Truncated TrkB-T1 mediates neurotrophin-evoked calcium signalling in glia cells.

Abstract:
The neurotrophin receptor TrkB is essential for normal function of the mammalian brain. It is expressed in three splice variants. Full-length receptors (TrkB(FL)) possess an intracellular tyrosine kinase domain and are considered as those TrkB receptors that mediate the crucial effects of brain-derived neurotrophic factor (BDNF) or neurotrophin 4/5 (NT-4/5). By contrast, truncated receptors (TrkB-T1 and TrkB-T2) lack tyrosine kinase activity and have not been reported to elicit rapid intracellular signalling. Here we show that astrocytes predominately express TrkB-T1 and respond to brief application of BDNF by releasing calcium from intracellular stores. The calcium transients are insensitive to the tyrosine kinase blocker K-252a and persist in mutant mice lacking TrkB(FL). By contrast, neurons produce rapid BDNF-evoked signals through TrkB(FL) and the Na(v)1.9 channel. Expression of antisense TrkB messenger RNA strongly reduces BDNF-evoked calcium signals in glia. Thus, our results show that, unexpectedly, TrkB-T1 has a direct signalling role in mediating inositol-1,4,5-trisphosphate-dependent calcium release; in addition, they identify a previously unknown mechanism of neurotrophin action in the brain.