Administration of GABA agonists into nucleus accumbens on naloxone induced morphine withdrawal

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Introduction

Opioid addiction is a serious public health problem. Chronic opioid use results in tolerance to and dependence on the drug. Withdrawal syndrome is characterized by a number of physiological symptoms after the rapid cease of drugs. Mesocorticolumbic (MCL) dopaminergic pathway consisting of the ventral tegmental area (VTA), nucleus accumbens (NAc) and medial prefrontal cortex (mPFC) are related to opiate withdrawal [1]. Recently researches have provided a premise that gamma-aminobutyric acid (GABA) receptors play a modulatory role in the mechanism of action of different drugs of abuse. Stimulation of the GABA 
 receptor with agonists prevented or weakened the rewarding effects of many drugs of abuse, including methamphetamine, nicotine, heroin or morphine ethanol [2]. GABA 
 receptor agonist baclofen has been shown to reduce naloxone-induced withdrawal jumping in morphine-dependent mice [3].

The aim of this project is to investigate the effects of local GABA agonists in NAc during naloxone precipitated withdrawal in morphine dependent rats.

Experimental Protocol

Male and female Sprague-Dawley rats weighing 250-320 g supplied from Marmara University Experimental Research and Animal Center were used. All the rats were housed in a quiet and temperature controlled room (21±3˚C) maintained on a 12-h light/dark cycle (07:00-19:00 light) and were allowed food and water ad libitum. Rats were anesthetized with the numbers of jumpings (0.37 ± 0.26) as compared to aCSF (4.33 ± 1.14) and equal dose of baclofen into NAc core significantly decreased the number of jumpings (1.14 ± 1.14), wet dog shakes (3.57 ± 0.73) and weight loss (6.84 ± 1.05) as compared to aCSF (respectively 4.50 ± 0.89, 9.22 ± 1.84 and 10.43 ± 0.84) (p<0.05). Muscimol had no effects on withdrawal symptoms and locomotor activity variances.

Conclusions

Our findings suggest that GABAergic transmission in NAc have some roles over some of the opioid withdrawal signs and locomotor activity should be examined as a potential mechanism that can be exploited for the treatment of opioid addiction.

References: