Supplementary information:

Table 1: Dendritic spine density after 24 or 72 hours of control and letrozole-treated cultures

Spine subtype	Spine density (spine/μm)			
	24 hours		72 hours	
	control	letrozole	control	letrozole
Stubby	0.43 ± 0.029	0.26 ± 0.018	0.42 ± 0.021	0.23 ± 0.019
Mushroom	0.72 ± 0.033	0.38 ± 0.032	0.59 ± 0.033	0.29 ± 0.026
Thin	0.73 ± 0.055	0.35 ± 0.055	0.72 ± 0.049	0.26 ± 0.054
Total	1.88 ± 0.10	0.99 ± 0.084	1.73 ± 0.073	0.78 ± 0.075

The data used to generate the contents of this table was also used for statistical analysis. Statistical analysis was done using two sample Student's *t*-test as described in the "Materials and Method" section. The calculated p-values are displayed and incorporated into the main text in the "Results" section. Data presented here correspond to Figure 2B and C.

Table 2: Dendritic spine density after 24 or 72 hours of control, letrozole, Aβ, or letrozole+Aβ-treated cultures.

Spine subtype	Spine density (spine/μm)							
	24 hours				72 hours			
	control	letrozole	$A\beta_{1-42}$	letrozole+ $A\beta_{1-42}$	control	letrozole	$A\beta_{1-42}$	letrozole+ $A\beta_{1-42}$
Stubby	0.43±0.029	0.26±0.018	0.37±0.025	0.28±0.022	0.42±0.021	0.23±0.019	0.36±0.029	0.29±0.028
Mushroom	0.72±0.033	0.38±0.032	0.35±0.031	0.40±0.022	0.59±0.033	0.29±0.026	0.34±0.020	0.23±0.029
Thin	0.73±0.055	0.35±0.055	0.45±0.063	0.42±0.032	0.72±0.049	0.26±0.054	0.33±0.027	0.20±0.030
Total	1.88±0.10	0.99±0.084	1.17±0.084	1.10±0.047	1.73±0.073	0.78±0.075	1.02±0.038	0.72±0.056

The data used to generate the contents of this table was also used for statistical analysis Statistical analysis was done using Two-tailed, One-way ANOVA followed by Tukey's multiple comparison test as described in the "Materials and Method" section. The calculated p-values are displayed and incorporated into the main text in the "Results" section. Data presented here correspond to Figure 4.

Table 3: Immunostaining punta density after 24 or 72 hours of control, letrozole, Aβ, or letrozole+-treated cultures

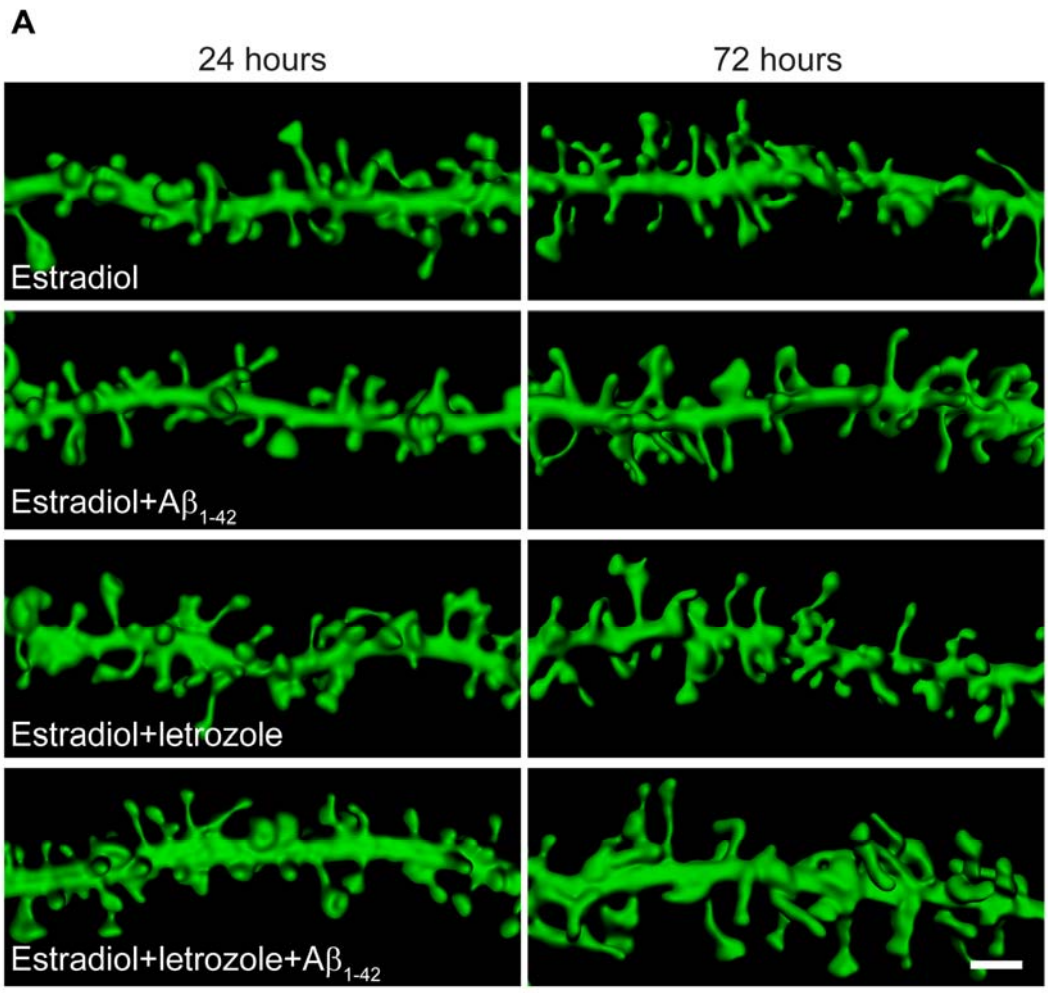
Synaptic protein	Spine density (spine/μm)							
	24 hours				72 hours			
	control	letrozole	$A\beta_{1-42}$	letrozole+ $A\beta_{1-42}$	control	letrozole	$A\beta_{1-42}$	letrozole+ $A\beta_{1-42}$
Synaptopodin	0.35±0.020	0.17±0.0096	0.22±0.016	0.19±0.013	0.41±0.028	0.14±0.013	0.26±0.022	0.092±0.015
Synaptophysin	1.06±0.090	0.64±0.035	0.84±0.050	0.65±0.043	0.94±0.067	0.37±0.025	0.53±0.049	0.31±0.026

The data used to generate the contents of this table was also used for statistical analysis Statistical analysis was done using Two-tailed, One-way ANOVA followed by Tukey's multiple comparison test as described in the "Materials and Method" section. The calculated p-values are displayed and incorporated into the main text in the "Results" section. Data presented here correspond to Figure 5.

Table 4: Dendritic spine density after 24 or 72 hours of estradiol, letrozole, Aβ, or letrozole+Aβ-treated cultures.

	Spine density (spine/μm)							
Spine subtype	24 hours				72 hours			
	estradiol	estradiol+ letrozole	estradiol+ $A\beta_{1-42}$	estradiol+ letrozole+ $A\beta_{1-42}$	estradiol	estradiol+ letrozole	estradiol+ $A\beta_{1-42}$	estradiol+ letrozole+ $A\beta_{1-42}$
Stubby	0.36±0.022	0.37±0.026	0.39±0.036	0.40±0.030	0.40±0.027	0.40±0.020	0.43±0.024	0.42±0.021
Mushroom	0.64±0.030	0.66±0.027	0.63±0.038	0.74±0.027	0.62±0.039	0.55±0.035	0.53±0.032	0.65±0.029
Thin	0.66±0.067	0.75±0.040	0.69±0.054	0.83±0.035	0.67±0.033	0.65±0.044	0.75±0.031	0.73±0.042
Total	1.66±0.094	1.78±0.059	1.71±0.089	1.78±0.065	1.68±0.050	1.60±0.075	1.70±0.051	1.78±0.061

The data used to generate the contents of this table was also used for statistical analysis Statistical analysis was done using Two-tailed, One-way ANOVA followed by Tukey's multiple comparison test as described in the "Materials and Method" section. The calculated p-values are displayed and incorporated into the main text in the "Results" section. Data presented here correspond to SI Figure 1.


A
24 hours
72 hours
Estradiol
Estradiol+Aβ1-42
Estradiol+letrozole
Estradiol+letrozole+Aβ1-42

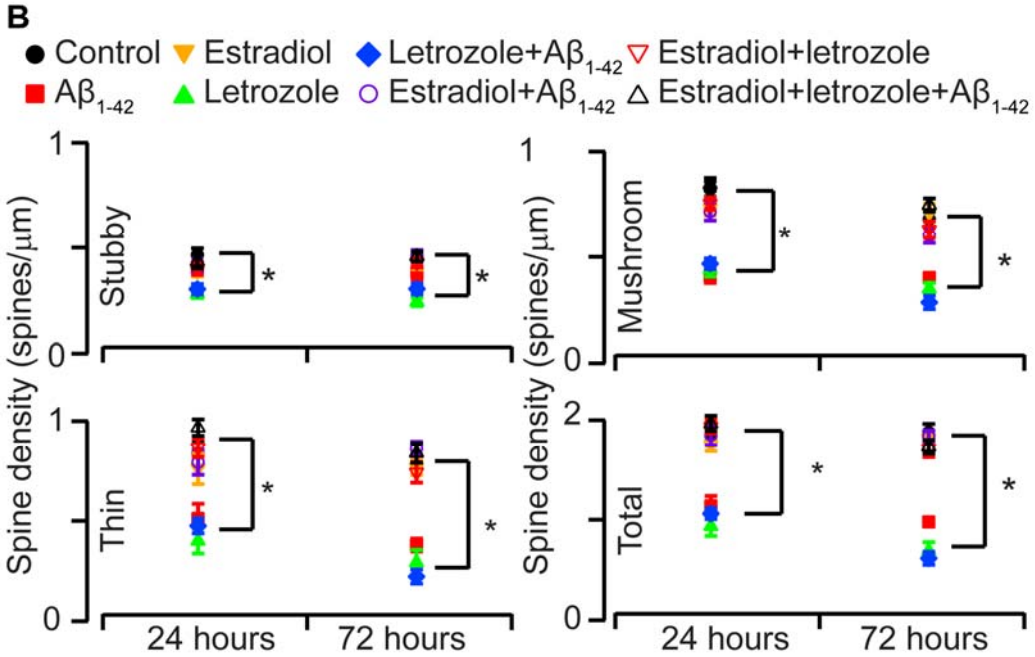

B
Control
Estradiol
Letrozole+Aβ1-42
Estradiol+letrozole
Aβ1-42
Letrozole
Estradiol+Aβ1-42
Estradiol+letrozole+Aβ1-42
Spine density (spines/μm)
Stubby
Mushroom
Thin
Total
1
0
2
*
24 hours
72 hours

Figure 1: Estradiol co-treatment prevents dendritic spine loss caused by letrozole and/or $A\beta_{1\text{-}42}$.
A, 3D-reconstructions of dendrites from sister-cultures that were treated with either estradiol (100 nM), estradiol (100 nM) + Aβ (1 μM), letrozole (1 μM) + estradiol (100 nM), or Aβ (1 μM) +letrozole (1 μM) +estradiol (100 nM) for 72 hours. Scale bar, 2 μm. **B**, Quantification of the spine subtype densities following treatments. There is a significant decrease in the total dendritic spine densities for $A\beta_{1\text{-}42}$, letrozole, and Letrozole+$A\beta_{1\text{-}42}$-treated cultures compared to control and cultures treated in the presence of estradiol after 24 hours. Estradiol prevented the dendritic spine loss caused by $A\beta_{1\text{-}42}$, letrozole, and letrozole+$A\beta_{1\text{-}42}$ at both 24 and 72 hours. 24 hours Control, *n* = total dendritic segment lengths of 441 μm from 10 cell in 4 cultures; estradiol, n = 625 μm of dendrite from 12 cell in 5 cultures; estradiol+$A\beta_{1\text{-}42}$, *n* = 725 μm of dendrite from 13 cell in 4 cultures; estradiol+letrozole, *n* = 862 μm of dendrite from 10 cell in 6 cultures; estradiol+letrozole+$A\beta_{1\text{-}42}$, *n* = 645 μm of dendrite from 11 cell in 5 cultures. 72 hours: Control, *n* = 500 μm of dendrite from 12 cell in 4 cultures; estradiol, n = 710 μm of dendrite from 10 cell in 5 cultures; estradiol+$A\beta_{1\text{-}42}$, *n* = 1016 μm of dendrite from 14 cell in 5 cultures; estradiol+letrozole, *n* = 688 μm of dendrite from 12 cell in 6 cultures; estradiol+letrozole+$A\beta_{1\text{-}42}$, *n* = 859 μm of dendrite from 10 cell in 4 cultures.