Fenofibrate (a PPAR-α Agonist) Administered During Ethanol Withdrawal Reverts Ethanol-Induced Astrogliosis and Restores the Levels of Glutamate Transporter in Ethanol-Administered Adolescent Rats

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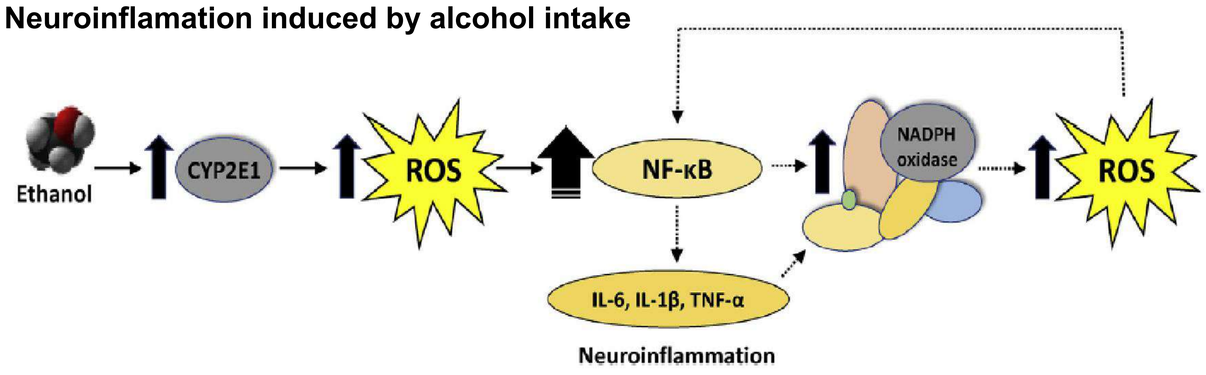
- **High-ethanol intake induces a neuroinflammatory response which decreases the expression of the main glutamater transporter (GLT-1). As a result, the extracellular level of this excitatory neurotransmitter is augmented.**
- **Glutamate is strongly implicated in the maintenance of chronic alcohol intake due to its capability of activating reward areas in the brain.**
- **The activation of peroxisome proliferator-activated receptor alpha (PPARα) by fibrates inhibits neuroinflammation in models other than alcohol consumption.**
- **We previously reported that the administration of fenofibrate to ethanol-drinking rats decreased ethanol consumption.**
- **In this work, we aimed to study if the reduction of alcohol consumption in rats treated with fenofibrate could be due to a decrease of ethanol-induced neuroinflammation, which would lead to the restoration of GLT-1 levels.**

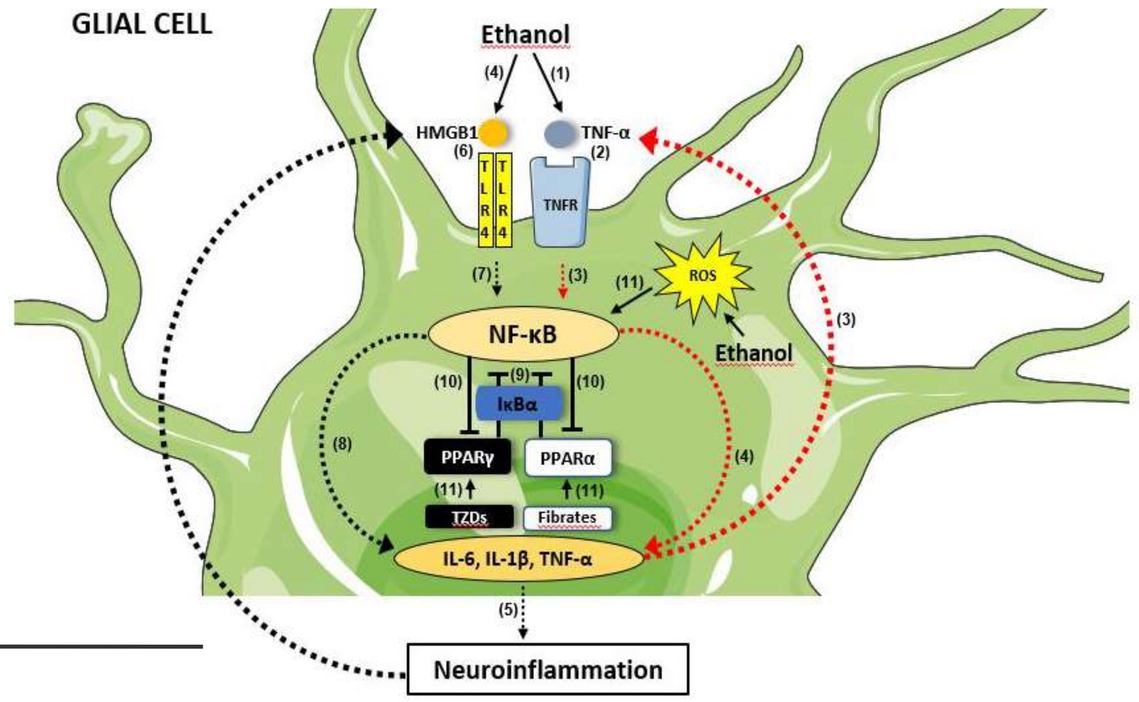
METHODS

- **30 day-old adolescent rats were administered ethanol on alternate days for 4 weeks (2 g/kg/day) by esophageal gavage.**
- **After ethanol withdrawal, fenofibrate was administered for 14 days (50 mg/kg/day) .**
- **The levels of glial fibrillary acidic protein (GFAP), phosphorylated NF-κB-inhibitory protein (plκBα) and GLT-1, were quantified in the prefrontal cortex, hippocampus, and hypothalamus by western blot.**

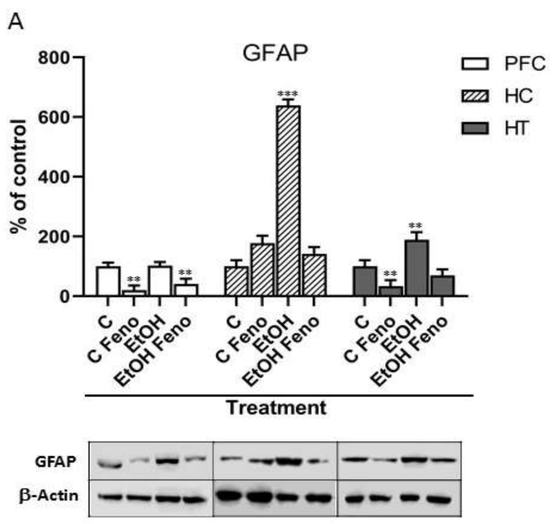
Neuroinflamation induced by alcohol intake

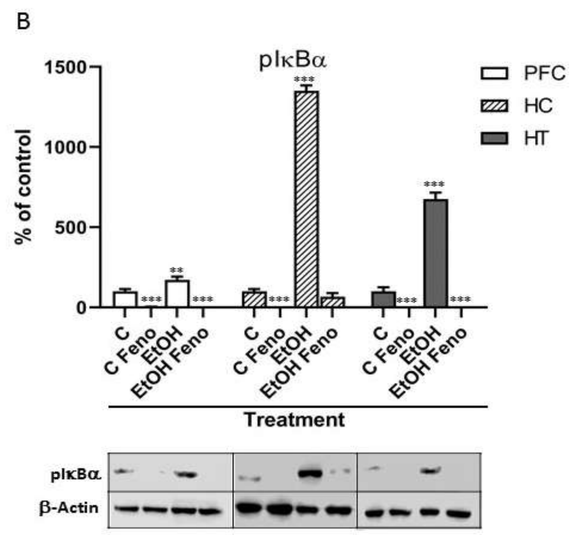


Possible mechanism of action of fenofibrate on etanol-induced neuroinflammation.

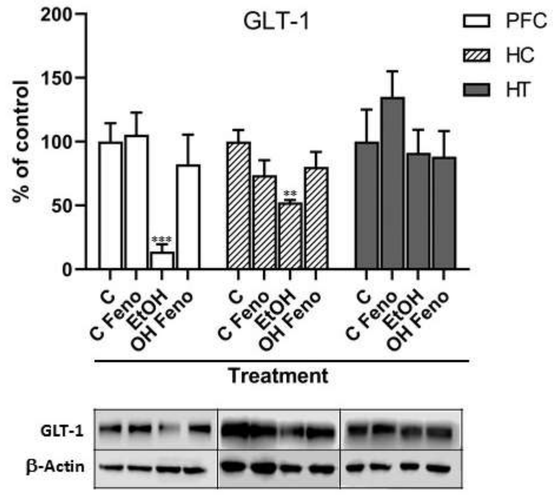


RESULTS





Expression levels of GFAP (A) and plκBα (B) in prefrontal cortex (PFC), hippocampus (HC) and hypothalamus (HT)



Expression levels of GLT-1 in prefrontal cortex (PFC), hippocampus (HC) and hypothalamus (HT)

CONCLUSIONS

i)Alcohol administration induces a marked glial activation and innate immune response in the prefrontal cortex, hippocampus and hypothalamus.

ii)Alcohol administration reduces GLT-1 levels in the prefrontal cortex and hippocampus.

iii) Fenofibrate administration reverts astrogliosis induced by alcohol intake in all the studied areas.

iv) Fenofibrate treatment restores GLt-1 levels, possibly due to decreased neuroinflammatory response.

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