Pioglitazone reduces the vulnerability to relapse to heroin seeking

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Addiction is a chronic relapsing disease characterized by loss of control over drug use, compulsive seeking and craving for a substance of abuse, and use that persists or resumes despite negative consequences. Dependence to opioid is recognized as one of the most pervasive form of addiction worldwide. In human addicts, reinstatement of heroin seeking could be triggered by stress, heroin associated cues or acute re-exposure to the drug.In addition, cue-induced reinstatement increases progressively after withdrawal, a phenomenon called incubation of heroin craving.

Recent evidence from our laboratory has demonstrated that activation of peroxisome proliferator-activated receptors (PPARγ) by pioglitazone, a drug currently used to treat insulin resistance in Type II diabetes, reduced the abuse liability associated with heroin and alcohol in rodents. Based on this finding we used four different animal models of relapse I) yohimbine stress-induced reinstatement, II) discriminative-cue induced reinstatement, III) drug priming induced reinstatement and IV) incubation of heroin craving to evaluate the effect of pioglitazone (10, 30 and 60 mg/kg), on attenuating the resumption of the heroin-reinforced operant response in the rat. Results demonstrated that activation of PPARγ by pioglitazone abolished the reinstatement of heroin seeking induced by yohimbine and reduced the priming induced relapse and the incubation of heroin craving. However, pioglitazone was not effective in attenuating the reinstatement induced by the re-exposure to the previously heroin associated cues.

The present study provides pre-clinical evidence of the efficacy of pioglitazone on reducing the vulnerability to relapse to heroin seeking. Based on these findings, we hypothesize that pioglitazone may represent a new therapeutic approach for the prevention of various forms of heroin relapse. Appropriate clinical investigation should be encouraged to thoroughly evaluate the potential of this drug.