Supplementary Table 1. Comparison of Adverse Events Between Atomoxetine and Placebo Treatments
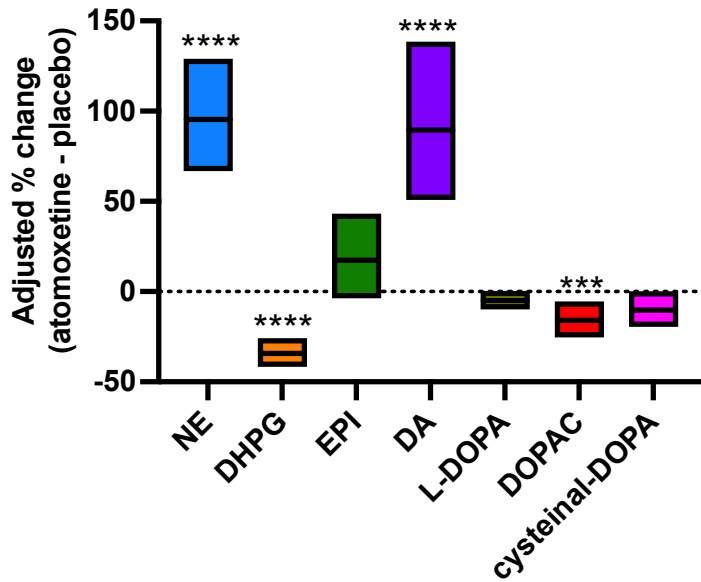
Symptom	Atomoxetine (n=39)	Placebo (n=37)
Serious Adverse Event, n (%)		
Fractured right pelvis	1 (2.6)	0
Acute appendicitis	0	1 (2.7)
Hypothermia/dizziness	1 (2.6)	0
Severe Elevated Blood Pressure	0	1 (2.7)
Dysautonomia	1 (2.6)	0
Headache Pain	0	1 (2.7)
Non-Serious Adverse Event, n (%)		
Gastrointestinal symptoms	12 (30.8)	4 (10.8)
Dry mouth	10 (25.6)	2 (5.4)
Dizziness	10 (25.6)	8 (21.6)
Falls	6 (15.4)	2 (5.4)
Upper respiratory infection	6 (15.4)	9 (24.3)
Headache	5 (12.8)	2 (5.4)
Constipation	4 (10.3)	1 (2.7)
Suicide	3 (7.7)	0
Tremor	3 (7.7)	0
Agitation	3 (7.7)	1 (2.7)
Loss of appetite	3 (7.7)	1 (2.7)
Fatigue	3 (7.7)	3 (8.1)
Fracture	2 (5.1)	0
Loss of Weigh	2 (5.1)	0
Anxiety	2 (5.1)	1 (2.7)
Injury	2 (5.1)	1 (2.7)
Rash	2 (5.1)	2 (5.4)
Hypokalemia	1 (2.6)	2 (5.4)
Pre-Cancerous	1 (2.6)	2 (5.4)
Back pain	1 (2.6)	3 (8.1)
Cancer	1 (2.6)	3 (8.1)
Cramp	0	2 (5.4)

*Only the Adverse Events above 5% threshold are listed under the Non-Serious Adverse Event.
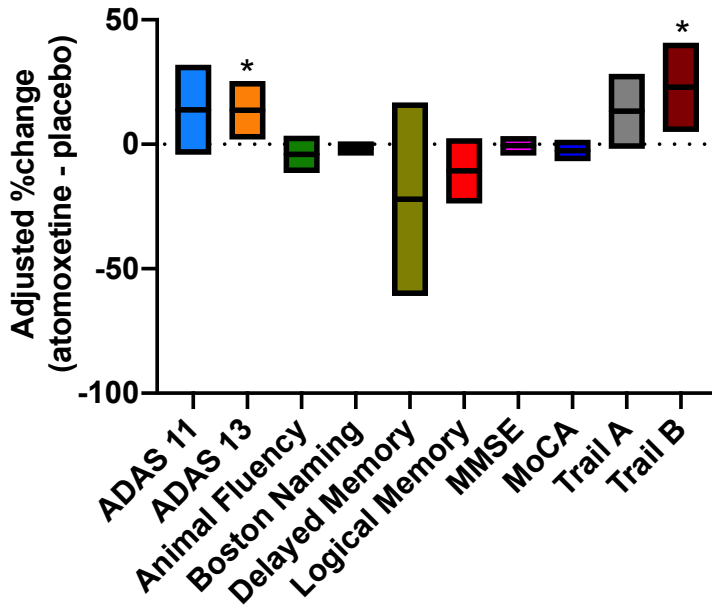
Supplementary Table 2. Comparison of Change in Blood Pressure and Heart Rate between two Treatment Arms

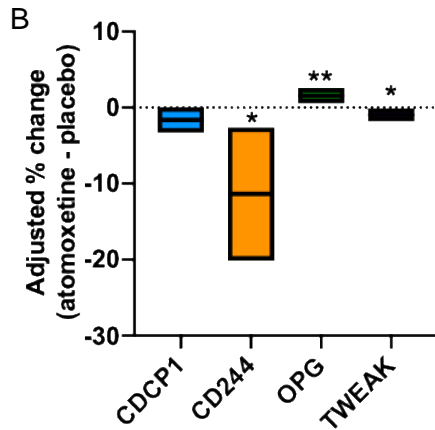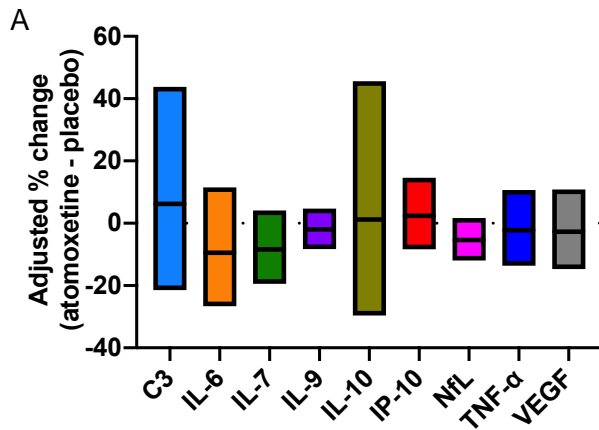| Variable	Visit	Active/Placebo Median (P25 - P75) (n)	Placebo/Active Median (P25 - P75) (n)	p value
Change in systolic BP from baseline	6 month	5.5 (-9.0, 12.0) (18)	4.0 (-6.0, 15.0) (19)	0.86
	12 month	-4.0 (-10, 10.0) (17)	3.0 (-7.0, 19.0) (19)	0.25
% Change in systolic BP from baseline	6 month	4.3 (-6.5, 7.6) (18)	2.6 (-4.6, 12.8) (19)	0.94
	12 month	-3.2 (-7.6, 6.8) (17)	3.0 (-5.3, 14.6) (19)	0.21
Change in diastolic BP from baseline	6 month	3.5 (-5.0, 6.0) (18)	1.0 (-5.0, 11.0) (19)	0.81
	12 month	-4.0 (-9.0, 2.0) (17)	-3.0 (-8.0, 7.0) (19)	0.22
% Change in diastolic BP from baseline	6 month	4.4 (-6.2, 8.3) (18)	1.4 (-6.2, 16.4) (19)	0.83
	12 month	-4.9 (-11, 3.1) (17)	-4.1 (-12, 9.2) (19)	0.27
Change in heart rate from baseline	6 month	9.0 (6.0, 12.0) (17)	1.0 (-4.0, 5.0) (19)	0.0006
	12 month	4.0 (-2.0, 8.0) (17)	8.0 (5.0, 12.0) (19)	0.012
% Change in heart rate from baseline	6 month	14.8 (10.3, 19.4) (17)	2.2 (-6.5, 8.6) (19)	0.0006
	12 month	6.9 (-3.4, 10.5) (17)	13.8 (8.7, 24.5) (19)	0.0107
Change in weight from baseline	6 month	-4.0 (-15, 0.0) (18)	-1.0 (-3.0, 1.0) (19)	0.07
	12 month	-1.0 (-6.0, 3.0) (17)	-4.0 (-7.0, -1.0) (19)	0.25
% Change in weight from baseline	6 month	-3.0 (-7.0, 0.0) (18)	-0.8 (-2.0, 0.6) (19)	0.07
	12 month	-0.9 (-3.3, 2.3) (17)	-2.3 (-4.8, -0.8) (19)	0.24

Supplementary Figure 1. Adjusted Effect of Atomoxetine vs Placebo on Plasma Biomarkers of Target Engagement. Catecholamine biomarkers show target engagement with norepinephrine (NE) reuptake inhibition, increasing levels of NE and dopamine (DA), both substrates for the NE transporter, and decreasing levels of catecholamine metabolites 3,4-dihydroxyphenylglycol (DHPG) and 3,4-dihydroxyphenylacetic acid (DOPAC). Values are estimated differences and corresponding 95% confidence (n=36). ***$p < 0.001$: ****$p < 0.0001$

Supplementary Figure 2. Adjusted Effect of Treatment of Atomoxetine vs Placebo on Neuropsychological Measures. Values are estimated differences and corresponding 95% confidence interval. The asterisked results for ADAS13 and Trails B were raw p values of *p<0.05, but were not significant after adjusting for multiple comparisons.

Supplementary Figure 3. Adjusted Effect of Treatment of Atomoxetine vs Placebo on Absolute Change in CSF Biomarkers of Inflammation. A) Immunoassays for targeted biomarkers shown. B) Proximity Extension Assays using Olink Inflammation panel. Only the significantly changed biomarkers are shown, from a panel of 92 analytes. Values are estimated differences and corresponding 95% confidence interval. * p<0.05; **p<0.01

Supplementary Figure 4. Adjusted Effect of Treatment of Atomoxetine vs Placebo on Absolute Change in Plasma Biomarkers. A) Luminex assay results for targeted plasma biomarkers shown (performed by Dr. William Hu). B) Mesoscale multi-plexed immune-assay results for plasma analytes (performed by Dr. Malú G. Tansey). Values are estimated differences and corresponding 95% confidence interval. *p<0.05