Therapeutic and preventive efficacy of mangiferin in an experimental model of schizophrenia

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INTRODUCTION

The connection between inflammatory processes occurring during the pregnancy as well as the consequences of subsequent oxidative stress in the development of schizophrenia points to the potential efficacy of anti-inflammatory and antioxidant drugs as therapeutic approaches for schizophrenia [1]. In this context, mangiferin a natural polyphenolic compound abundant in the leaves of Mangifera indica L. with robust antioxidant and anti-inflammatory properties, could represent a potential candidate for schizophrenia treatment, particularly interesting as preventive or coadjuvant therapy in this disorder [2].

Therefore, the aim of this study was to evaluate the therapeutic and preventive efficacy of mangiferin on behavioural and brain structural alterations induced by an experimental model of schizophrenia based on maternal immune activation.

METHODS

Model of schizophrenia: Poly I:C was administered in wistar pregnant rats (4 mg/kg, i.v.) on gestational day (GD) 15.

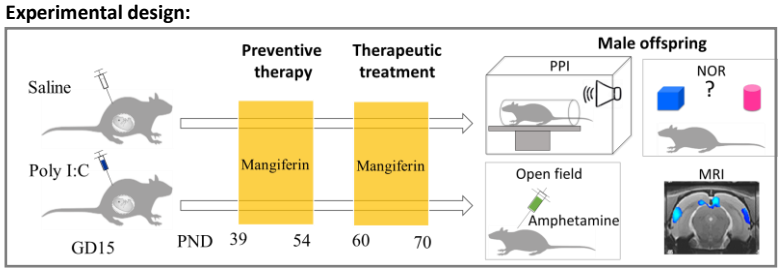
Mangiferin extract: Supercritical fluid extraction from mango leaves were applied in order to obtain extracts with high phenolic content and potent antioxidant activity [3].

Treatment: Male offspring received daily mangiferin extract (50 mg/kg, p.o.) **(i)** as **a therapeutic treatment** in young adults (postnatal day (PND) 60-70) or **(ii)** as **a preventive therapy** in adolescents (PND 39-54). Risperidone (0.3 mg/kg, i.p.) was administered as preventive reference treatment [4].

Behavioural tests (PND 70-80): Prepulse inhibition (PPI), novel object recognition (NOR) to evaluate short term memory (STM) and long-term memory (LTM), open field and amphetamine induced activity tests were performed in adult offspring.

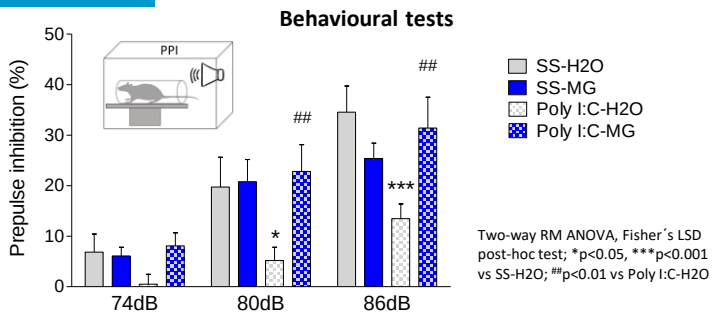
T2-weighted MRI (PND 120): Brain images were acquired in the mangiferin preventive treatment.

Experimental design:

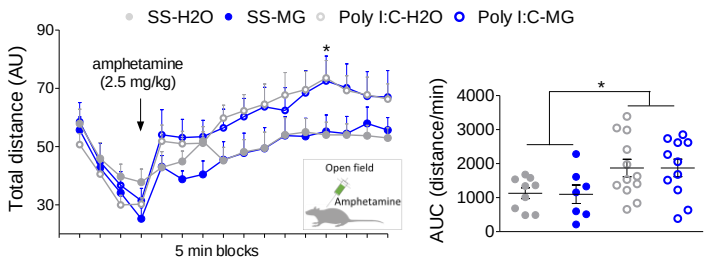


RESULTS

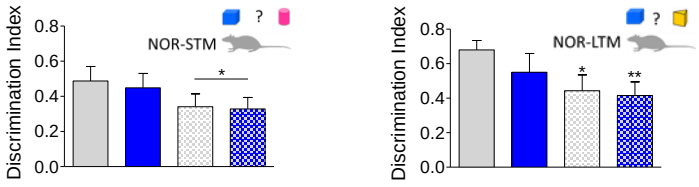
Therapeutic treatment



Two-way RM ANOVA, Fisher´s LSD post-hoc test; *p<0.05, ***p<0.001 vs SS-H2O; ##p<0.01 vs Poly I:C-H2O

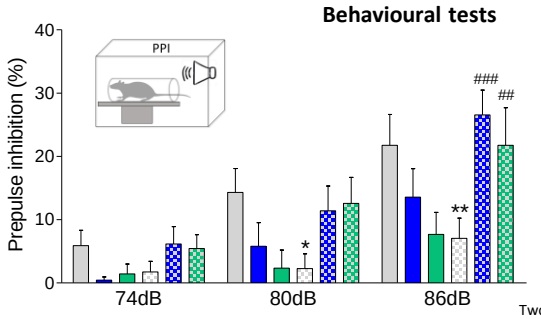


Two-way RM and Two-way ANOVAs, Fisher's LSD post-hoc test; *p<0.05 vs SS-H2O

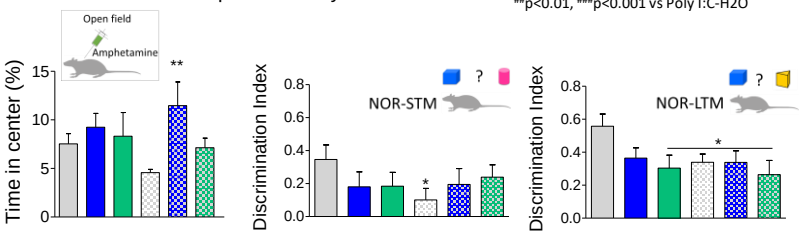


Two-way ANOVA, Fisher´LSD post-hoc test; *p<0.05, **p<0.01 vs SS-H2O

Preventive therapy



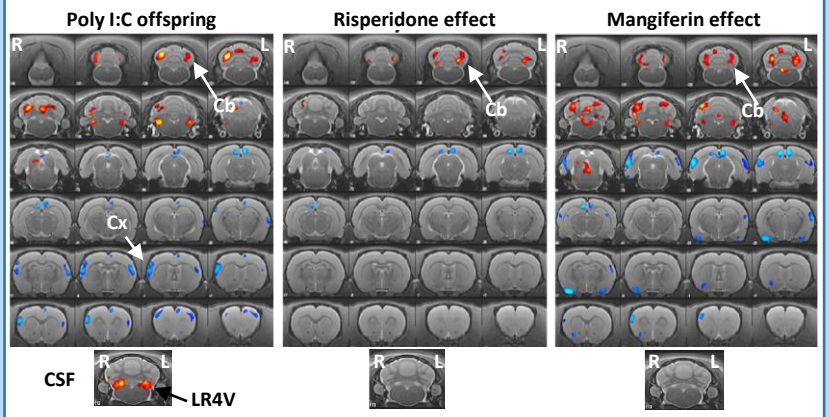
Two-way RM ANOVA, Fisher´s LSD post-hoc test; *p<0.05, **p<0.01 vs SS-H2O; ##p<0.01, ###p<0.001 vs Poly I:C-H2O



Two-way ANOVA, Fisher´s LSD post-hoc test; *p<0.05 vs SS-H2O

Two-way ANOVA, Fisher´s LSD post-hoc test; *p<0.05 vs SS-H2O

T2-weighted MRI



**p<0.01: Lateral recess of 4th Ventricle (LR4V);
***p<0.001: Cortex (Cx), Cerebellum (Cb); T= 2.43; k>1500.

CONCLUSION

These findings demonstrate that mangiferin was able to improve behavioural and morphometric abnormalities in the schizophrenia model. Therefore, these data suggest that mangiferin might be an alternative therapeutic or preventive strategy to improve clinical signs in the adulthood besides to modify the time course of this disease at the early stage of population with high-risk. Further studies would be necessary to demonstrate anti-inflammatory and antioxidant mechanisms involved in the efficacy of mangiferin for schizophrenia treatment.

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