

Neurotrophins, neuronal plasticity and neuroprotection: role of antidepressant drugs

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Neuronal plasticity is active during the early postnatal life, when neuronal networks are modified by environmental guidance, but plasticity is much more restricted in adult brain. Antidepressant treatments have been shown to promote different forms of neuronal plasticity, including neurogenesis, synaptogenesis and neuronal maturation in the hippocampus. We have shown that antidepressants activate signaling of TrkB, the receptor for the neurotrophin brain-derived neurotrophic factor (BDNF) in adult brain and BDNF-TrkB signaling appears critical for the behavioral effects of antidepressants in rodents. By using the well-characterized developmental plasticity of the mammalian visual cortex as a model in collaboration with Prof. Maffei's lab, we recently showed that chronic antidepressant treatment reactivates the critical period-like plasticity in the visual cortex adult rats. Furthermore, we have showed that the impaired vision brought about by a closure of one eye throughout development (amblyopia) was completely rescued in adult rats if adult antidepressant treatment was combined with the opening of the amblyopic eye and patching of the better eye in rats in adulthood. These effects were associated with increased BDNF and could be inhibited by blocking BDNF signaling through TrkB receptors, emphasizing the important role of BDNF in adult plasticity. Very recently, we have observed that antidepressant fluoxetine reactivates a developmental-like state also in the fear-conditioning circuitry including amygdala and that a combination of fluoxetine treatment and fear extinction training leads to a long-term erasure of the conditioned fear response. Our data suggest that pharmacological agents, such as antidepressants, can reactivate developmental-type cortical plasticity and help to repair malfunctioning neuronal networks brought about by imbalanced early experiences, when antidepressant treatment is combined with environmental rehabilitation. These findings open up a novel view of antidepressant drug action where the drug treatment does not work alone, but act by relaxing neuronal plasticity facilitates the effects of psychotherapy and other types of rehabilitation.