BDNF is a member of the neurotrophic family and is the most abundant neurotrophin in the brain. BDNF plays a key role in the neuronal plasticity and survival of midbrain dopaminergic neurons. Evidence from animal and clinical studies suggests that increased brain BDNF activity may act through cleavage of pro-BDNF to increase risk of substance abuse.

To the Editor:

Substance abuse is a complex trait that is influenced by neurobiological, psychosocial, and environmental factors. While the ventral tegmental area/nucleus accumbens dopamine system is crucial to acute reward and the initiation of addiction, evidence suggests that permanent neuroplastic changes occur at the cellular and molecular levels that underlie the addictive process. The tissue-type plasminogen activator (tPA)/plasmin proteolytic cascade is known to be important for thrombolysis. However, recent evidence has uncovered new roles for this cascade in various aspects of synaptic plasticity and in the pathogenesis of substance abuse. For example, a single injection of morphine induced tPA mRNA and protein expression in the nucleus accumbens of mice. In the same study, morphine-induced conditioned place preference and hyperlocomotion were significantly reduced in tPA-knockout mice; the defect of morphine-induced hyperlocomotion in tPA-knockout mice was reversed by microinjections of either exogenous tPA or plasmin into the nucleus accumbens. Furthermore, other drugs of abuse such as methamphetamine, nicotine, and ethanol increase tPA expression and activity in the nucleus accumbens, and behavioral analyses of tPA-knockout mice revealed that the tPA/plasmin system plays a crucial role in the rewarding effects of methamphetamine and nicotine.

The above findings suggest that the tPA/plasminogen system could be regarded as a pro-addictive factor for substance abuse. However, the mechanisms underlying this substance abuse risk induced by the tPA/plasminogen system are poorly understood. The regulation of dopamine release evoked by morphine and nicotine in the nucleus accumbens by the tPA/plasminogen has been proposed as a possible mechanism. It has been recognized recently that drugs of abuse influence neuronal plasticity, possibly via the mechanisms of long-term potentiation, which enhances the dopamine transmission or activation in ventral tegmental area. In this report, we proposed that the role of tPA/plasmin in risk of substance abuse may arise from their action on brain-derived neurotrophic factor (BDNF) to influence the neuroplastic change in this respect.

References


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To the Editor:

Early identification of psychosis is one of the fields of contemporary psychiatry where pioneering efforts to promote evidence-based practices is closely coupled with an original, translation-oriented concept development. Gradually, in the last 15 years, the focus has moved from timely...