Chronic (-)cannabidiol produces antidepressant-like effects in OBX mice acting on 5-HT$_{1A}$ and CB$_1$ receptors functionality

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INTRODUCTION

Depression is one of the most prevalent psychiatric disorders in our society, affecting around 17 % of women and 9 % of men. Unfortunately, treatments are highly ineffective and with an inconvenient delay in the onset of action.

Recently, it has been described a strong implication of the endocannabinoid system in mood and also in the regulation of the neurotransmission systems that are involved in the depression pathology.

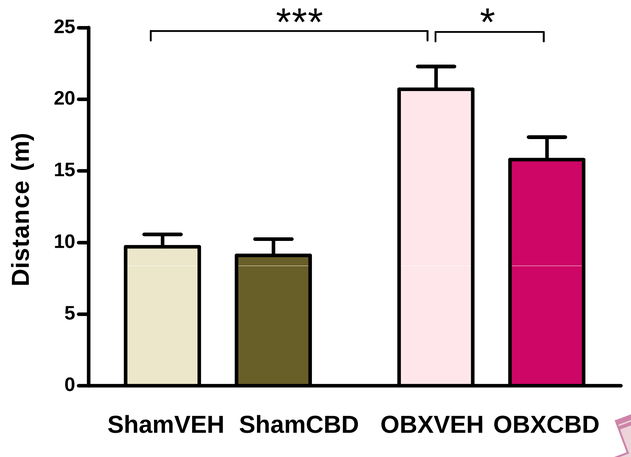
In this sense, cannabidiol (CBD), a non-psychoactive and anxiolytic component of marihuana, produced promising effects after acute administration in tests of antidepressant screening.

The aim of this study was to test the chronic administration of CBD in an animal model of depression as a putative novel antidepressant strategy and to investigate the consequences on CB$_1$ and 5HT-$_{1A}$ receptor functionality.

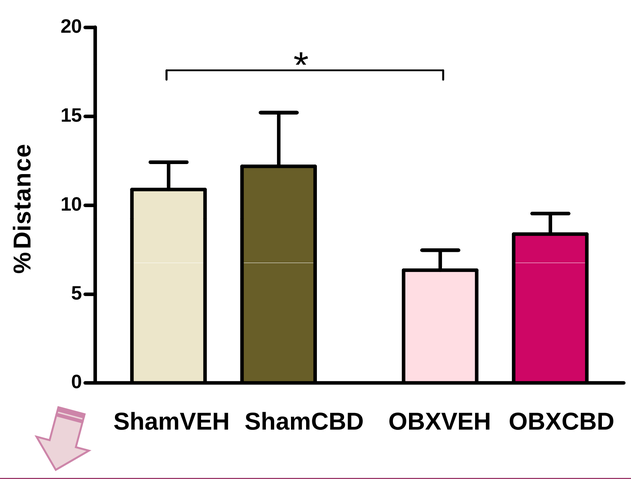
RESULTS

Behavioural characterization

OFT- Peripheral Distance

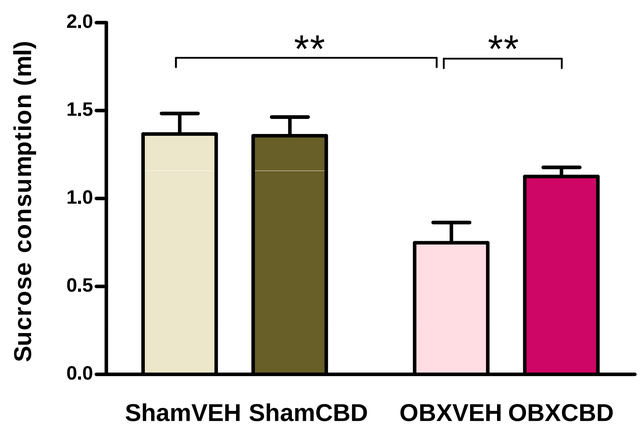


% Distance in the Central zone



Chronic CBD reverted the OBX-induced hyperactivity as antidepressant drugs

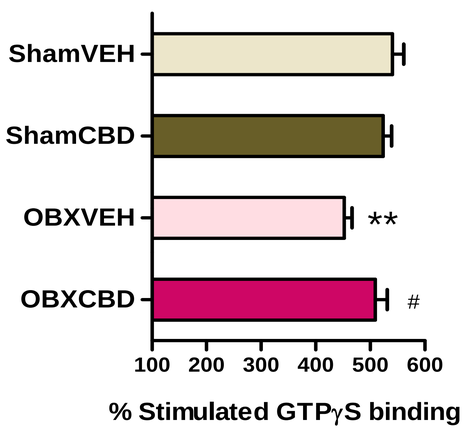
Sucrose intake test (1 hour)



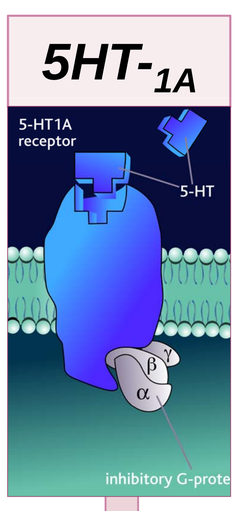
Chronic CBD reverted the OBX-induced anhedonia

5-HT$_{1A}$ and CB$_1$ receptor functionality

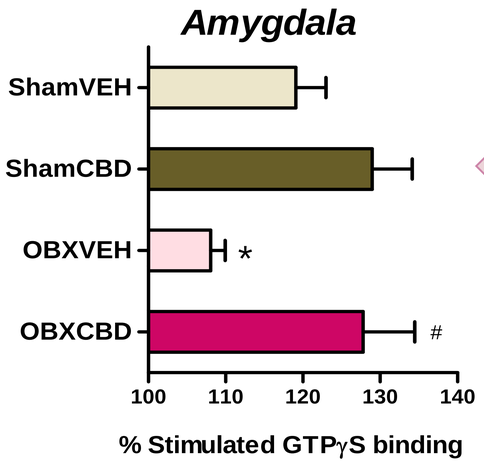
Hippocampus CA$_1$-CA$_2$



5HT-$_{1A}$

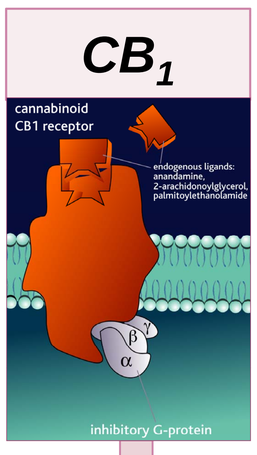


Amygdala

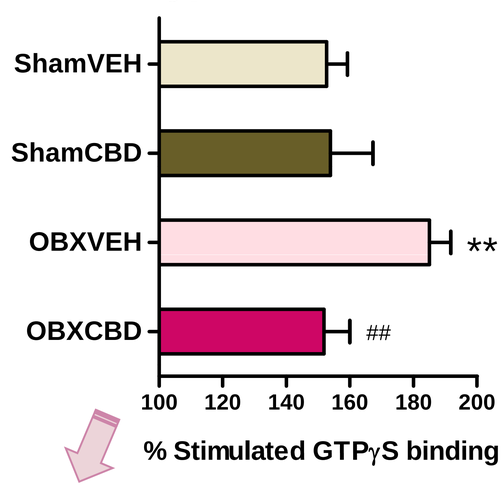


- CBD reverted OBX-induced alterations of functionality in amygdala and hippocampus
- CBD increased the functionality in medial PFC

CB$_1$

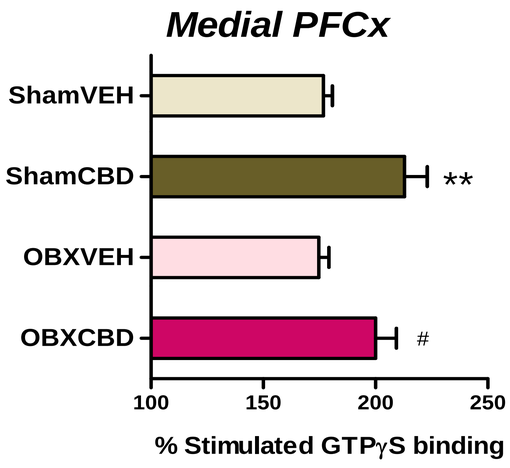


Hypothalamus



CBD reverted the increased CB$_1$ functionality in the hypothalamus

Medial PFCx

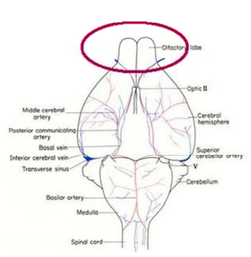


CONCLUSIONS

- ✓ ***Chronic administration of cannabidiol improves the depressive phenotype of OBX mice in behavioural tests.***
- ✓ ***Cannabidiol shows a faster onset of action than common antidepressant drugs.***
- ✓ ***Chronic cannabidiol regulates the functionality of CB$_1$ and 5-HT$_{1A}$ receptors in limbic brain areas. This could underlie the behavioural improvement observed.***

MATERIALS AND METHODS

- Olfactory bulbectomy (OBX) was performed as a chronic model of comorbid depression and anxiety.



- CBD 50 mg/kg/day (3 days) followed by 10 mg/kg/day i.p. (until 2 weeks) was administered.
- Behavioural characterization: aversive open field test (OFT) and sucrose intake test
- Neuroadaptive responses of CB$_1$ and 5-HT$_{1A}$ receptors functionality analysed by [^{35}S]GTPγS binding autoradiography

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