

## Statistical analysis

Fig. 1B: Ca<sub>v</sub>2.2 (*trkBTK*<sup>+/+</sup> 1.00 ± 0.04, Q<sub>2</sub> 1.01, n = 6, N = 78; *trkBTK*<sup>-/-</sup> 0.54 ± 0.10, Q<sub>2</sub> 0.47, n = 4, N = 66; p = 0.0015, unpaired t-test (two-tailed), t = 4.714, df = 8), Ca<sub>v</sub>2.2/tau (*trkBTK*<sup>+/+</sup> 1.00 ± 0.08, Q<sub>2</sub> 0.95; *trkBTK*<sup>-/-</sup> 0.65 ± 0.06, Q<sub>2</sub> 0.67; p = 0.0118, unpaired t-test (two-tailed), t = 3.247, df = 8)

Fig. 1C: Ca<sup>2+</sup> transients per min (Control 0.92 ± 0.13, Q<sub>2</sub> 0.60, IQR 1.35, N = 72; *trkBTK*<sup>-/-</sup> 0.55 ± 0.09, Q<sub>2</sub> 0.30, IQR 0.9, N = 64; p = 0.0337, Mann Whitney test (two-tailed), Mann Whitney U 1827)

Fig. 1D: Axon length in [μm] (*trkBTK*<sup>+/+</sup> 262.9 ± 11.79, Q<sub>2</sub> 278.8, n = 7, N = 283; *trkBTK*<sup>-/-</sup> 316.4 ± 12.65, Q<sub>2</sub> 314.5, n = 7, N = 298; p = 0.0093, unpaired t-test (two-tailed), t = 3.093, df = 12)

Fig. 1E: Axon length in [μm] (*trkBTK*<sup>+/+</sup> (A) 285.4 ± 4.26, Q<sub>2</sub> 284.1, n = 3, N = 140; *trkBTK*<sup>-/-</sup> (B) 348.2 ± 4.04, Q<sub>2</sub> 345.4, n = 3, N = 130; *trkBTK*<sup>+/+</sup> +CTX (C) 342.6 ± 20.20, Q<sub>2</sub> 331.3, n = 3, N = 177; *trkBTK*<sup>-/-</sup> +CTX (D) 360.3 ± 7.26, Q<sub>2</sub> 360, n = 3, N = 155; p = 0.0168 (A-B), p = 0.0273 (A-C), p = 0.0062 (A-D), one-way ANOVA with Tukey's Multiple Comparison)

Fig. 2A: Ca<sub>v</sub>2.2 (BDNF (B) 1.00 ± 0.11, Q<sub>2</sub> 1.00, n = 5, N = 130; CNTF (C) 0.65 ± 0.05, Q<sub>2</sub> 0.65, n = 6, N = 133; GDNF (G) 0.47 ± 0.04, Q<sub>2</sub> 0.47, n = 6, N = 145; p (B-C) = 0.0081, p (B-G) = 0.0002, one-way ANOVA with Tukey's Multiple Comparison), Ca<sub>v</sub>2.2/APP (BDNF (B) 1.00 ± 0.14, Q<sub>2</sub> 1.00, n = 5, N = 130; CNTF (C) 0.45 ± 0.05, Q<sub>2</sub> 0.47, n = 6, N = 133; GDNF (G) 0.49 ± 0.06, Q<sub>2</sub> 0.50, n = 6, N = 145; p (B-C) = 0.0014, p (B-G) = 0.0028, one-way ANOVA with Tukey's Multiple Comparison)

Fig. 2B: Ca<sup>2+</sup> transients per min (BDNF (B) 0.89 ± 0.11, Q<sub>2</sub> 0.6, IQR 3, N = 75; CNTF (C) 0.69 ± 0.13, Q<sub>2</sub> 0.3, IQR 3, N = 77; GDNF (G) 0.50 ± 0.08, Q<sub>2</sub> 0.3, IQR 2.5, N = 73; p (B-C) = 0.0306, p (B-G) = 0.0078, Kruskal-Wallis test with Dunn's multiple comparison tests)

Fig. 2C: Axon length in [μm] (BDNF (B) 356 ± 22.16, Q<sub>2</sub> 342, n = 6, N = 275; CNTF (C) 466.6 ± 35.41, Q<sub>2</sub> 465.6, n = 6, N = 263; GDNF (G) 454.8 ± 19.28, Q<sub>2</sub> 440.9, n = 6, N = 200; p (B-C) = 0.0256, p (B-G) = 0.0470, one-way ANOVA with Tukey's Multiple Comparison)

Fig. 3A: Ca<sub>v</sub>2.2 (no pulse 1.00 ± 0.04, Q<sub>2</sub> 1.00, n = 9, N = 221; 5' BDNF 1.93 ± 0.24, Q<sub>2</sub> 1.75, n = 9, N = 245; p = 0.0014, unpaired t-test (two-tailed), t = 3.839, df = 16), Ca<sub>v</sub>2.2/APP (no pulse 1.00 ± 0.02, Q<sub>2</sub> 1.00, n = 9, N = 221; 5' BDNF 1.55 ± 0.24, Q<sub>2</sub> 1.36, n = 9, N = 245; p = 0.0370, unpaired t-test (two-tailed), t = 2.275, df = 16)

Fig. 3B: Ca<sup>2+</sup> transients per min (no pulse 0.16 ± 0.08, Q<sub>2</sub> 0, IQR 0, N = 32; 5' BDNF 0.30 ± 0.08, Q<sub>2</sub> 0, IQR 2, N = 32; p = 0.0104, Mann Whitney test (two-tailed), Mann-Whitney U 357.5)

Fig. 3C: 5' BDNF/no pulse - Ca<sub>v</sub>2.2 (*trkBTK*<sup>+/+</sup> 1.00 ± 0.06, Q<sub>2</sub> 1.00, n = 7, N (no pulse) = 88, N (5' BDNF) = 102; *trkBTK*<sup>-/-</sup> 0.75 ± 0.07, Q<sub>2</sub> 0.79, n = 7, N (no pulse) = 100, N (5' BDNF) = 106; p = 0.0184, unpaired t-test (two-tailed), t = 2.725, df = 12), Ca<sub>v</sub>2.2/SynPhys (*trkBTK*<sup>+/+</sup> 1.00 ± 0.09, Q<sub>2</sub> 1.00, IQR 0.15; *trkBTK*<sup>-/-</sup> 0.67 ± 0.05, Q<sub>2</sub> 0.65, IQR 0.27; p = 0.0072, Mann Whitney test (two-tailed), Mann-Whitney U 3.000)

Fig. 4A: Growth cone size in [ $\mu\text{m}^2$ ] (Control  $26.14 \pm 1.13$ ,  $Q_2$  25.4,  $n = 13$ ,  $N = 226$ ; CTX  $19.51 \pm 1.17$ ,  $Q_2$  19.96,  $n = 17$ ,  $N = 274$ ;  $p = 0.0005$ , unpaired t-test (two-tailed),  $t = 3.964$ ,  $df = 28$ ),  $\beta$ -actin (Control  $1.00 \pm 0.05$ ,  $Q_2$  1.00; CTX  $0.71 \pm 0.07$ ,  $Q_2$  0.68;  $p = 0.0037$ , unpaired t-test (two-tailed),  $t = 3.170$ ,  $df = 28$ ), tau (Control  $1.00 \pm 0.03$ ,  $Q_2$  1.00; 30nM CTX  $0.94 \pm 0.08$ ,  $Q_2$  0.95;  $p = 0.5168$ , unpaired t-test (two-tailed),  $t = 0.6566$ ,  $df = 28$ )

Fig. 4B: Growth cone size in [ $\mu\text{m}^2$ ] (shLUC (A)  $22.02 \pm 1.68$ ,  $Q_2$  16.89, IQR 13.07,  $N = 76$ ; shAct $\beta$  (B)  $14.85 \pm 1.18$ ,  $Q_2$  11.70, IQR 11.45,  $N = 74$ ; Rescue (C)  $23.54 \pm 2.44$ ,  $Q_2$  17.09, IQR 13.15,  $N = 62$ ;  $p$  (AB)  $< 0.0001$ ,  $p$  (AC)  $> 0.9999$ ,  $p$  (BC)  $< 0.0001$ , Kruskal-Wallis test with Dunn's multiple comparison tests),  $\beta$ -actin (shLUC (A)  $1.00 \pm 0.09$ ,  $Q_2$  0.90, IQR 0.92,  $N = 76$ ; shAct $\beta$  (B)  $0.38 \pm 0.05$ ,  $Q_2$  0.27, IQR 0.53,  $N = 74$ ; Rescue (C)  $0.98 \pm 0.09$ ,  $Q_2$  0.96, IQR 0.82,  $N = 62$ ;  $p$  (AB)  $< 0.0001$ ,  $p$  (AC)  $> 0.9999$ ,  $p$  (BC)  $< 0.0001$ , Kruskal-Wallis test with Dunn's multiple comparison tests), tau (shLUC (A)  $1.00 \pm 0.07$ ,  $Q_2$  0.92, IQR 0.76,  $N = 76$ ; shAct $\beta$  (B)  $1.10 \pm 0.08$ ,  $Q_2$  0.97, IQR 0.89,  $N = 74$ ; Rescue (C)  $1.07 \pm 0.09$ ,  $Q_2$  0.90, IQR 0.73,  $N = 62$ ;  $p$  (AB)  $> 0.9999$ ,  $p$  (AC)  $> 0.9999$ ,  $p$  (BC)  $> 0.9999$ , Kruskal-Wallis test with Dunn's multiple comparison tests)

Fig. 4C: Ca $_v$ 2.2 (shLUC (A)  $1.00 \pm 0.09$ ,  $Q_2$  0.84, IQR 0.75,  $N = 54$ ; shAct $\beta$  (B)  $0.70 \pm 0.06$ ,  $Q_2$  0.52, IQR 0.46,  $N = 63$ ; Rescue (C)  $1.04 \pm 0.07$ ,  $Q_2$  1.05, IQR 0.90,  $N = 64$ ;  $p$  (AB) = 0.0053,  $p$  (AC)  $> 0.9999$ ,  $p$  (BC) = 0.0007; Kruskal-Wallis test with Dunn's multiple comparison tests), SynPhys (shLUC (A)  $1.00 \pm 0.08$ ,  $Q_2$  0.85, IQR 0.64,  $N = 54$ ; shAct $\beta$  (B)  $1.03 \pm 0.09$ ,  $Q_2$  0.83, IQR 0.87,  $N = 63$ ; Rescue (C)  $1.24 \pm 0.10$ ,  $Q_2$  1.02, IQR 1.04,  $N = 64$ ;  $p$  (AB)  $> 0.9999$ ,  $p$  (AC) = 0.5022,  $p$  (BC) = 0.2002, Kruskal-Wallis test with Dunn's multiple comparison tests)

Fig. 5A: Growth cone size in [ $\mu\text{m}^2$ ] (*trkBTK* $^{+/+}$   $34.23 \pm 2.77$ ,  $Q_2$  29.45,  $n = 20$ ,  $N = 308$ ; *trkBTK* $^{-/-}$   $21.22 \pm 1.41$ ,  $Q_2$  22.81,  $n = 19$ ,  $N = 341$ ;  $p = 0.0002$ , unpaired t-test (two-tailed),  $t = 4.119$ ,  $df = 37$ ),  $\beta$ -actin/tau (*trkBTK* $^{+/+}$   $1.00 \pm 0.10$ ,  $Q_2$  1.00,  $n = 8$ ,  $N = 154$ ; *trkBTK* $^{-/-}$   $0.55 \pm 0.12$ ,  $Q_2$  0.45,  $n = 8$ ,  $N = 167$ ;  $p = 0.0140$ , unpaired t-test (two-tailed),  $t = 2.805$ ,  $df = 14$ ), F-actin/tau (*trkBTK* $^{+/+}$   $1.00 \pm 0.04$ ,  $Q_2$  0.99, IQR 0.15,  $n = 19$ ,  $N = 254$ ; *trkBTK* $^{-/-}$   $0.76 \pm 0.11$ ,  $Q_2$  0.64, IQR 0.44,  $n = 18$ ,  $N = 298$ ;  $p = 0.0005$ , Mann Whitney test (two-tailed), Mann Whitney U 60)

Fig. 5B: Growth cone size in [ $\mu\text{m}^2$ ] (BDNF (B)  $31.59 \pm 1.75$ ,  $Q_2$  31.05,  $n = 18$ ,  $N = 385$ ; CNTF (C)  $23.01 \pm 2.12$ ,  $Q_2$  20.73,  $n = 17$ ,  $N = 425$ ; GDNF (G)  $21.79 \pm 1.69$ ,  $Q_2$  18.27,  $n = 17$ ,  $N = 435$ ;  $p$  (B-C) = 0.0054,  $p$  (B-G) = 0.0014, one-way ANOVA with Tukey's Multiple Comparison), tau (BDNF (B)  $1.00 \pm 0.03$ ,  $Q_2$  1.00,  $n = 15$ ,  $N = 323$ ; CNTF (C)  $1.13 \pm 0.09$ ,  $Q_2$  1.08,  $n = 13$ ,  $N = 336$ ; GDNF (G)  $1.05 \pm 0.08$ ,  $Q_2$  1.07,  $n = 13$ ,  $N = 334$ ;  $p$  (B-C) = 0.4044,  $p$  (B-G) = 0.8411, one-way ANOVA with Tukey's Multiple Comparison),  $\beta$ -actin (BDNF (B)  $1.00 \pm 0.03$ ,  $Q_2$  1.00, IQR 0.03,  $n = 11$ ,  $N = 267$ ; CNTF (C)  $0.85 \pm 0.10$ ,  $Q_2$  0.83, IQR 0.85,  $n = 9$ ,  $N = 274$ ; GDNF (G)  $0.73 \pm 0.06$ ,  $Q_2$  0.70, IQR 0.73,  $n = 9$ ,  $N = 274$ ;  $p$  (B-C) = 0.5874,  $p$  (B-G) = 0.0163, Kruskal-Wallis test with Dunn's multiple comparisons test), F-actin (BDNF (B)  $1.00 \pm 0.04$ ,  $Q_2$  1.00, IQR 0.01,  $n = 14$ ,  $N = 276$ ; CNTF (C)  $0.76 \pm 0.10$ ,  $Q_2$  0.79, IQR 0.33,  $n = 13$ ,  $N = 308$ ; GDNF (G)  $0.54 \pm 0.06$ ,  $Q_2$  0.49, IQR 0.37,  $n = 13$ ,  $N = 314$ ;  $p$  (B-C) = 0.0112,  $p$  (B-G)  $< 0.0001$ , Kruskal-Wallis test with Dunn's multiple comparisons test)

Fig. 6A: Axon length in [ $\mu\text{m}$ ] (*trkBTK* $^{+/+}$   $468.8 \pm 39.31$ ,  $Q_2$  454.9,  $n = 9$ ,  $N = 615$ ; *trkBTK* $^{-/-}$   $357.2 \pm 29.33$ ,  $Q_2$  363,  $n = 8$ ,  $N = 579$ ;  $p = 0.0417$ , unpaired t-test (two-tailed),  $t = 2.227$ ,  $df = 15$ )

Fig. 6C: Growth cone size in [ $\mu\text{m}^2$ ] (*trkBTK*<sup>+/+</sup>  $27.51 \pm 4.58$ ,  $Q_2$  25.06,  $n = 7$ ,  $N = 113$ ; *trkBTK*<sup>-/-</sup>  $16.55 \pm 1.26$ ,  $Q_2$  17.12,  $n = 11$ ,  $N = 178$ ;  $p = 0.0132$ , unpaired t-test (two-tailed),  $t = 2.788$ ,  $df = 16$ ),  $\beta$ -actin (*trkBTK*<sup>+/+</sup>  $1.00 \pm 0.07$ ,  $Q_2$  0.99,  $n = 7$ ,  $N = 113$ ; *trkBTK*<sup>-/-</sup>  $1.11 \pm 0.07$ ,  $Q_2$  1.15,  $n = 11$ ,  $N = 178$ ;  $p = 0.2696$ , unpaired t-test (two-tailed),  $t = 1.144$ ,  $df = 16$ ), F-actin (*trkBTK*<sup>+/+</sup>  $1.00 \pm 0.09$ ,  $Q_2$  1.00,  $n = 7$ ,  $N = 113$ ; *trkBTK*<sup>-/-</sup>  $0.81 \pm 0.06$ ,  $Q_2$  0.80,  $n = 11$ ,  $N = 178$ ;  $p = 0.0819$ , unpaired t-test (two-tailed),  $t = 1.856$ ,  $df = 16$ ), tau (*trkBTK*<sup>+/+</sup>  $1.00 \pm 0.06$ ,  $Q_2$  1.00,  $n = 7$ ,  $N = 113$ ; *trkBTK*<sup>-/-</sup>  $1.40 \pm 0.19$ ,  $Q_2$  1.25,  $n = 11$ ,  $N = 178$ ;  $p = 0.1287$ , unpaired t-test (two-tailed),  $t = 1.602$ ,  $df = 16$ )

Fig. 6D: Axon length in [ $\mu\text{m}$ ] (BDNF (B)  $425.3 \pm 14.93$ ,  $Q_2$  423.3,  $n = 5$ ,  $N = 256$ ; CNTF (C)  $439.0 \pm 18.37$ ,  $Q_2$  439.9,  $n = 6$ ,  $N = 258$ ; GDNF (G)  $388.6 \pm 24.47$ ,  $Q_2$  412.1,  $n = 5$ ,  $N = 273$ ;  $p$  (B-C) = 0.8710,  $p$  (B-G) = 0.4295, one-way ANOVA with Tukey's Multiple Comparison)

Fig. 6F: Growth cone size in [ $\mu\text{m}^2$ ] (BDNF (B)  $32.83 \pm 4.93$ ,  $Q_2$  29.04,  $n = 6$ ,  $N = 165$ ; CNTF (C)  $33.01 \pm 4.41$ ,  $Q_2$  30.96,  $n = 6$ ,  $N = 175$ ; GDNF (G)  $37.85 \pm 4.72$ ,  $Q_2$  38.52,  $n = 6$ ,  $N = 172$ ;  $p$  (B-C) = 0.9996,  $p$  (B-G) = 0.7352, one-way ANOVA with Tukey's Multiple Comparison), F-actin (BDNF (B)  $1.00 \pm 0.02$ ,  $Q_2$  1.00, IQR 0.04,  $n = 6$ ,  $N = 165$ ; CNTF (C)  $1.14 \pm 0.22$ ,  $Q_2$  0.95, IQR 0.97,  $n = 6$ ,  $N = 175$ ; GDNF (G)  $0.99 \pm 0.28$ ,  $Q_2$  0.79, IQR 1.02,  $n = 6$ ,  $N = 172$ ;  $p$  (B-C) > 0.9999,  $p$  (B-G) > 0.9999, Kruskal-Wallis test with Dunn's multiple comparisons test), tau (BDNF (B)  $1.00 \pm 0.03$ ,  $Q_2$  1.00, IQR 0.05,  $n = 6$ ,  $N = 165$ ; CNTF (C)  $0.92 \pm 0.08$ ,  $Q_2$  0.93, IQR 0.34,  $n = 6$ ,  $N = 175$ ; GDNF (G)  $0.82 \pm 0.11$ ,  $Q_2$  0.82, IQR 0.43,  $n = 6$ ,  $N = 172$ ;  $p$  (B-C) > 0.9999,  $p$  (B-G) = 0.3449, Kruskal-Wallis test with Dunn's multiple comparisons test), F-actin/tau (BDNF (B)  $1.00 \pm 0.08$ ,  $Q_2$  1.00, IQR 0.15,  $n = 6$ ,  $N = 165$ ; CNTF (C)  $1.25 \pm 0.16$ ,  $Q_2$  1.05, IQR 0.52,  $n = 6$ ,  $N = 175$ ; GDNF (G)  $1.12 \pm 0.24$ ,  $Q_2$  1.14, IQR 1.13,  $n = 6$ ,  $N = 172$ ;  $p$  (B-C) = 0.2459,  $p$  (B-G) = 0.6953, Kruskal-Wallis test with Dunn's multiple comparisons test)

Fig. 7A: pTrk/SynPhys (no pulse  $1.00 \pm 0.08$ ,  $Q_2$  1.00,  $n = 10$ ,  $N = 136$ ; 5' BDNF  $1.72 \pm 0.25$ ,  $Q_2$  1.63,  $n = 10$ ,  $N = 137$ ;  $p = 0.0154$ , unpaired t-test (two-tailed),  $t = 2.677$ ,  $df = 18$ )

Fig. 7B: pCof/Cofilin (no pulse  $1.00 \pm 0.03$ ,  $Q_2$  1.00,  $n = 11$ ,  $N = 174$ ; 5' BDNF  $1.73 \pm 0.17$ ,  $Q_2$  1.69,  $n = 11$ ,  $N = 176$ ;  $p = 0.0003$ , unpaired t-test (two-tailed),  $t = 4.303$ ,  $df = 20$ ), pCof/SynPhys (no pulse  $1.00 \pm 0.04$ ,  $Q_2$  1.00,  $n = 11$ ,  $N = 174$ ; 5' BDNF  $1.68 \pm 0.15$ ,  $Q_2$  1.70,  $n = 11$ ,  $N = 176$ ;  $p = 0.0003$ , unpaired t-test (two-tailed),  $t = 4.424$ ,  $df = 20$ )

Fig. 7C: pProf/SynPhys (no pulse  $1.00 \pm 0.04$ ,  $Q_2$  1.00, IQR 0.09,  $n = 13$ ,  $N = 200$ ; 5' BDNF  $1.59 \pm 0.12$ ,  $Q_2$  1.67, IQR 0.57,  $n = 14$ ,  $N = 226$ ;  $p = 0.0012$ , Mann Whitney test (two-tailed), Mann-Whitney U 24)

Fig. 7D:  $\beta$ -actin (no pulse  $1.00 \pm 0.07$ ,  $Q_2$  1.00,  $n = 7$ ,  $N = 194$ ; 5' BDNF  $1.00 \pm 0.09$ ,  $Q_2$  0.98,  $n = 9$ ,  $N = 236$ ;  $p = 0.9861$ , unpaired t-test (two-tailed),  $t = 0.0178$ ,  $df = 14$ ), F-actin (no pulse  $1.00 \pm 0.06$ ,  $Q_2$  1.00,  $n = 7$ ,  $N = 194$ ; 5' BDNF  $1.49 \pm 0.13$ ,  $Q_2$  1.48,  $n = 9$ ,  $N = 236$ ;  $p = 0.0088$ , unpaired t-test (two-tailed),  $t = 3.040$ ,  $df = 14$ ), tau (no pulse  $1.00 \pm 0.05$ ,  $Q_2$  1.00,  $n = 7$ ,  $N = 194$ ; 5' BDNF  $1.06 \pm 0.05$ ,  $Q_2$  1.08,  $n = 9$ ,  $N = 236$ ;  $p = 0.4391$ , unpaired t-test (two-tailed),  $t = 0.7965$ ,  $df = 14$ )

Fig. 7F: Velocity in  $\mu\text{m}/\text{sec}$  (no pulse  $0.25 \pm 0.02$ ,  $Q_2$  0.27, IQR 0.20,  $N = 49$ ; 5' BDNF  $0.18 \pm 0.02$ ,  $Q_2$  0.14, IQR 0.16,  $N = 44$ ;  $p = 0.0044$ , Mann Whitney test (two-tailed), Mann-Whitney U 707)

Fig. S1A:  $\text{Ca}^{2+}$  transients per min (Control  $0.45 \pm 0.09$ ,  $Q_2$  0.30, IQR 0.6,  $N = 85$ ; CTX  $0.24 \pm 0.06$ ,  $Q_2$  0.00, IQR 0.3,  $N = 86$ ;  $p = 0.0063$ , Mann Whitney test (two-tailed), Mann Whitney U 2873)

Fig. S1C:  $\text{Ca}_v2.2/\text{SynPhys}$  (Control\_Laminin-221/211  $1.58 \pm 0.49$ ,  $Q_2$  1.18,  $n = 3$ ,  $N = 32$ ; Control\_Laminin-111  $1.02 \pm 0.16$ ,  $Q_2$  0.91,  $n = 3$ ,  $N = 38$ ;  $\text{trkBTK}^{-/-}$ \_Laminin-221/211  $0.86 \pm 0.12$ ,  $Q_2$  0.86,  $n = 3$ ,  $N = 38$ ;  $\text{trkBTK}^{-/-}$ \_Laminin-111  $1.07 \pm 0.12$ ,  $Q_2$  1.09,  $n = 3$ ,  $N = 36$ ),  $\text{Ca}_v2.2/\text{SynPhys}$  – Laminin-221/211 vs Laminin-111 (Control  $1.48 \pm 0.21$ ,  $Q_2$  1.30,  $n = 3$ ;  $\text{trkBTK}^{-/-}$   $0.83 \pm 0.16$ ,  $Q_2$  0.98,  $n = 3$ )

Fig. S1D: Protrusion vs core ( $\text{trkB}$   $1.40 \pm 0.09$ ,  $Q_2$  1.28, IQR 0.81;  $\text{c-ret}$   $1.08 \pm 0.07$ ,  $Q_2$  1.00, IQR 0.61;  $N = 72$ ,  $p = 0.0021$ , Mann Whitney test (two-tailed), Mann Whitney U 1820)

Fig. S2A: Soma size in [ $\mu\text{m}^2$ ] ( $\text{trkBTK}^{+/+}$   $216.9 \pm 10.13$ ,  $Q_2$  226.4,  $n = 7$ ,  $N = 124$ ;  $\text{trkBTK}^{-/-}$   $203.6 \pm 6.815$ ,  $Q_2$  201.6,  $n = 5$ ,  $N = 72$ ;  $p = 0.3445$ , unpaired t-test (two tailed),  $t = 0.9921$ ,  $\text{df} = 10$ ), number of dendrites per soma ( $\text{trkBTK}^{+/+}$   $4.93 \pm 0.25$ ,  $Q_2$  5,  $n = 7$ ,  $N = 124$ ;  $\text{trkBTK}^{-/-}$   $4.40 \pm 0.24$ ,  $Q_2$  4,  $n = 5$ ,  $N = 72$ ;  $p = 0.1796$ , unpaired t-test (two tailed),  $t = 1.443$ ,  $\text{df} = 10$ ), mean dendrite length in [ $\mu\text{m}$ ] ( $\text{trkBTK}^{+/+}$   $25.13 \pm 1.31$ ,  $Q_2$  23.9,  $n = 7$ ,  $N = 640$ ;  $\text{trkBTK}^{-/-}$   $28.67 \pm 2.11$ ,  $Q_2$  28.29,  $n = 5$ ,  $N = 328$ ;  $p = 0.1625$ , unpaired t-test (two tailed),  $t = 1.508$ ,  $\text{df} = 10$ ), total dendrite length in [ $\mu\text{m}$ ] ( $\text{trkBTK}^{+/+}$   $133 \pm 9.14$ ,  $Q_2$  124.1, IQR 48.1,  $n = 7$ ,  $N = 124$ ;  $\text{trkBTK}^{-/-}$   $137.1 \pm 18.52$ ,  $Q_2$  123.1, IQR 54.4,  $n = 5$ ,  $N = 72$ ;  $p = 1.0000$ , Mann Whitney (two tailed), Mann Whitney U 17)

Fig. S2C: Soma size in [ $\mu\text{m}^2$ ] (BDNF (B)  $205.8 \pm 13.37$ ,  $Q_2$  195.3,  $n = 6$ ,  $N = 106$ ; CNTF (C)  $207.4 \pm 15.69$ ,  $Q_2$  207.2,  $n = 6$ ,  $N = 106$ ; GDNF (G)  $187.9 \pm 7.59$ ,  $Q_2$  193.9,  $n = 6$ ,  $N = 96$ ;  $p$  (B-C) = 0.9962,  $p$  (B-G) = 0.6233, one-way ANOVA with Tukey's Multiple Comparison), number of dendrites per soma (BDNF (B)  $4.42 \pm 0.20$ ,  $Q_2$  4.25,  $n = 6$ ,  $N = 106$ ; CNTF (C)  $4.42 \pm 0.20$ ,  $Q_2$  4.25,  $n = 6$ ,  $N = 106$ ; GDNF (G)  $3.92 \pm 0.20$ ,  $Q_2$  4,  $n = 6$ ,  $N = 96$ ;  $p$  (B-C) > 0.9999,  $p$  (B-G) = 0.2159, one-way ANOVA with Tukey's Multiple Comparison), mean dendrite length in [ $\mu\text{m}$ ] (BDNF (B)  $27.81 \pm 0.70$ ,  $Q_2$  28.28,  $n = 6$ ,  $N = 488$ ; CNTF (C)  $28.49 \pm 1.21$ ,  $Q_2$  27.8,  $n = 6$ ,  $N = 457$ ; GDNF (G)  $31.03 \pm 1.36$ ,  $Q_2$  30,  $n = 6$ ,  $N = 391$ ;  $p$  (B-C) = 0.9050,  $p$  (B-G) = 0.1407, one-way ANOVA with Tukey's Multiple Comparison), total dendrite length in [ $\mu\text{m}$ ] (BDNF (B)  $138.2 \pm 7.92$ ,  $Q_2$  134.5,  $n = 6$ ,  $N = 106$ ; CNTF (C)  $131.5 \pm 8.41$ ,  $Q_2$  127.1,  $n = 6$ ,  $N = 106$ ; GDNF (G)  $133.6 \pm 7.00$ ,  $Q_2$  137.4,  $n = 6$ ,  $N = 96$ ;  $p$  (B-C) = 0.8194,  $p$  (B-G) = 0.6233, one-way ANOVA with Tukey's Multiple Comparison)

Fig. S2D: Cell survival in % (BDNF (B)  $51.91 \pm 2.87$ ,  $Q_2$  53.19,  $n = 12$ ; CNTF (C)  $50.74 \pm 2.46$ ,  $Q_2$  49.89,  $n = 12$ ; GDNF (G)  $50.38 \pm 2.44$ ,  $Q_2$  50.37,  $n = 12$ ; no factor (NF)  $24.35 \pm 2.00$ ,  $Q_2$  21.48,  $n = 12$ ;  $p$  (B-C) = 0.9864,  $p$  (B-G) = 0.9712,  $p$  (B-NF) < 0.0001, one-way ANOVA with Tukey's Multiple Comparison)

Fig. S2E: Soma size in [ $\mu\text{m}^2$ ] ( $\text{trkBTK}^{+/+}$   $195.2 \pm 14.97$ ,  $Q_2$  181,  $n = 7$ ,  $N = 143$ ;  $\text{trkBTK}^{-/-}$   $198.0 \pm 13.46$ ,  $Q_2$  199.1,  $n = 7$ ,  $N = 124$ ;  $p = 0.8950$ , unpaired t-test (two tailed),  $t = 0.1348$ ,  $\text{df} = 12$ ), number of dendrites per soma ( $\text{trkBTK}^{+/+}$   $4.29 \pm 0.18$ ,  $Q_2$  4, IQR 1,  $n = 7$ ,  $N = 143$ ;  $\text{trkBTK}^{-/-}$   $4.00 \pm 0.29$ ,  $Q_2$  4, IQR 1.5,  $n = 7$ ,  $N = 124$ ;  $p = 0.3328$ , Mann Whitney (two tailed), Mann Whitney U 17), mean dendrite length in [ $\mu\text{m}$ ] ( $\text{trkBTK}^{+/+}$   $26.82 \pm 1.42$ ,  $Q_2$  26.09,  $n = 7$ ,  $N = 661$ ;  $\text{trkBTK}^{-/-}$   $29.82 \pm 1.84$ ,  $Q_2$  30.53,  $n = 7$ ,  $N = 560$ ;  $p = 0.2219$ , unpaired t-test (two tailed),  $t = 1.288$ ,  $\text{df} = 12$ ), total dendrite length in [ $\mu\text{m}$ ] ( $\text{trkBTK}^{+/+}$   $128.5 \pm 3.91$ ,  $Q_2$  133.1,  $n = 7$ ,  $N = 143$ ;  $\text{trkBTK}^{-/-}$   $137.8 \pm 5.26$ ,  $Q_2$  143,  $n = 7$ ,  $N = 124$ ;  $p = 0.1835$ , unpaired t-test (two-tailed),  $t = 1.411$ ,  $\text{df} = 12$ )

Fig. S2F: Soma size in [ $\mu\text{m}^2$ ] (BDNF (B)  $185.3 \pm 12.64$ ,  $Q_2$  181.4,  $n = 5$ ,  $N = 99$ ; CNTF (C)  $187.3 \pm 9.87$ ,  $Q_2$  195.1,  $n = 6$ ,  $N = 124$ ; GDNF (G)  $198.8 \pm 10.12$ ,  $Q_2$  201.1,  $n = 5$ ,  $N = 124$ ;  $p$  (B-C) = 0.9904,  $p$  (B-G) = 0.6784, one-way ANOVA with Tukey's Multiple Comparison), number of dendrites per soma (BDNF (B)  $4.40 \pm 0.24$ ,  $Q_2$  4.00, IQR 1.00,  $n = 5$ ,  $N = 99$ ; CNTF (C)  $4.33 \pm 0.31$ ,  $Q_2$  4.50, IQR 1.25,  $n = 6$ ,  $N = 124$ ; GDNF (G)  $4.40 \pm 0.24$ ,  $Q_2$  4.00, IQR 1.00,  $n = 5$ ,  $N = 124$ ;  $p$  (B-C) > 0.9999,  $p$  (B-G) > 0.9999, Kruskal-Wallis test with Dunn's multiple comparisons test), mean dendrite length in [ $\mu\text{m}$ ] (BDNF (B)  $26.58 \pm 1.34$ ,  $Q_2$  25.61,  $n = 5$ ,  $N = 447$ ; CNTF (C)  $27.30 \pm 0.75$ ,  $Q_2$  26.9,  $n = 6$ ,  $N = 583$ ; GDNF (G)  $27.74 \pm 1.43$ ,  $Q_2$  27.04,  $n = 5$ ,  $N = 517$ ;  $p$  (B-C) = 0.8965,  $p$  (B-G) = 0.7771, one-way ANOVA with Tukey's Multiple Comparison), total dendrite length in [ $\mu\text{m}$ ] (BDNF (B)  $124.4 \pm 7.66$ ,  $Q_2$  127.7,  $n = 5$ ,  $N = 99$ ; CNTF (C)  $129.4 \pm 6.74$ ,  $Q_2$  130.3,  $n = 6$ ,  $N = 124$ ; GDNF (G)  $133.9 \pm 11.54$ ,  $Q_2$  125.5,  $n = 5$ ,  $N = 124$ ;  $p$  (B-C) = 0.9103,  $p$  (B-G) = 0.7396, one-way ANOVA with Tukey's Multiple Comparison)

Fig. S3A:  $\text{Ca}_v2.2$  – 5' BDNF vs no pulse (Control  $1.52 \pm 0.19$ ,  $Q_2$  1.38,  $n = 5$ ,  $N$  (no pulse) = 129,  $N$  (5' BDNF) = 140; Acetone  $0.90 \pm 0.08$ ,  $Q_2$  0.92,  $n = 5$ ,  $N$  (no pulse) = 140,  $N$  (5' BDNF) = 145;  $p$  (Control) = 0.0491,  $t = 2.793$ ,  $df = 4$ ;  $p$  (Acetone) = 0.3055,  $t = 1.174$ ,  $df = 4$ ; one sample t-test with theoretical mean set as 1)

Fig. S3B: F-actin – 5' BDNF vs no pulse (Control  $1.24 \pm 0.02$ ,  $Q_2$  1.24,  $n = 3$ ,  $N$  (no pulse) = 118,  $N$  (5' BDNF) = 116; Acetone  $1.22 \pm 0.04$ ,  $Q_2$  1.20,  $n = 3$ ,  $N$  (no pulse) = 119,  $N$  (5' BDNF) = 91;  $p$  (Control) = 0.0072,  $t = 11.73$ ,  $df = 2$ ;  $p$  (Acetone) = 0.0241,  $t = 6.329$ ,  $df = 2$ ; one sample t-test with theoretical mean set as 1)

Fig. S3D: PP1 –  $\text{Ca}_v2.2$  (Control\_no pulse (A)  $1.00 \pm 0.02$ ,  $Q_2$  1.00,  $n = 5$ ,  $N = 136$ ; Control\_5' BDNF (B)  $1.76 \pm 0.28$ ,  $Q_2$  1.51,  $n = 6$ ,  $N = 169$ ; PP1\_no pulse (C)  $1.07 \pm 0.09$ ,  $Q_2$  1.07,  $n = 4$ ,  $N = 116$ ; PP1\_5' BDNF (D)  $1.01 \pm 0.18$ ,  $Q_2$  1.07,  $n = 5$ ,  $N = 130$ ;  $p$  (AB) = 0.0496,  $p$  (BD) = 0.0538,  $p$  (CD) = 0.9970, one-way ANOVA with Tukey's Multiple Comparison), PP1 – APP (Control\_no pulse (A)  $1.00 \pm 0.03$ ,  $Q_2$  1,  $n = 5$ ,  $N = 136$ ; Control\_5' BDNF (B)  $1.33 \pm 0.18$ ,  $Q_2$  1.18,  $n = 6$ ,  $N = 169$ ; PP1\_no pulse (C)  $1.05 \pm 0.14$ ,  $Q_2$  1.06,  $n = 4$ ,  $N = 116$ ; PP1\_5' BDNF (D)  $1.22 \pm 0.24$ ,  $Q_2$  1.34,  $n = 5$ ,  $N = 130$ ;  $p$  (AB) = 0.5279,  $p$  (BD) = 0.9720,  $p$  (CD) = 0.9046, one-way ANOVA with Tukey's Multiple Comparison), CytD –  $\text{Ca}_v2.2$  (Control\_no pulse (A)  $1.00 \pm 0.06$ ,  $Q_2$  1.00,  $n = 7$ ,  $N = 166$ ; Control\_5' BDNF (B)  $1.69 \pm 0.31$ ,  $Q_2$  1.43,  $n = 6$ ,  $N = 151$ ; CytD\_no pulse (C)  $1.24 \pm 0.30$ ,  $Q_2$  0.98,  $n = 3$ ,  $N = 85$ ; CytD\_5' BDNF (D)  $0.93 \pm 0.26$ ,  $Q_2$  0.95,  $n = 5$ ,  $N = 114$ ;  $p$  (AB) = 0.1266,  $p$  (BD) = 0.1182,  $p$  (CD) = 0.8441, one-way ANOVA with Tukey's Multiple Comparison), CytD – APP (Control\_no pulse (A)  $1.00 \pm 0.04$ ,  $Q_2$  1.00,  $n = 7$ ,  $N = 166$ ; Control\_5' BDNF (B)  $1.11 \pm 0.09$ ,  $Q_2$  1.04,  $n = 6$ ,  $N = 151$ ; CytD\_no pulse (C)  $0.84 \pm 0.22$ ,  $Q_2$  1.05,  $n = 3$ ,  $N = 85$ ; CytD\_5' BDNF (D)  $1.20 \pm 0.21$ ,  $Q_2$  0.95,  $n = 5$ ,  $N = 114$ ;  $p$  (AB) = 0.9186,  $p$  (BD) = 0.9477,  $p$  (CD) = 0.3769, one-way ANOVA with Tukey's Multiple Comparison; the BDNF pulse *per se* resulted in increased  $\text{Ca}_v2.2$  immunoreactivity under control conditions, unpaired t-test (two-tailed),  $p = 0.0353$ ,  $t = 2.400$ ,  $df = 11$ )

Fig. S4A: actin mRNA (no pulse  $1.00 \pm 0.05$ ,  $Q_2$  1.00,  $n = 10$ ,  $N = 225$ ; 5' BDNF  $1.72 \pm 0.19$ ,  $Q_2$  1.56,  $n = 10$ ,  $N = 233$ ;  $p = 0.0021$ , unpaired t-test (two-tailed),  $t = 3.583$ ,  $df = 18$ )

Fig. S4B: actin mRNA (*trkBTK*<sup>+/+</sup>  $1.00 \pm 0.06$ ,  $Q_2$  1.00,  $n = 7$ ,  $N = 190$ ; *trkBTK*<sup>-/-</sup>  $0.62 \pm 0.06$ ,  $Q_2$  0.69,  $n = 9$ ,  $N = 229$ ;  $p = 0.0006$ , unpaired t-test (two-tailed),  $t = 4.429$ ,  $df = 14$ )

Fig. S4C: actin mRNA (BDNF (B)  $1.00 \pm 0.08$ ,  $Q_2$  0.97,  $n = 8$ ,  $N = 186$ ; CNTF (C)  $0.62 \pm 0.06$ ,  $Q_2$  0.63,  $n = 5$ ,  $N = 148$ ; GDNF (G)  $0.63 \pm 0.10$ ,  $Q_2$  0.72,  $n = 6$ ,  $N = 211$ ;  $p$  (B-C) = 0.0175,  $p$  (B-G) = 0.0147, one-way ANOVA with Tukey's Multiple Comparison)

Fig. S4D: Glu-Tub (*trkBTK*<sup>+/+</sup>  $1.00 \pm 0.11$ ,  $Q_2$  0.94,  $n = 7$ ,  $N = 91$ ; *trkBTK*<sup>-/-</sup>  $1.09 \pm 0.18$ ,  $Q_2$  1.01,  $n = 4$ ,  $N = 66$ ;  $p = 0.6634$ , unpaired t-test (two-tailed),  $t = 0.4500$ ,  $df = 9$ ), YL1/2-Tub (*trkBTK*<sup>+/+</sup>  $1.00 \pm 0.07$ ,  $Q_2$  0.97,  $n = 7$ ,  $N = 91$ ; *trkBTK*<sup>-/-</sup>  $1.03 \pm 0.10$ ,  $Q_2$  1.06,  $n = 4$ ,  $N = 66$ ;  $p = 0.8251$ , unpaired t-test (two-tailed),  $t = 0.2275$ ,  $df = 9$ )

Fig. S4E: Glu-Tub (BDNF (B)  $1.00$ ,  $Q_2$  1.00,  $n = 7$ ,  $N = 198$ ; CNTF (C)  $0.93 \pm 0.05$ ,  $Q_2$  0.92,  $n = 7$ ,  $N = 186$ ; GDNF (G)  $0.98 \pm 0.04$ ,  $Q_2$  0.93,  $n = 7$ ,  $N = 180$ ;  $p$  (B-C) = 0.3290,  $p$  (B-G) = 0.8892, one-way ANOVA with Tukey's Multiple Comparison), YL1/2-Tub (BDNF (B)  $1.00$ ,  $Q_2$  1.00,  $n = 7$ ,  $N = 198$ ; CNTF (C)  $0.98 \pm 0.05$ ,  $Q_2$  0.96,  $n = 7$ ,  $N = 186$ ; GDNF (G)  $1.05 \pm 0.02$ ,  $Q_2$  1.05,  $n = 7$ ,  $N = 180$ ;  $p$  (B-C) = 0.9476,  $p$  (B-G) = 0.5673, one-way ANOVA with Tukey's Multiple Comparison)

Fig. S4F: F-actin/tau (Control\_Laminin-221/211  $2.05 \pm 1.08$ ,  $Q_2$  1.59,  $n = 3$ ,  $N = 20$ ; Control\_Laminin-111  $0.54 \pm 0.04$ ,  $Q_2$  0.55,  $n = 3$ ,  $N = 25$ ; *trkBTK*<sup>-/-</sup>\_Laminin-221/211  $0.74 \pm 0.18$ ,  $Q_2$  0.75,  $n = 3$ ,  $N = 26$ ; *trkBTK*<sup>-/-</sup>\_Laminin-111  $0.66 \pm 0.13$ ,  $Q_2$  0.60,  $n = 3$ ,  $N = 25$ ), F-actin/tau – Laminin-221/211 vs Laminin-111 (Control  $3.57 \pm 1.74$ ,  $Q_2$  2.87,  $n = 3$ ; *trkBTK*<sup>-/-</sup>  $1.30 \pm 0.50$ ,  $Q_2$  1.25,  $n = 3$ )

Fig. S5A: trkB – immunoreactivity (no pulse  $1.00 \pm 0.01$ ,  $Q_2$  1.00,  $n = 9$ ,  $N = 165$ ; 5' BDNF  $1.26 \pm 0.12$ ,  $Q_2$  1.33,  $n = 9$ ,  $N = 139$ ;  $p = 0.0474$ , unpaired t-test (two-tailed),  $t = 2.148$ ,  $df = 16$ ), trkB – protrusion vs core (no pulse  $1.00 \pm 0.03$ ,  $Q_2$  1.00,  $n = 9$ ,  $N = 165$ ; 5' BDNF  $1.31 \pm 0.11$ ,  $Q_2$  1.29,  $n = 9$ ,  $N = 139$ ;  $p = 0.0117$ , unpaired t-test (two-tailed),  $t = 2.843$ ,  $df = 16$ )

Fig. S5B: trkB/APP (non-transduced (A)  $1.08 \pm 0.06$ ,  $Q_2$  1.00, IQR 0.28,  $N = 49$ ; GFP control (B)  $1.15 \pm 0.12$ ,  $Q_2$  1.00, IQR 0.82,  $N = 29$ ; shtrkB (C)  $0.45 \pm 0.04$ ,  $Q_2$  0.40, IQR 0.31,  $N = 37$ ;  $p$  (AB) > 0.9999,  $p$  (AC) < 0.0001,  $p$  (BC) < 0.0001, Kruskal-Wallis test with Dunn's multiple comparison tests)

Fig. S5C: pTrk/TrkB (no pulse  $0.16 \pm 0.07$ ,  $Q_2$  0.15,  $n = 3$ ; 5' BDNF  $1.11 \pm 0.11$ ,  $Q_2$  1.21,  $n = 3$ ), pAKT/AKT (no pulse  $0.60 \pm 0.12$ ,  $Q_2$  0.71,  $n = 3$ ; 5' BDNF  $1.26 \pm 0.12$ ,  $Q_2$  1.20,  $n = 3$ ), pMAPK/MAPK (no pulse  $0.58 \pm 0.13$ ,  $Q_2$  0.63,  $n = 3$ ; 5' BDNF  $1.27 \pm 0.25$ ,  $Q_2$  1.17,  $n = 3$ ), pLIMK1+2/LIMK1 (no pulse  $0.53 \pm 0.17$ ,  $Q_2$  0.42,  $n = 3$ ; 5' BDNF  $1.31 \pm 0.58$ ,  $Q_2$  1.11,  $n = 3$ ), pCof/AKT (no pulse  $0.19 \pm 0.05$ ,  $Q_2$  0.22,  $n = 3$ ; 5' BDNF  $0.36 \pm 0.10$ ,  $Q_2$  0.27,  $n = 3$ )

Fig. S5D: F/G Ratio  $\beta$ -actin (no pulse  $1.13 \pm 0.10$ ,  $Q_2$  1.07,  $n = 3$ ; 5' BDNF  $2.17 \pm 0.35$ ,  $Q_2$  2.00,  $n = 3$ )

Fig. S5E: pTrk/SynPhys (no pulse  $1.00 \pm 0.16$ ,  $Q_2$  1.00,  $n = 3$ ,  $N = 56$ ; 5' BDNF  $1.34 \pm 0.17$ ,  $Q_2$  1.27,  $n = 4$ ,  $N = 68$ )

Fig. S5F:  $\beta$ -actin/tau (no pulse  $1.00 \pm 0.10$ ,  $Q_2$  1.00,  $n = 3$ ,  $N = 48$ ; 5' BDNF  $1.56 \pm 0.25$ ,  $Q_2$  1.34,  $n = 4$ ,  $N = 68$ ), F-actin/tau (no pulse  $1.00 \pm 0.15$ ,  $Q_2$  1.00,  $n = 3$ ,  $N = 48$ ; 5' BDNF  $0.94 \pm 0.05$ ,  $Q_2$  0.94,  $n = 4$ ,  $N = 68$ )