PPAR gamma Activation reduces alcohol drinking through Modulation of the Mesolimbic Dopamine Transmission in Genetically selected Alcohol-Preferring Rats.

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The peroxisome proliferator-activated receptor gamma (PPAR□□ is one of the three isoforms of the PPARs family, known for its role in cellular differentiation, adipogenesis and metabolism (Desvergne et al., 1999). The discovery of PPAR□ in the ventral tegmental area (VTA) dopaminergic neurons (Sarruf et al., 2009) suggests the potential role of this receptor in the regulation of rewarded processing and motivated behavior in drug addiction. Furthermore, pioglitazone, a selective agonist of PPAR□ has been shown to suppress alcohol drinking and relapse to alcohol seeking in msP alcohol-preferring rats (Stopponi et al., 2011). However, the mechanisms underlying these effects are still to be elucidated.

Here, behavioral and electrophysiological studies have been carried out to explore the effect of pioglitazone in selected brain areas on alcohol drinking. To this end we have injected two doses of pioglitazone (5µg/µl and 10µg/µl in 0.3µl of vehicle per site) in the rostromedial tegmental nucleus (RMTg), in the ventral tegmental area (VTA), in the shell portion of the nucleus accumbens (NAcshell) and in the central nucleus of the amygdala (CeA) and we have evaluated the response in a two-bottle choice paradigm of alcohol drinking. Results showed that only the activation of PPAR□□ in RMTg reduces voluntary alcohol drinking. This is in agreement with ongoing ex vivo electrophysiological experiments, which suggest that activation of PPAR□ counteract ethanol-induced enhancement of the firing rate of DA neurons in the mesolimbic rewarding system. Conversely, pioglitazone (15 µM) was not able to induce this effect in PPAR□ KO mice, indicating that its action is strictly mediated by the binding with PPAR□□ So, our results extend the previous finding on the involvement of PPAR□ on alcohol abuse-related behaviors and confirm its potential role in the treatment of alcoholism.

Key words: Alcohol drinking, PPAR□□□msP rats

References

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