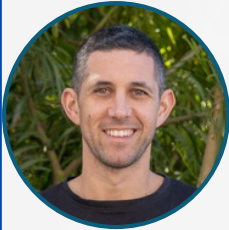


INTERNATIONAL CONFERENCE ON CELL SCIENCE AND REGENERATIVE MEDICINE



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BDNF-induced synaptic plasticity: the role of mitochondrial fission

Abstract: Brain-Derived Neurotrophic Factor (BDNF) is an important regulator of synaptic activity and a mediator of LTP of hippocampal synapses. Furthermore, synaptic activity controls mitochondrial fission and dynamic control of fission regulates plasticity induction in hippocampus. Given the important role of mitochondrial fission in establishing LTP and knowing the key role of BDNF in LTP induction, we hypothesized that the effects of BDNF on synaptic potentiation could be mediated by mitochondrial fission. We observed that local protein synthesis of Drp1, a key mediator of mitochondrial fission, is enhanced after stimulation of cultured hippocampal neurons with BDNF. FUNCAT-PLA experiments showed that BDNF upregulates the ‘de novo’ synthesis of Drp1 in the dendritic compartment, and at the synapses of cultured hippocampal neurons. Furthermore, immunocytochemistry experiments showed that BDNF stimulation increases Drp1 phosphorylation on Serine 616 in dendrites of cultured hippocampal neurons, which is known to increase the rate of mitochondrial fission. We have also analysed the effects of BDNF on mitochondrial dynamics in the dendritic compartment, labelling mitochondria through transfection with mito-DsRed and using video microscopy. These studies showed an increase of overall mitochondrial dynamics following stimulation of hippocampal neurons with BDNF. Moreover, inhibition of Drp1 with P110 decreased LTP in hippocampal CA1 synapses induced by 5 trains of theta burst-stimulation, and this effect was not additive with the inhibition by TrkB-Fc, which prevents the effect of endogenous BDNF. The results show a key role for mitochondrial dynamics in the effects of BDNF as mediator of synaptic plasticity.

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Keywords: Brain-Derived Neurotrophic Factor (BDNF), Mitochondria, Synapse