DIFFERENT STRIATAL C-FOS EXPRESSION FOLLOWING CO-
ADMINISTRATION OF DELTA-9-TETRAHYDROCANNABINOL WITH
HALOPERIDOL OR CLOzapINE

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Dopaminergic and cannabinoidergic systems are both involved in the control of movement and functional interaction between two systems have been demonstrated. Recent studies indicated that CB1 stimulation might exacerbate extra-pyramidal symptoms (EPS) induced by D2 blockade. In line with these evidences, we demonstrated in a previous study, that haloperidol but not clozapine administration in rats induced high level of catalepsy when associated with Δ9-tetrahydrocannabinol (THC).

Furthermore, several studies demonstrated that haloperidol, but not clozapine increases c-Fos immunoreactivity (IM) in rat striatum. These results indicate that the different propensity of typical with respect to atypical antipsychotics in inducing EPS is related to the different levels of D2 blockade in nigro-striatal system, and suggest that c-Fos is a suitable tool to investigate on activation of brain areas following drugs administration.

In this study we investigated the physiological mechanisms underlying the different cataleptic states induced by haloperidol and clozapine when associated with THC, by analysing the level of c-Fos expression in striatum through western blot and stereological immunocytochemistry techniques.

Western Blot and stereological immunocytochemistry analyses indicated that Δ9-THC (0.5 mg/kg, i.p) administration increased striatal c-Fos IM induced by haloperidol (0.1 mg/kg, s.c.). Conversely, clozapine (10 mg/kg, s.c.), Δ9-THC and co-administration of clozapine with Δ9-THC did not alter c-Fos IM in striatum compared to vehicle. Furthermore stereological data highlighted that enhancement of c-Fos expression induced by Δ9-THC and haloperidol association is highest in dorsal-lateral part of striatum, where dopamine D2-receptors are more densely distributed and co-localized with CB1 receptors.

The present results indicate that the different cataleptic states induced by Δ9-THC in haloperidol- and clozapine-treated rats are correlated with different level of c-Fos IM in striatum, suggesting that CB1- and D2-receptor systems might also concur in regulating striatal c-Fos expression.