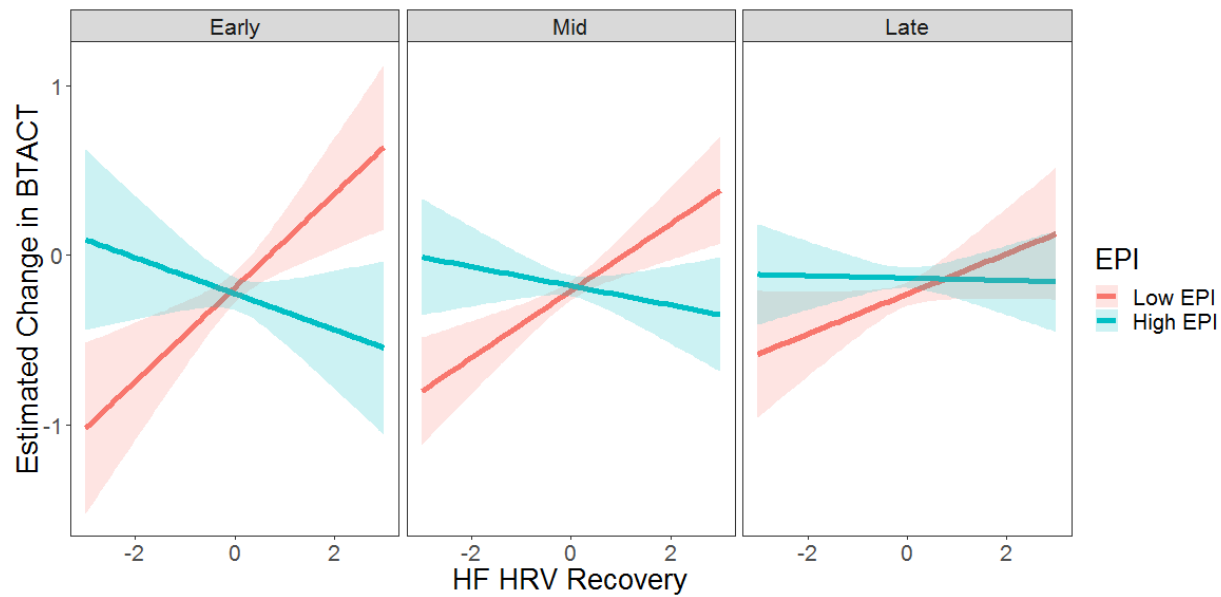|	Baseline HRV			HRV Reactivity			HRV Recovery		
	Estimates	*CI*	*p*	*Estimates*	*CI*	*p*	*Estimates*	*CI*	*p*
Years between Waves	-0.157	-0.215 – -0.100	**<0.001**	-0.164	-0.222 – -0.106	**<0.001**	-0.168	-0.226 – -0.110	**<0.001**
Circulatory	-0.181	-0.347 – -0.015	**0.033**	-0.194	-0.361 – -0.027	**0.023**	-0.196	-0.362 – -0.029	**0.021**
Heart Disease	-0.091	-0.268 – 0.087	0.317	-0.095	-0.274 – 0.084	0.300	-0.097	-0.276 – 0.082	0.289
High BP	-0.131	-0.246 – -0.016	**0.026**	-0.123	-0.239 – -0.006	**0.039**	-0.130	-0.246 – -0.013	**0.030**
Heart Murmur	0.080	-0.059 – 0.219	0.260	0.071	-0.070 – 0.211	0.324	0.085	-0.056 – 0.225	0.239
TIA/Stroke	-0.090	-0.367 – 0.186	0.522	-0.073	-0.357 – 0.212	0.616	-0.091	-0.371 – 0.188	0.521
Emphysema/COPD	-0.077	-0.377 – 0.222	0.614	-0.092	-0.394 – 0.210	0.549	-0.083	-0.385 – 0.219	0.589
Major Depressive Disorder	-0.038	-0.156 – 0.079	0.520	-0.031	-0.149 – 0.088	0.611	-0.029	-0.147 – 0.090	0.634
Medication	-0.059	-0.120 – 0.003	0.062	-0.049	-0.111 – 0.014	0.126	-0.047	-0.110 – 0.015	0.137
Random Effects									
σ^2		0.16			0.15			0.16	
τ_{00}		0.38			0.39			0.39	
ICC		0.71			0.72			0.72	
N		867			854			843	
Observations		1666			1642			1622	
Marginal R^2 / Conditional R^2		0.196 / 0.766			0.190 / 0.772			0.187 / 0.768	

Figure S1. Estimated change in BTACT scores (MIDUS 3 – MIDUS 2) at ±1SD EPI concentration for a 40 (early), 50 (mid), and 60 (late) year old at MIDUS 2 (and thus, approximately 50, 60, and year old at MIDUS 3) across a range of HF HRV recovery values. Larger positive HF HRV recovery values indicate a stronger recovery following a cognitive challenge. Point estimates of change in BTACT represent the slope connecting MIDUS 3 and MIDUS 2 and were derived from the multilevel model.

Table S8: Norepinephrine moderates HRV association with change in cognitive functioning (BTACT scores)

	Baseline HRV			HRV Reactivity			HRV Recovery		
	Estimates	*CI*	*p*	*Estimates*	*CI*	*p*	*Estimates*	*CI*	*p*
Intercept	1.956	1.418 – 2.494	**<0.001**	1.943	1.401 – 2.484	**<0.001**	1.956	1.415 – 2.497	**<0.001**
MIDUS Wave	-0.185	-0.224 – -0.146	**<0.001**	-0.182	-0.221 – -0.143	**<0.001**	-0.180	-0.220 – -0.141	**<0.001**
HF HRV	-0.055	-0.096 – -0.014	**0.009**	0.073	-0.016 – 0.161	0.108	-0.083	-0.165 – -0.000	**0.049**
Norepinephrine (NE)	-0.075	-0.199 – 0.048	0.232	-0.052	-0.178 – 0.074	0.419	-0.048	-0.174 – 0.078	0.454
Wave x NE	0.048	-0.042 – 0.138	0.295	0.020	-0.069 – 0.110	0.660	0.017	-0.073 – 0.107	0.710
Wave x HF HRV	0.032	0.001 – 0.063	**0.045**	-0.058	-0.126 – 0.011	0.100	0.077	0.013 – 0.141	**0.019**
HF HRV x NE	0.029	-0.060 – 0.117	0.526	-0.254	-0.457 – -0.051	**0.014**	0.222	0.032 – 0.413	**0.022**
Wave x HF HRV x NE	-0.005	-0.074 – 0.063	0.877	0.161	0.001 – 0.321	**0.048**	-0.158	-0.308 – -0.008	**0.039**
Covariates									
Age	-0.026	-0.031 – -0.021	**<0.001**	-0.025	-0.030 – -0.020	**<0.001**	-0.024	-0.029 – -0.020	**<0.001**
Gender	0.049	-0.048 – 0.147	0.322	0.042	-0.057 – 0.141	0.405	0.037	-0.062 – 0.136	0.469
Years between Waves	-0.170	-0.228 – -0.113	**<0.001**	-0.170	-0.228 – -0.112	**<0.001**	-0.171	-0.229 – -0.113	**<0.001**
Circulatory	-0.183	-0.350 – -0.016	**0.031**	-0.204	-0.371 – -0.038	**0.016**	-0.208	-0.374 – -0.041	**0.015**
Heart Disease	-0.084	-0.262 – 0.095	0.358	-0.102	-0.281 – 0.076	0.262	-0.099	-0.279 – 0.080	0.277
High BP	-0.118	-0.234 – -0.002	**0.046**	-0.121	-0.238 – -0.004	**0.043**	-0.128	-0.245 – -0.011	**0.032**
Heart Murmur	0.069	-0.071 – 0.208	0.333	0.071	-0.069 – 0.211	0.320	0.078	-0.062 – 0.218	0.274
TIA/Stroke	-0.093	-0.369 – 0.183	0.509	-0.090	-0.373 – 0.192	0.531	-0.106	-0.382 – 0.171	0.454
Emphysema/COPD	-0.068	-0.369 – 0.234	0.660	-0.083	-0.385 – 0.219	0.591	-0.082	-0.383 – 0.218	0.591

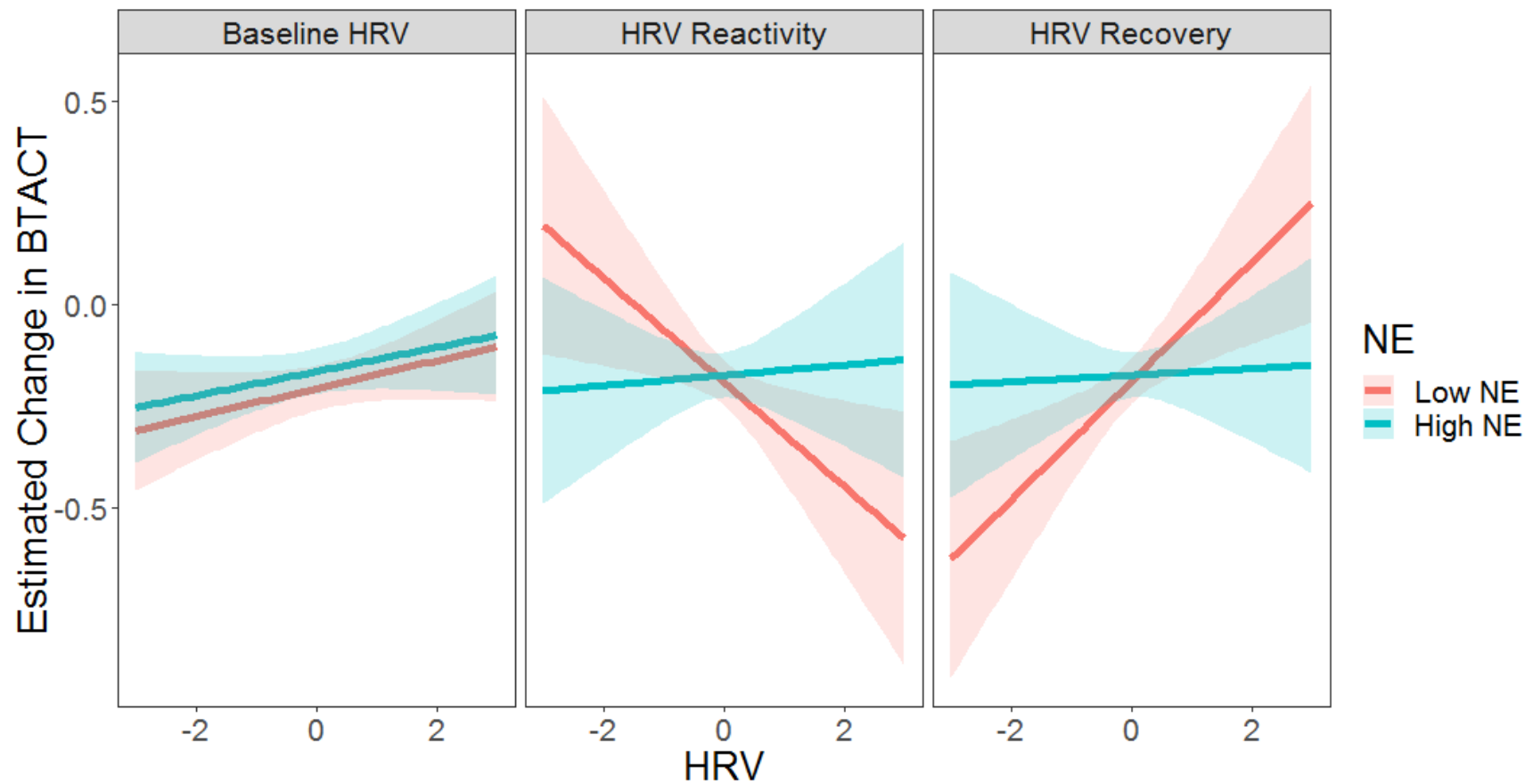|	Baseline HRV			HRV Reactivity			HRV Recovery		
	Estimates	*CI*	*p*	*Estimates*	*CI*	*p*	*Estimates*	*CI*	*p*
Major Depressive Disorder	-0.026	-0.143 – 0.092	0.668	-0.022	-0.141 – 0.096	0.710	-0.019	-0.137 – 0.099	0.757
Medication	-0.058	-0.120 – 0.004	0.068	-0.052	-0.115 – 0.010	0.102	-0.051	-0.113 – 0.011	0.110
Random Effects									
σ^2		0.16			0.16			0.16	
τ_{00}		0.39			0.39			0.39	
ICC		0.71			0.72			0.71	
N		867			854			843	
Observations		1666			1642			1622	
Marginal R^2 / Conditional R^2		0.188 / 0.764			0.186 / 0.768			0.184 / 0.765	

Figure S2: Estimated change in BTACT scores (MIDUS 3 – MIDUS 2) at ±1SD norepinephrine concentration across range of HF HRV values. Point estimates of change in BTACT represent the slope connecting MIDUS 2 to MIDUS 3 derived from the multilevel model. Larger HRV values for baseline and recovery represent stronger vagal tone; larger values for reactivity represent strong HRV withdrawal, indicative of weaker vagal tone.

Table S9: HF HRV reactivity to orthostatic challenge and EPI levels do not interactively predict change in cognitive functioning (BTACT scores)

	HF HRV Reactivity to Orthostatic Challenge		
	Estimates	*CI*	*p*
Intercept	2.048	1.501 – 2.595	**<0.001**
MIDUS Wave	-0.196	-0.251 – -0.141	**<0.001**
HF HRV (reactivity)	0.040	-0.019 – 0.099	0.182
EPI	-0.048	-0.174 – 0.078	0.456
Wave x EPI	0.077	-0.020 – 0.174	0.119
Wave x HF HRV	-0.022	-0.067 – 0.024	0.352
HF HRV x EPI	-0.012	-0.120 – 0.095	0.822
Wave x HF HRV x EPI	0.030	-0.053 – 0.113	0.483
Covariates			
Age	-0.024	-0.029 – -0.020	**<0.001**
Gender	0.028	-0.069 – 0.126	0.568
Years between Waves	-0.177	-0.235 – -0.119	**<0.001**
Circulatory	-0.224	-0.394 – -0.054	**0.010**
Heart Disease	-0.088	-0.271 – 0.096	0.349
High BP	-0.142	-0.260 – -0.023	**0.019**
Heart Murmur	0.095	-0.048 – 0.238	0.192
TIA/Stroke	-0.073	-0.358 – 0.212	0.614
Emphysema/COPD	-0.073	-0.376 – 0.230	0.638
Major Depressive Disorder	-0.012	-0.132 – 0.108	0.844
Medication	-0.049	-0.112 – 0.014	0.128
Random Effects			
σ^2		0.16	
τ_{00}		0.39	
ICC		0.71	
N		827	
Observations		1590	
Marginal R^2 / Conditional R^2		0.182 / 0.762	