

Neuregulin 1 signalling modulates mGluR1 function in mesencephalic dopaminergic neurons

A Ledonne, A Nobili, EC Latagliata, V Cavallucci, E Guatteo, S Puglisi-Allegra, M D'Amelio and NB Mercuri

Neuregulin 1 (NRG1) is a trophic factor that has an essential role in the nervous system by modulating neurodevelopment, neurotransmission and synaptic plasticity. Despite the evidence that NRG1 and its receptors, ErbB tyrosine kinases, are expressed in mesencephalic dopaminergic nuclei and their functional alterations are reported in schizophrenia and Parkinson's disease, the role of NRG1/ErbB signalling in dopaminergic neurons remains unclear. Here we found that NRG1 selectively increases the metabotropic glutamate receptor 1 (mGluR1)-activated currents by inducing synthesis and trafficking to membrane of functional receptors and stimulates phosphatidylinositol 3-kinase-Akt-mammalian target of rapamycin (PI3K-Akt-mTOR) pathway, which is required for mGluR1 function. Notably, an endogenous NRG1/ErbB tone is necessary to maintain mGluR1 function, by preserving its surface membrane expression in dopaminergic neurons. Consequently, it enables striatal mGluR1-induced dopamine outflow in *in vivo* conditions. Our results identify a novel role of NRG1 in the dopaminergic neurons, whose functional alteration might contribute to devastating diseases, such as schizophrenia and Parkinson's disease.