## Differential Expression of Arc in the Mesocorticolimbic System Is Involved in Drug and Natural Rewarding Behavior in Rats

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**Abstract :** Aim: To investigate the different effects of heroin and milk in activating the corticostriatal system that plays a critical role in reward reinforcement learning. Methods: Male SD rats were trained daily for 15 d to self-administer heroin or milk tablets in a classic runway drug self-administration model. Immunohistochemical assay was used to quantify Arc protein expression in the medial prefrontal cortex (mPFC), the nucleus accumbens (NAc), the dorsomedial striatum (DMS) and the ventrolateral striatum (VLS) in response to chronic self-administration of heroin or milk tablets. NMDA receptor antagonist MK801 (0.1 mg/kg) or dopamine D1 receptor antagonist SCH23390 (0.03 mg/kg) were intravenously injected at the same time as heroin was infused intravenously. Results: Runway training with heroin resulted in robust enhancement of Arc expression in the mPFC, the NAc and the DMS on d 1, 7, and 15, and in the VLS on d 1 and d 7. However, runway training with milk led to increased Arc expression in the mPFC, the NAc and the DMS only on d 7 and/or d 15 but not on d 1. Moreover, runway training with milk failed to induce increased Arc protein in the VLS. Both heroin-seeking behavior and Arc protein expression were blocked by MK801 or SCH23390 administration. Conclusion: The VLS is likely to be critically involved in drug-seeking behavior.

Keywords : arc, mesocorticolimbic system, drug rewarding behavior, NMDA receptor

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