The signaling pathways underlying BDNF-induced Nrf2 hippocampal nuclear translocation involve ROS, RyR-Mediated Ca2+ signals, ERK and PI3K

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 The neurotrophin Brain-Derived Neurotrophic Factor (BDNF) induces complex neuronal signaling cascades that are critical for the cellular changes underlying synaptic plasticity. These pathways include activation of Ca2+ entry via N-methyl-D-aspartate receptors and sequential activation of nitric oxide synthase and NADPH oxidase, which via generation of reactive nitrogen/oxygen species stimulate Ca2+-induced Ca2+ release mediated by Ryanodine Receptor (RyR) channels. These sequential events underlie BDNF-induced spine remodeling and type-2 RyR up-regulation. In addition, BDNF induces the nuclear translocation of the transcription factor Nrf2, a master regulator of antioxidant protein expression that protects cells against the oxidative damage caused by injury and inflammation. To investigate the possible BDNF-induced signaling cascades that mediate Nrf2 nuclear translocation in primary hippocampal cultures, we tested here whether reactive oxygen species, RyR-mediated