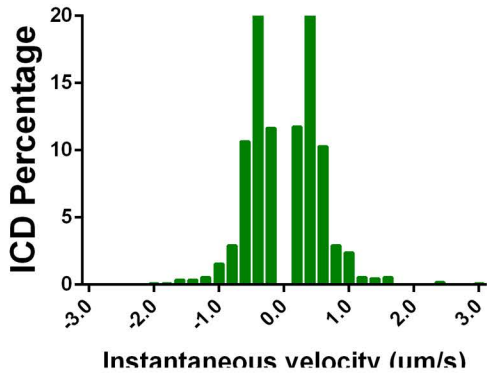
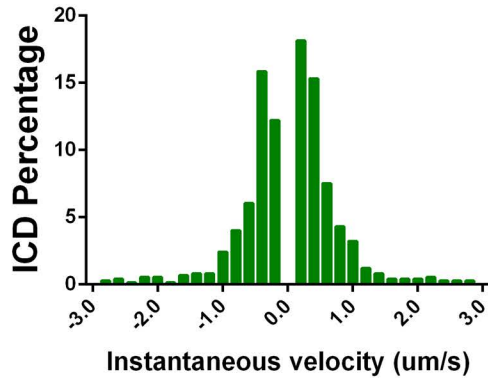


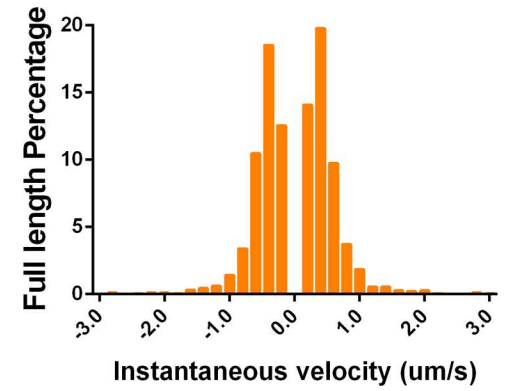
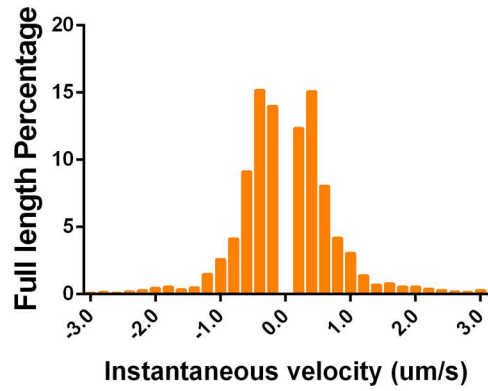
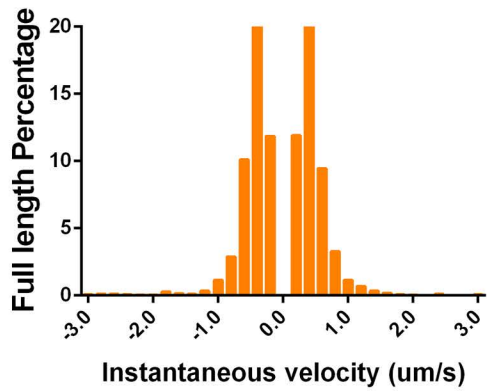
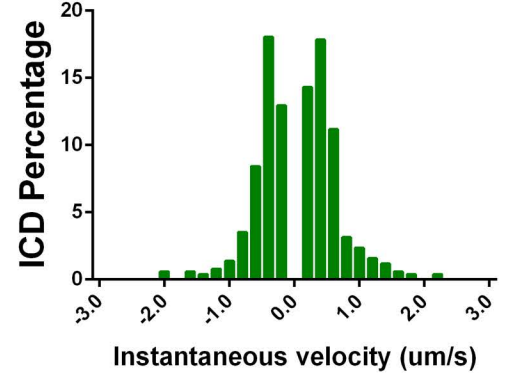
# KCI



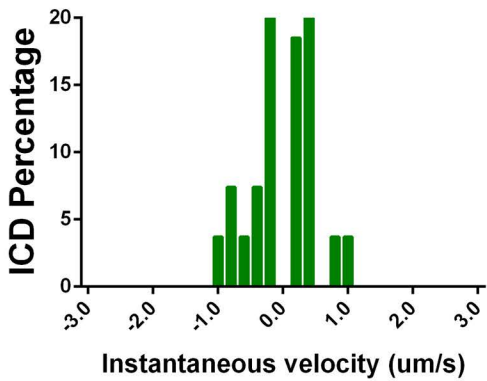
# BDNF



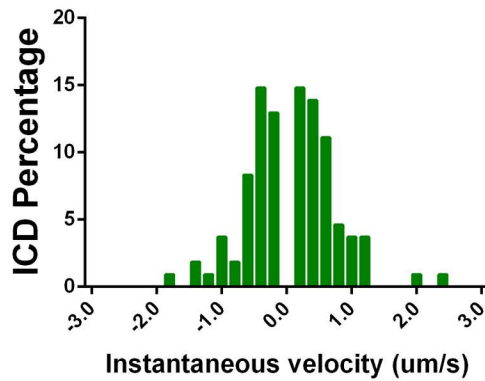
# BDNF+MS



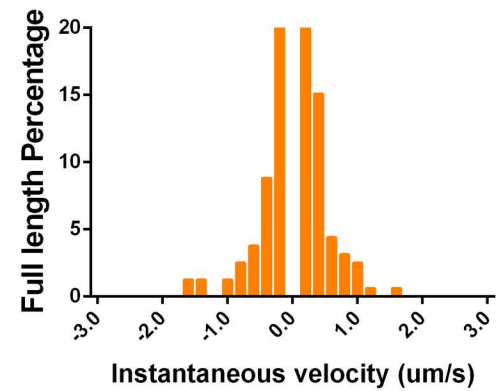
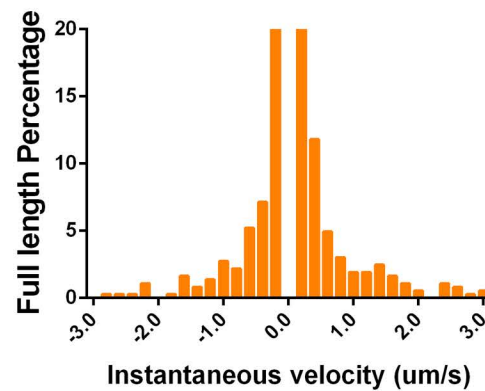
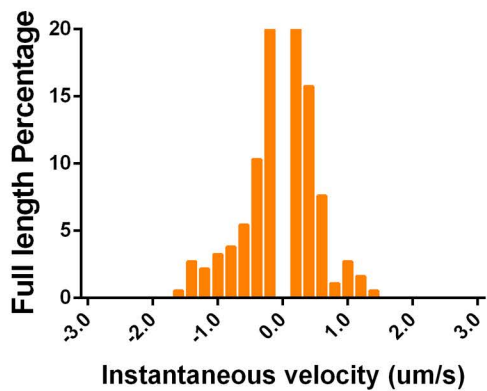
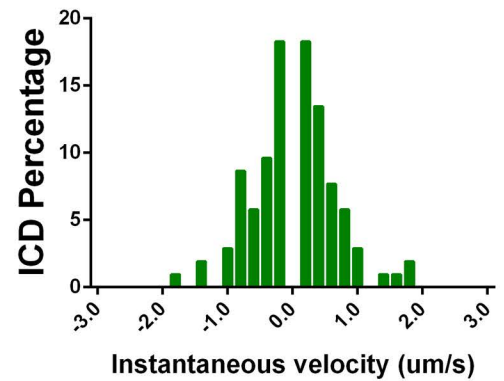
# NGF



# TFD



# TFD+MS



## Supplemental Information titles and legends

### **Supplementary figure S1 related to Figure 2: P75NTR cleavage in distal axons.**

(A) Representative image of axons showing full length p75NTR (yellow), ECD (red) and the cleaved ICD (green) in GFP tagged p75NTR overexpressing lentivirus. (B) Quantification of the number of p75NTR ICD only and full length p75NTR puncta in axons after treatment with BDNF or BDNF+DAPT for 2 hrs after pretreatment with DAPT for 1 hr. Depicted are the means + SEM from at least 3 different experiments; \*,  $p < 0.0001$ , 2 way Anova with Sidak's multiple comparison test. Primary sympathetic neurons were grown in microfluidic devices and infected with GFP tagged p75NTR lentivirus. Neurons were stained with ATTO-550 tagged antibody against p75NTR-ECD, then fixed and stained with GFP. (C) Visualization of mCherry-p75NTR-GFP electroporated neuron stained with ATTO-550 antibody against p75-ECD, TUJ1 and DAPI. (D) Western blot showing the cleavage of mCherry-p75NTR-GFP wildtype (mCh-p75WT-GFP), V243D mutant (mch-p75VD-GFP) and V243N mutant (mch-p75-GFP) transfected HEK293 cells treated with PMA and/or TAPI as indicated. Shown here are the full length, c-terminal fragment (CTF) and ICD of p75NTR. (E) Darker exposure of the same western blot shown in D, for better visualization of ICD.

### **Supplementary figure S2, related to figure 3: HDAC1 expression and activity in peripheral axons is necessary for retrograde apoptotic signaling.**

(A) Treatment of axons with sodium butyrate prevents p75NTR-mediated neuronal apoptosis. Neurons were cultured in microfluidics chambers with NGF and after the axons reached the distal sides, NGF was removed and cell bodies (CB) and distal axons (DAX) were treated with 12.5 mM KCl (K) or 200 ng/ml BDNF (B) +/- 10 mM sodium butyrate (N) for 48 hrs, as indicated. Thereafter, the neurons were immunostained with TUJ1 and the nuclei labeled with DAPI to quantify pyknotic nuclei as a measure of apoptosis. The data shown in the bar graph is the mean from two different experiments. (B). HDAC1 immunostaining in rat cerebral cortex. Paraffin embedded sections from P4-5 rats were fixed and immunostained for HDAC1, TUJ1 and DAPI. Scale bar 20um.

### **Supplementary figure S3, related to figure 5: Speed distribution of anterograde and retrograde traffic.**

Negative values towards the left of the graph are for the movement in anterograde direction while the positive values are for the movement in retrograde direction towards the cell body. p75NTR-ICD is displayed by green while the full length p75NTR is shown by yellow graphs under different conditions as indicated. Data is pooled from at least two different experiments for each condition with at least 500 puncta analyzed for ICD and 1500 puncta analyzed for Full length.