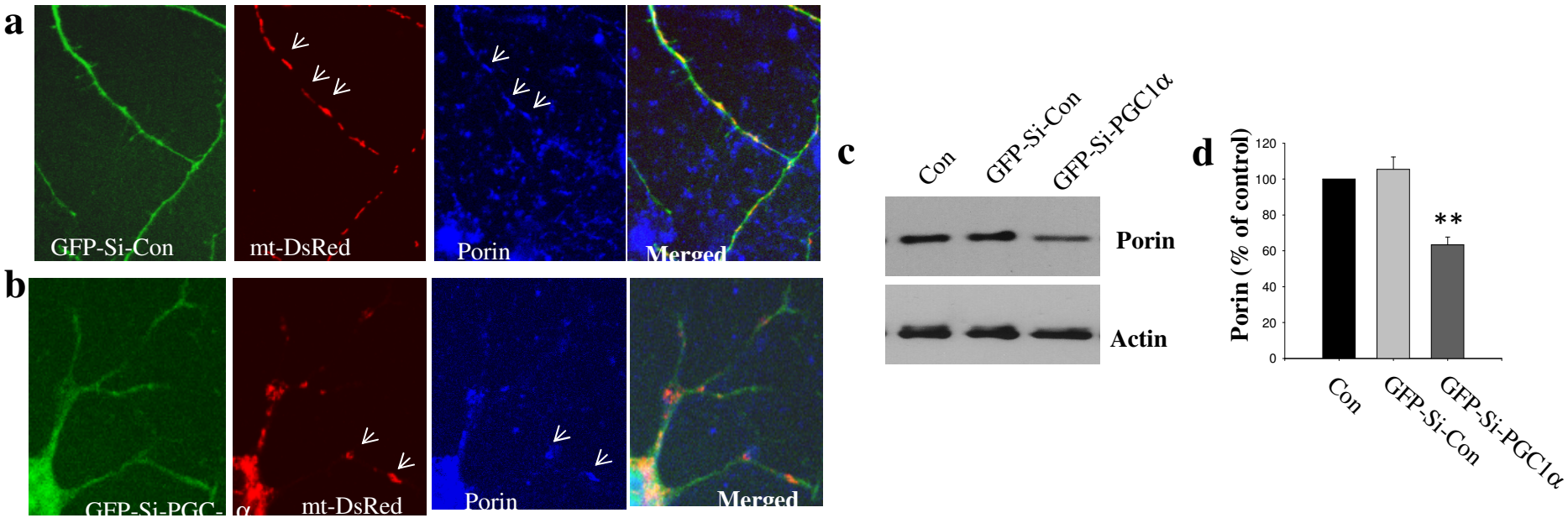
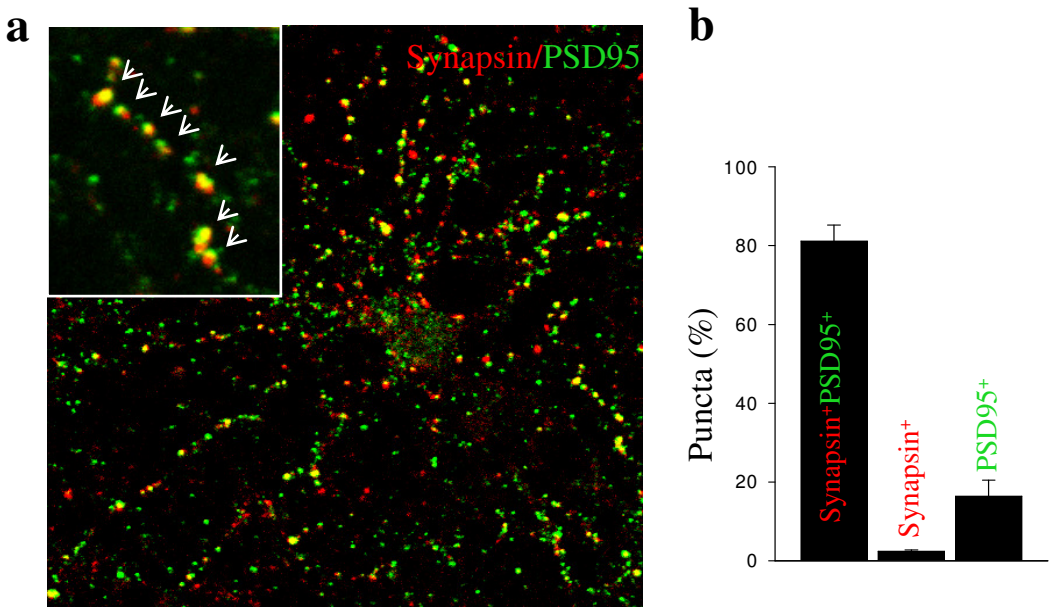
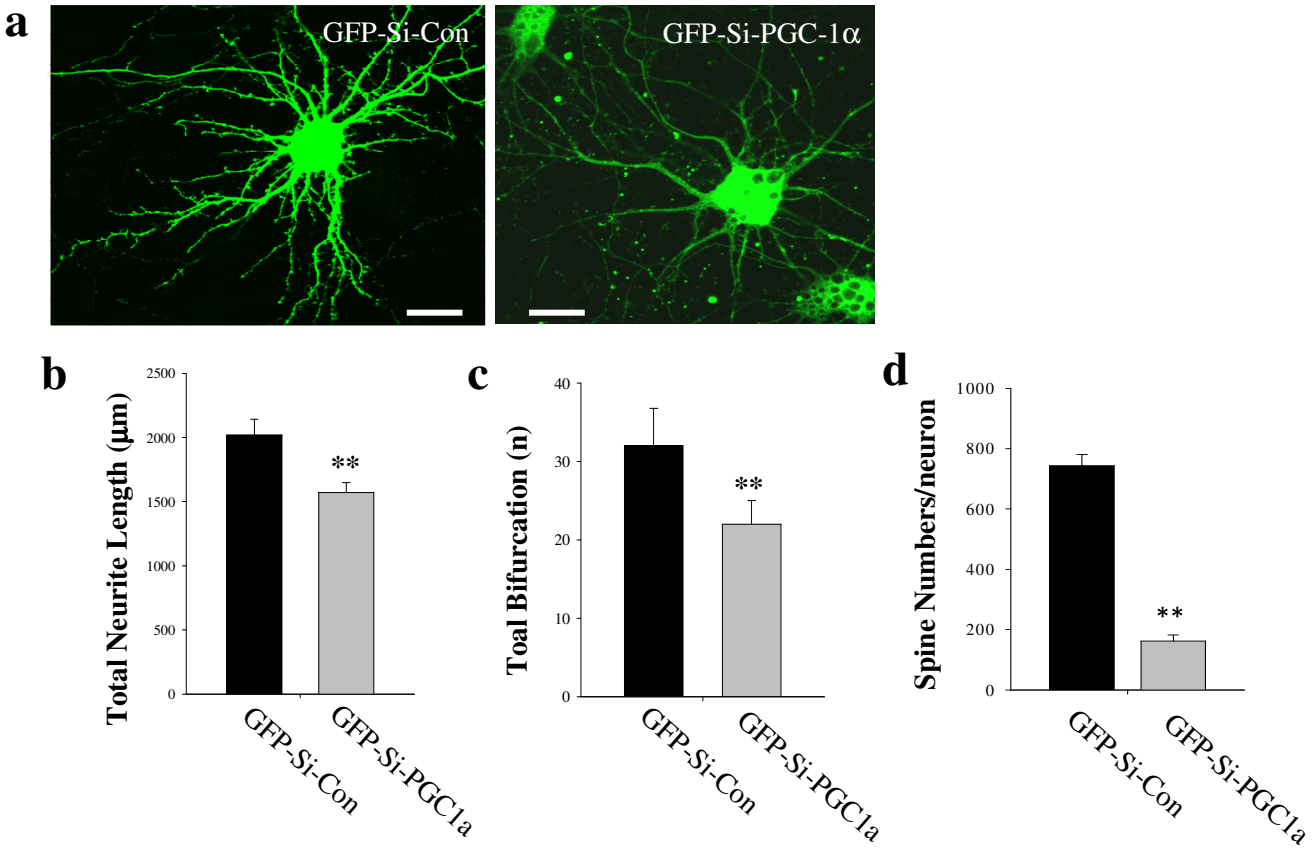


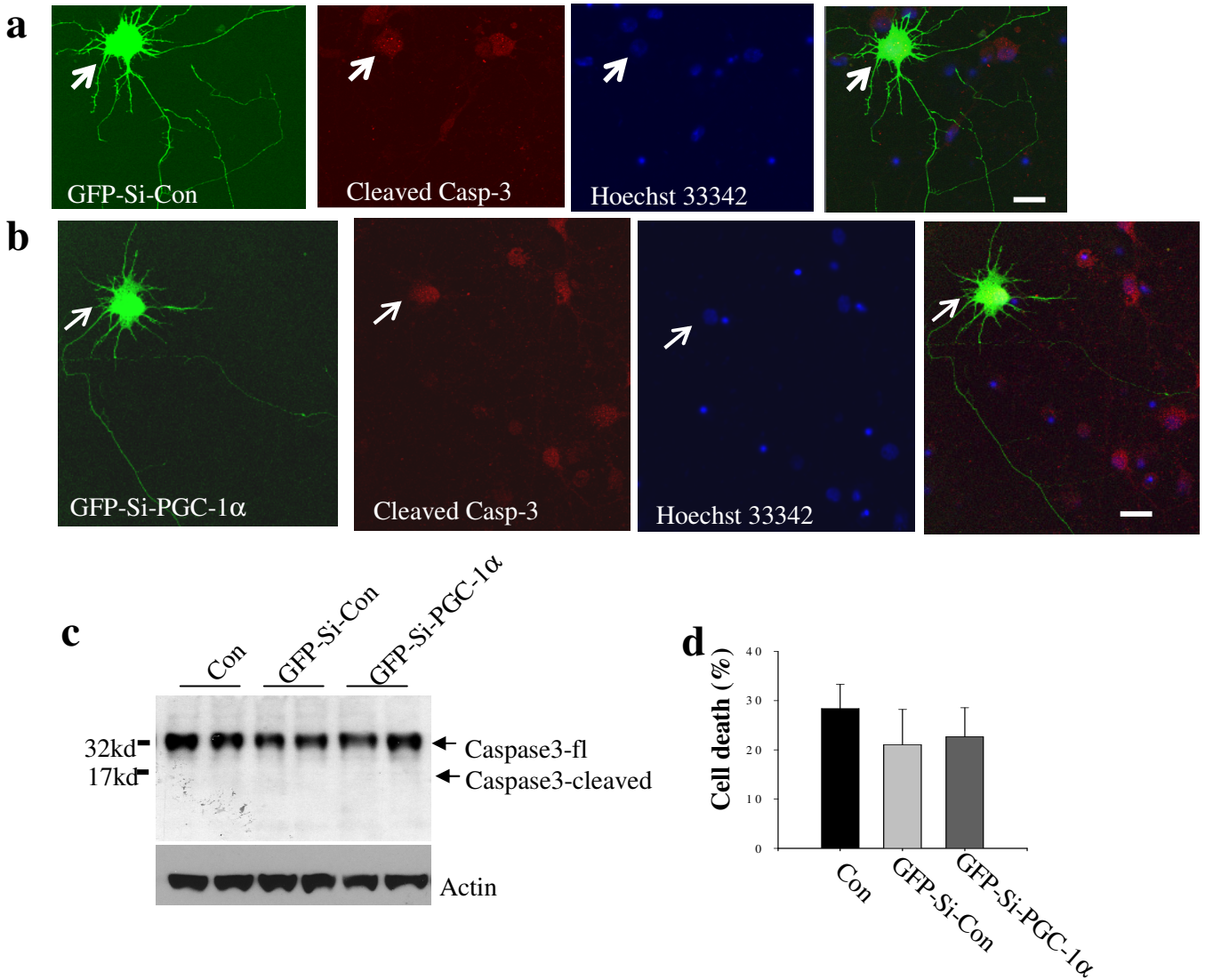
Supplementary Figure S1. mt-Dsred labeled mitochondria co-localize with the mitochondrial proein porin in cultured neurons. **(a, b)** Representative confocal images of hippocampal neurons that had been tranfected with either GFP-Si-con or GFP-Si-PGC1α constructs with mt-Dsred on culture day 5, and then fixed for immunostaining on culture day 12 day. Note that mt-Dsred (red) and porin immunoreactivity (blue) are highly co-localized. (**c**) Immunoblot analysis of Porin levels 7 days after infection (from culture days 5-12) of neurons with Ad- GFP-Si-con or Ad-GFP-Si-PGC1α, or in uninfected neurons (con). (**d**) Results of densitometric analysis of blots normalized to actin levels. Values are mean ± S.D. (n = 3 independent experiments). **p<0.01.



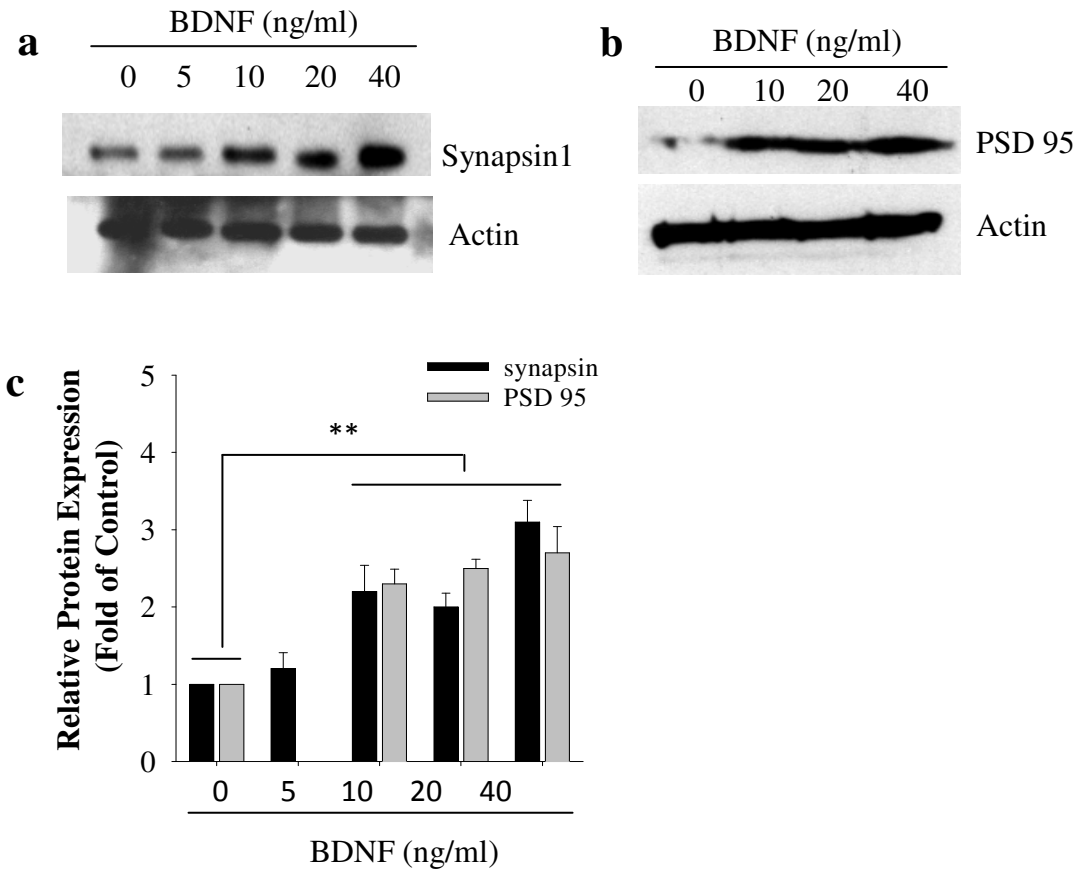
Supplementary Figure S2. Double immunostaining of synapsin and PSD95 in 12 day cultured hippocampal neurons.
(**a**) representative confocal image (approximately one neuronal field) demonstrating double immunostaining of synapsin (red) and PSD95 (green) with with arrows in inset box showing the typical synapsin/PSD95 aligned synaptic punctas. (**b**) the quantitative results of synapsin+/PSD95+ synaptic puncta, synapsin$^+$ or PSD95$^+$ only puncta. Values are the mean ± S.D. (n = 10 random fields).



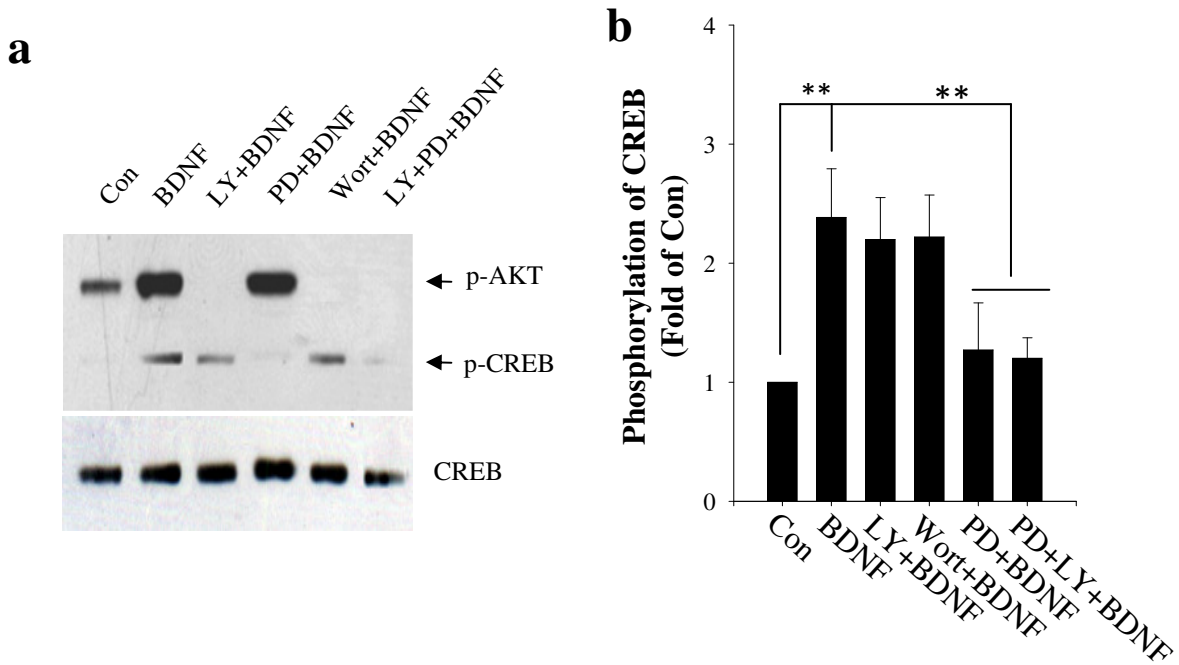
Supplementary Figure S3. PGC-1a depeletion inhibits dendrite growth in cultured embryonichippocampal neurons.
(**a**) Representative confocal images of 12 day-old hippocampal neurons that had been transfected with either GFP-Si-con or GFP-Si-PGC1α constructs on culture day 5. Scale bars = 20 mm. (**b-d**) Results of quantitative analysis of total dendritic length, number ofbifurcations and dendritic spine number per neuron in 12 day-old hippocampal neurons expressing either GFP-Si-Con or GFP-Si-PGC-1α. Values are the mean ± S.D. (n = 10-15 neurons analyzed). **p<0.01.



Supplementary Figure S4. Knockdown of PGC-1α does not affect the viability of cultured hippocampal neurons.
(a, b) Representative confocal images of hippocampal neurons that had been infected with either Ad-GFP-Si-Con or Ad-GFP-Si-PGC-1α constructs on culture day 5, and then fixed on culture day 12 and immunostained using an antibody against cleaved caspase-3 (red) in combination with the DNA-binding dye Hoechst 33342 (blue). **(c)** Immunoblot analysis of caspase-3 using an antibody that recognizes both full-length caspase-3 (32 kd) and the cleaved (active) form of caspase-3 (17 kd). (**d**) The percentage of cells displaying nuclear apoptotic morphology (condensed and fragmented nuclear DNA visualize by Hoechst 33342 staining) was determined for neurons in untreated control cultures compared to neurons infected with either Ad-GFP-Si-con or Ad-GFP-Si-PGC-1α . Values are the means ± S.D. of three independent experiments.



Supplementary Figure S5. BDNF treatment enhances the expression of synaptic proteins.
(**a, b**) Representative immunoblots of synapsin 1 and postsynaptic density protein 95 (PSD95) in 12 day-old hippocampal neuron cultures that were treated with the indicated concentrations of BDNF (ng/ml) for 7 days (from culture days 5-12) or left untreated (control). (**c**) Results of densitometric analysis of blots. Values are mean ± S.D. (n = 4-5 independent experiments).
*p<0.05, **p<0.01.



Supplementary Figure S6. Activation of CREB by BDNF does not require PI3 kinase activation.
(**a**) Immunoblot analysis of phosphorylation of Akt and CREB in control and BDNF-treated neurons. Neurons were pretreated with vehicle or kinase inhibitors 30 min prior to exposure to BDNF (40 ng/ml) for 30 min: MAPK inhibitor, PD980059 (PD, 20 mM); PI3K inhibitor LY290043 (LY, 20 μM); PI3K inhibitor wortmannin (Wort, 20 μM). p-AKT and p-CREB are bands in blots probed with antibodies that selectively recognize phospho-AKT and phospho-CREB; the same blots were reprobed with an antibody against total CREB (phosphorylation independent antibody). (**b**) Results of densitometric analysis of p-CREB immunoreactive bands in cell lysates from hippocampal cultures treated as indicated. Values are the means ±S.D. of determinations made in three separate experiments. $^{**}p < 0.01$.