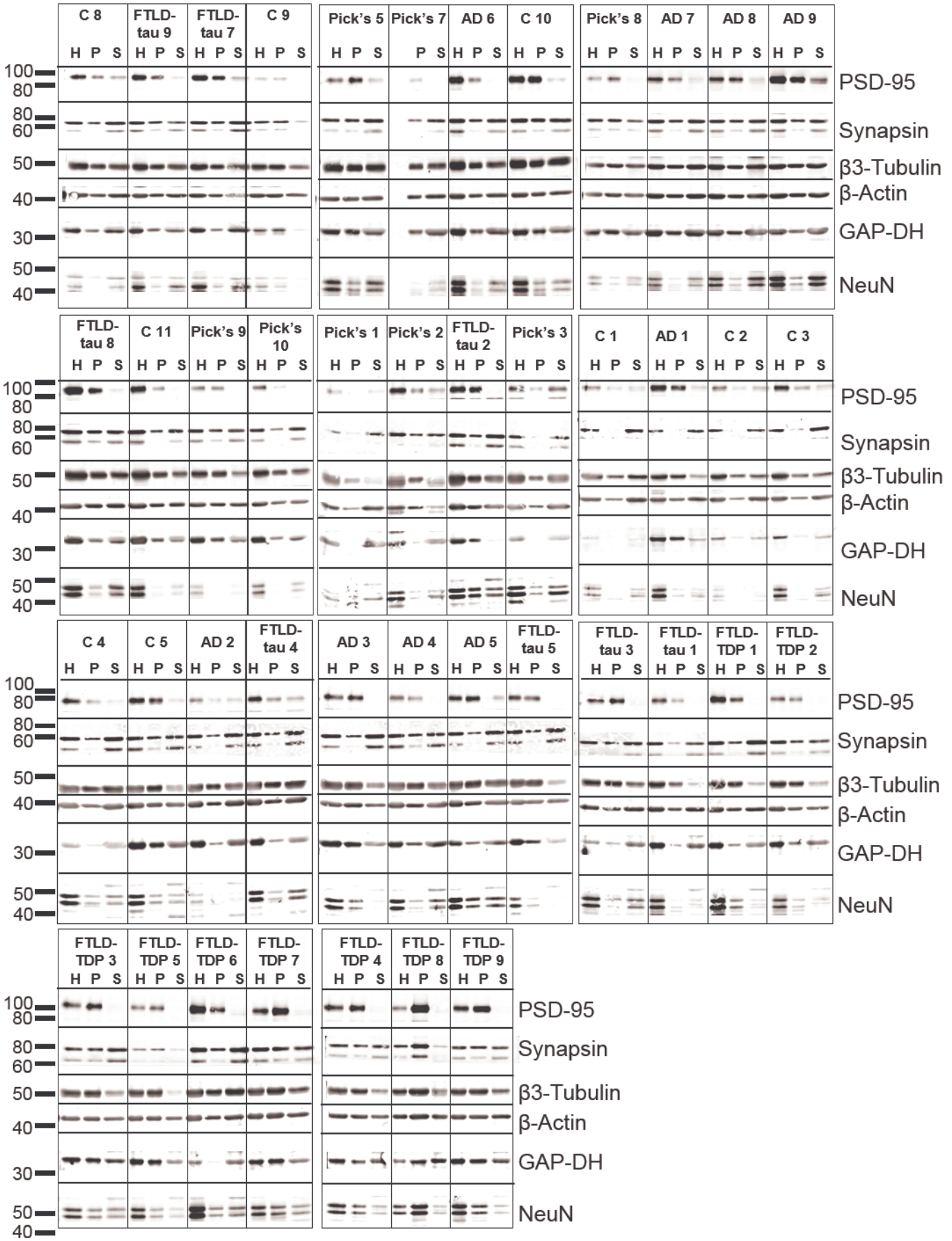

Figure Supplemental Digital Content 1: Separation of a crude synaptoneurosome fraction from frozen human brain tissues. Western blots showing PSD-95, Synapsin 1a/b, NeuN, β3-tubulin, β-actin and GAPDH in samples from human frontal cortex tissue extracts from non-demented controls (C) and individuals with AD, FTLD-tau (FTLD-tau), Pick's disease or FTLD-TDP type B (FTLD-TDP). For each case total homogenates (H), pelleted synaptoneurosomes (P) and non-synaptic cytoplasmic supernatant (S) were run next to each other to asses success of the fractionation process. Due to significant levels of NeuN in the pellet fraction, cases FTLD-Tau 2, AD 5, FTLD 7-9 were excluded from the synaptoneurosome analysis.

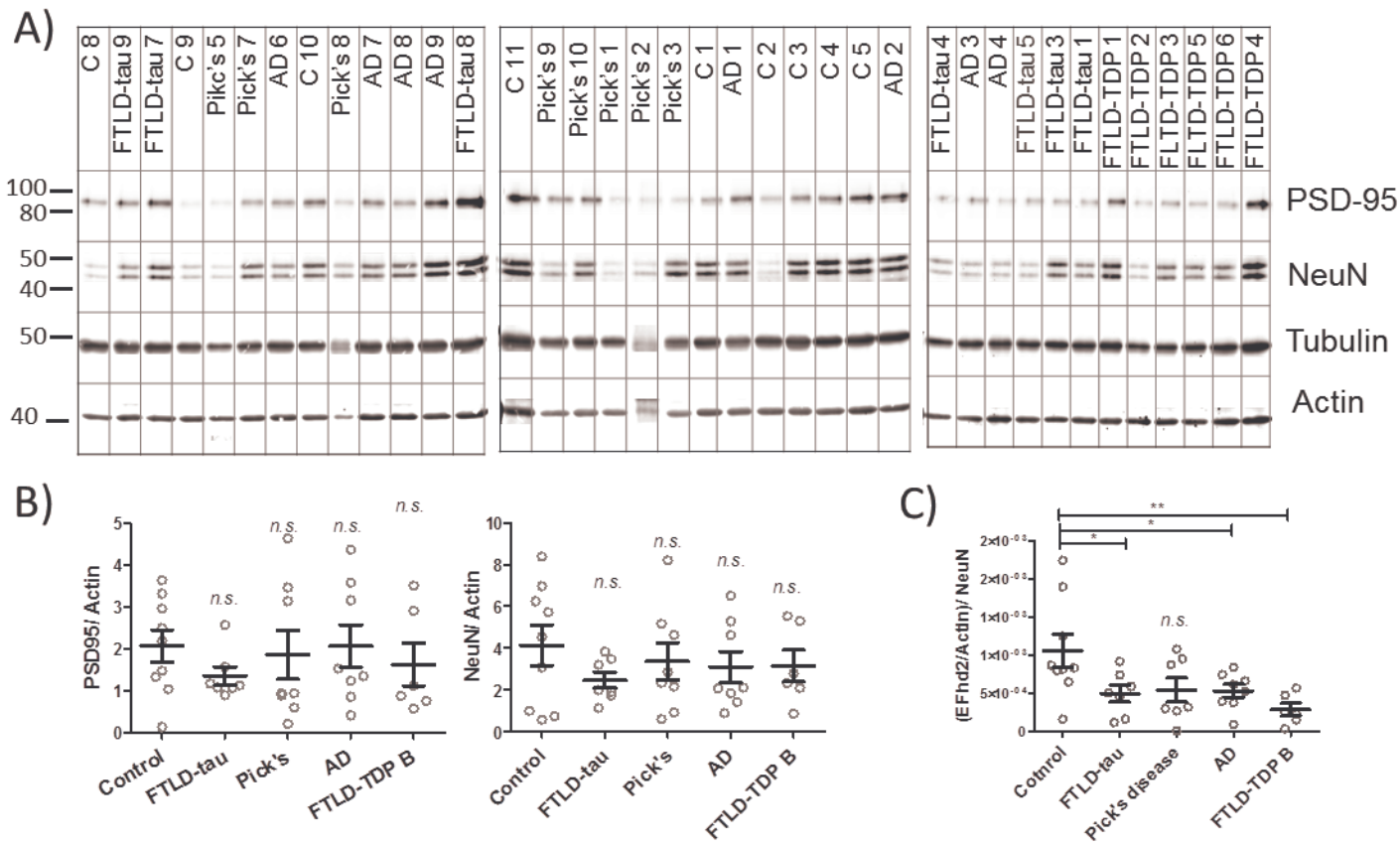

Figure Supplemental Digital Content 2: Protein levels of PSD-95 and NeuN in total homogenates from human brain tissues. **A**) Western blots showing EFhd2 protein levels in human frontal cortex tissue extracts from non-demented controls and individuals with AD, FTLD-tau (FTLD-tau), Pick's disease or FTLD-TDP type B (FTLD-TDP). β-Actin was used as loading control. **B**) Quantification of PSD-95 (left) and NeuN (right) stained bands by densitometry. Error bars = SEM. N.s. = non-significant compared to control by 1-way ANOVA with Dunnett's post-hoc test. C) Adjustment of EFhd2 densitometry results to NeuN per sample. Error bars = SEM. *p<0.05 and **p<0.01 compared to control by 1-way ANOVA with Dunnett's post-hoc test.

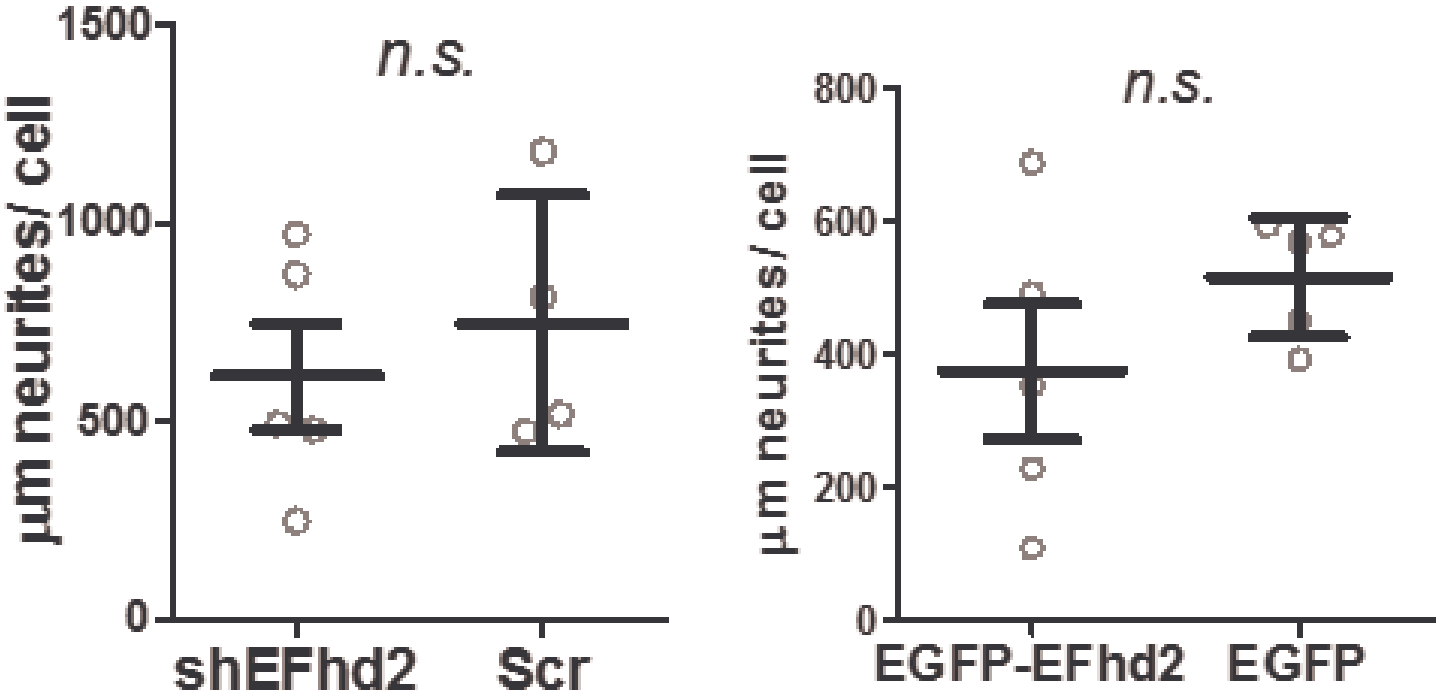

Figure Supplemental Digital Content 3: Neurite development in shEFhd2 and EGFP-EFhd2 8 DIV transgenic neuronal cultures. Neurons were infected with shEFhd2 or EGFP-EFhd2 vectors or respective controls at 1 DIV and fixed and stained for MAP2 at 8 DIV. MAP2 stained neurites were quantified from 5 fluorescence images (20 x magnifications) per group. n.s. = non-significant by 2-tailed T-test, error bars = SD . Results are representative of 3 independent experiments.