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Neuroadaptive Changes in the Dopaminergic System Associated with Cocaine Addiction: A Preclinical Study

Yousra A. El-Maradny*

Pharmaceutical and Fermentation Industries Development Center, City of Scientific Research and Technological Applications (SRTA-City), Egypt

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Introduction

Cocaine addiction is a neuropsychiatric disorder driven by compulsive drug seeking and consumption, despite adverse consequences. Central to this pathology are neuroadaptive changes in the brain's dopaminergic system, particularly within the mesolimbic reward pathway encompassing the ventral tegmental area (VTA) and nucleus accumbens (NAc)0020[1-5]. Chronic cocaine exposure disrupts normal dopaminergic signaling, leading to tolerance, sensitization, and altered reward processing. Preclinical animal models offer critical insights into the molecular and cellular underpinnings of addiction. This study investigates the long-term effects of repeated cocaine administration on dopamine receptor expression, transporter function, and synaptic plasticity in a rodent model [6-10].

Discussion

Using male Wistar rats, the study administered cocaine intraperitoneally over a 21-day period, followed by a 14-day withdrawal phase. Neurochemical analyses revealed a marked downregulation of D2 receptors in the NAc and upregulation of dopamine transporter (DAT) activity. Electrophysiological recordings showed increased excitatory postsynaptic potentials, indicating enhanced synaptic strength. Behavioral assays confirmed locomotor sensitization and increased drug-seeking behavior upon re-exposure. These findings are consistent with the theory of incentive sensitization, wherein repeated drug use amplifies the salience of drug-related cues through dopaminergic system remodeling. While preclinical findings cannot fully replicate human complexity, they provide a foundational understanding of addiction mechanisms and potential therapeutic targets. Interventions aimed at restoring dopaminergic balance, such as D2 receptor agonists or synaptic plasticity modulators, may offer novel treatment avenues.

Conclusion

Chronic cocaine use induces persistent neuroadaptive changes in the brain's reward system, particularly within the dopaminergic circuitry. Understanding these alterations is vital for developing pharmacological strategies that target the biological roots of addiction. Preclinical models remain indispensable for advancing our knowledge of substance use disorders and informing clinical innovation.

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***Corresponding author:** Yousra A. El-Maradny, Pharmaceutical and Fermentation Industries Development Center, City of Scientific Research and Technological Applications (SRTA-City), Egypt, E-mail: yousra789@gmail.com

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