

**Figure S1.** Synaptic stimulation inhibited MTOR and activated TFEB in primary cultured neurons. (**A**, **B**) gLTP-stimulation increased levels (+50±9%) of TFE3 in the nucleus of Tg neurons compared to CTRL (n=3; two-tailed unpaired t-test \*\*p<0.01; scale bar: 10 μm). (**C**, **D**) gLTP-stimulation decreased levels (-40±10%) of MAPT/Tau oligomers in Tg neurons (n=5; two-tailed unpaired t-test \*p<0.05). (**E**, **F**) Inhibition of MTOR via torin 1 treatment reduced phospho-TFEB (-78±6%) similarly to gLTP stimulation (-74±10%) in Tg neurons (n=3; one-way ANOVA test, p=0.0121, followed by Tukey’s multiple comparison post-hoc test: CTRL vs gLTP \*p<0.05; CTRL vs gLTP+torin 1 \*p<0.05; CTRL vs torin 1 \*p<0.05; scale bar: 10 μm). (**G-J**) Western blot analyses revealed no changes in levels of ATP6V1H and ATP6V1D in gLTP-stimulated compared to CTRL Tg neurons (n=3; unpaired t-test, p>0.05). (**K**) Quantitative RT-PCR revealed no changes of TFEB transcripts in gLTP-stimulated compared to CTRL neurons (n=5, 6; two-tailed unpaired t-test; p>0.05).



**Figure S2.** DBS restored levels of LAMP1 in Tg-S mice back to WT-NS. (**A-F**) Levels of MCOLN1, ATP6V1H and ATP6V1D were measured by western blot analyses in Tg-NS compared to Tg-S hippocampi. (n=4; two-tailed unpaired t-test; p>0.05). (**G**, **H**) DBS reduced of 46±3% LAMP1 levels in Tg-S compared to Tg-NS mice (n=4; two-tailed unpaired t-test \*p<0.05). (**I**, **J**) A 49±9% increase of LAMP1 levels was measured in Tg-NS hippocampus compared to WT-NS; in Tg-S mice levels of LAMP1 were restored back to WT levels (n=3, 4; one-way ANOVA test, p= 0.0173 followed by Tukey’s multiple comparison post-hoc test: WT-NS vs Tg-NS \*p<0.05; Tg-S vs Tg-NS #p<0.05). (**K**, **L**) Confocal immunofluorescence showing 11±3% increased levels of LAMP1 in Tg-NS compared to WT-NS hippocampal neurons. In Tg-S mice, DBS was able to restore LAMP1 back to WT (n=4,5; one-way ANOVA test, p=0.0187 followed by Tukey’s multiple comparison post-hoc test: WT-NS vs Tg-NS \*p<0.05; Tg-S vs Tg-NS #p<0.05; scale bar 10 μm).



**Figure S3.** CTRL and DBS PD patient groups had comparable levels of pathological MAPT/Tau and accumulated SQSTM1 in non-stimulated brain areas. (**A**, **B**) Quantification of AT8 in the cortex of CTRL and DBS PD patients (n=3; two-tailed unpaired t-test, p>0.05; scale bar: 50 μm). (**C**) Nissl staining combined with AT8 immunostaining of PD (CTRL and DBS) GPi sections. Nissl staining was used to precisely locate the GPi (yellow dotted lines). (**D**) Quantification of AT8 in neurites of GPi of CTRL and DBS PD brains (n=3; two-tailed unpaired t-test, p>0.05). (**E-G**) Quantification of SQSTM1 in the cortex of CTRL and DBS brains of PD patients (quantification in **C** for puncta density, and **F** for puncta size, respectively; n=3; two-tailed unpaired t-test, p>0.05; scale bars: 100 μm). (**H**, **I**) Immunofluorescence of TFEB (green) and nuclei (DAPI, blue) in GPi of PD controls (left panels) and DBS (right panels; scale bar: 10 μm). Higher magnification panels (below) show a trend for increased immunostaining of TFEB in the nuclei of DBS-stimulated neurons (quantification in **I**; n=3; two-tailed unpaired t-test, p>0.05).



**Figure S4.** Inhibition of PPP3/calcineurin did not prevent dephosphorylation of TFEB during gLTP. (**A**, **B**) Confocal immunofluorescence showing effects of cyclosporin A (CsA) treatment on phospho-TFEB in Tg neurons, with or without gLTP (n=3; one-way ANOVA test, p=0.0066, followed by Tukey’s multiple comparison post-hoc test: CTRL vs gLTP \*\*p<0.01; CTRL vs gLTP-CsA p=0.052; scale bar: 10 µm).