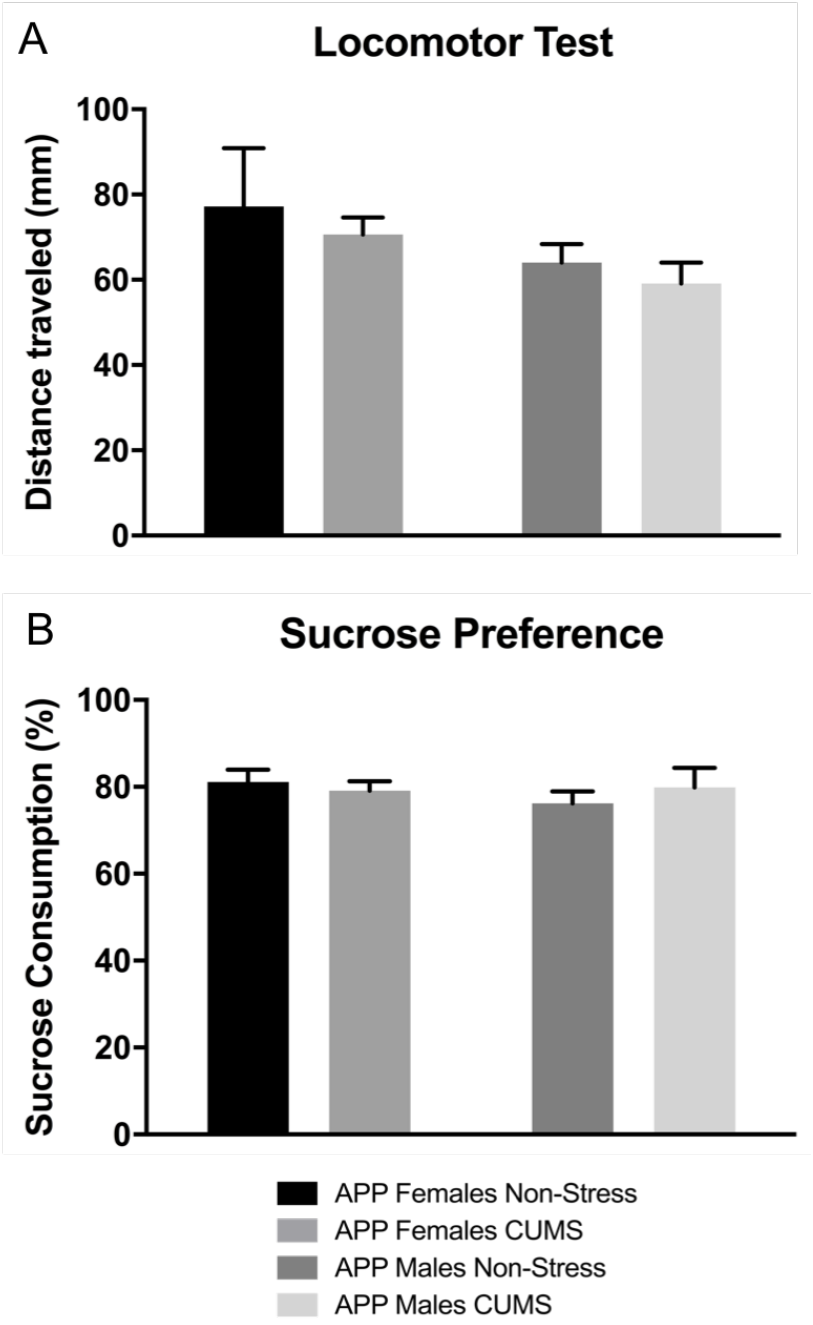
Supplementary Material

Sex Differences of the Phosphoproteomic Profiles in APP/PS1 Mice after Chronic Unpredictable Mild Stress

Stressor	Duration
No bedding	2 hours
Wet Bedding	2 hours
Cage Tilt	2 hours
Restraint	1 hour
Cold Water Swim	3 minutes
Food Deprivation	8 hours
Water Deprivation	8 hours
Isolation	Overnight
Light/Dark Cycle Alternation	2 days

Supplementary Figure 1. Timings of Stressors in our Chronic Unpredictable Mild Stress Model. A table of the stressors used for our chronic unpredictable stress model along with the duration of each stressor.



Supplementary Figure 2. Additional Behavioral Assessments. A) Locomotor test, showed no significant differences between sex or stress-condition in terms of total distance traveled. B) Sucrose preference, showed no significant differences among conditions or sexes in terms of amount of sucrose consumed, shown in percent of total consumption, as there was an overwhelming preference for sucrose water suggesting little anhedonia in any group.

Enriched motifs for significant phospho-peptides in male cohort

Motifs	Total size	Selection size	Category size	Intersection size	Enrichment factor	P value	Benj. Hoch. FDR
Calmodulin-dependent protein kinase II substrate motif	27161	841	5919	227	1.2386	4.53E-05	0.001617
WW domain binding motif	27161	841	11300	402	1.1489	3.17E-05	0.001617
GSK-3, ERK1, ERK2, CDK5 substrate motif	27161	841	11300	402	1.1489	3.17E-05	0.001617
Casein kinase I substrate motif	27161	841	3063	65	0.68536	0.000124	0.003313
Aurora-A kinase substrate motif	27161	841	290	21	2.3387	0.00019	0.004073
14-3-3 domain binding motif	27161	841	4923	188	1.2333	0.000237	0.004219
PKC epsilon kinase substrate motif	27161	841	1365	62	1.4669	0.000645	0.009861
PAK2 kinase substrate motif	27161	841	1144	53	1.4962	0.000942	0.012595
PKC kinase substrate motif	27161	841	11620	395	1.0978	0.00128	0.015222
ERK1,2 kinase substrate motif	27161	841	9954	341	1.1064	0.001725	0.018458

Enriched motifs for significant phospho-peptides in female cohort

Motifs	Total size	Selection size	Category size	Intersection size	Enrichment factor	P value	Benj. Hoch. FDR
WW domain binding motif	27161	909	11300	435	1.1503	1.52E-05	0.00081463
GSK-3, ERK1, ERK2, CDK5 substrate motif	27161	909	11300	435	1.1503	1.52E-05	0.00081463
Calmodulin-dependent protein kinase II substrate motif	27161	909	5919	236	1.1914	0.000307	0.010965
MAPKAPK2 kinase substrate motif	27161	909	4490	183	1.2178	0.000507	0.012601
ERK1,2 kinase substrate motif	27161	909	9954	373	1.1197	0.000589	0.012601
14-3-3 domain binding motif	27161	909	4923	197	1.1957	0.000726	0.012941
Casein kinase I substrate motif	27161	909	3063	77	0.75115	0.000882	0.013483
MAPKAPK1 kinase substrate motif	27161	909	1170	57	1.4557	0.001141	0.015255

Supplementary Table 1. Motif Analysis. Sustained motif sequences for males and females individually were identified and the top motifs per sex are shown.