Presynaptic c-Jun N-terminal Kinase 2 regulates NMDA receptor-dependent glutamate release

R. Nisticò[1], F. Florenzano[1], D. Mango[1], M. Grilli[2], S. Marcelli[1], F. Iannuzzi[1],M. Morbin[3], M. Marchi[2], N.B. Mercuri[4], R.J. Davis[5], A. Pittaluga[2],M. Feligioni[1]

[1]Laboratory of Pharmacology of Synaptic Plasticity, EBRI 'Rita Levi-Montalcini' Foundation, Rome, 00143, Italy
[2]Dept. of Pharmacy, Pharmacology and Toxicology Section, University of Genoa, Genoa, 16148, Italy
[3]Neuropathology & Neurology V - IRCCS Foundation C. Besta Milan, 20133, Italy
[4]Laboratory of Experimental Neurology, IRCCS Fondazione Santa Lucia, Rome, 00143, Italy
[5]Dept. of Biochemistry and Molecular Biology, Howard Hughes Medical Institute and Program in Molecular Medicine, University of Massachusetts Medical School, Worcester, Massachusetts, 01605, USA

Activation of c-Jun N-terminal kinase (JNK) signaling pathway is a critical step for neuronal death occurring in several neurological conditions. JNKs can be activated via receptor tyrosine kinases, cytokine receptors, G-protein coupled receptors and ligand-gated ion channels, including the NMDA glutamate receptors. While JNK has been generally associated with postsynaptic NMDA receptors, its presynaptic role remains largely unexplored. Here, by means of biochemical, morphological and functional approaches, we demonstrate that JNK and its scaffold protein JIP1 are also expressed at the presynaptic level and that the NMDA-evoked glutamate release is controlled by presynaptic JNK-JIP1 interaction. Moreover, using knockout mice for single JNK isoforms, we proved that JNK2 is the essential isoform in mediating this presynaptic event. Overall the present findings unveil a novel JNK2 localization and function, which is likely to play a role in different physiological and pathological conditions (1).

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