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The role of the liver-brain axis in a rotenone-induced rat model of Parkinson's disease

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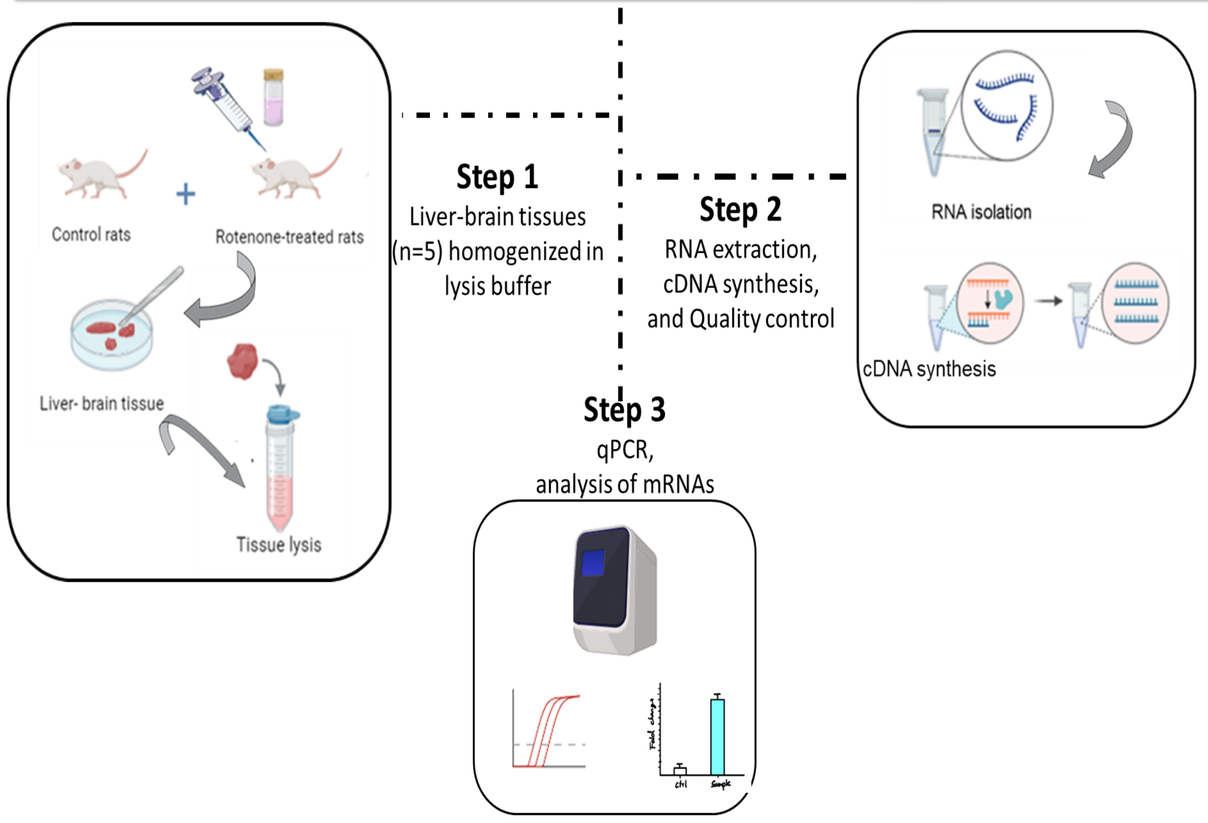
INTRODUCTION & AIM

- Evidence indicates the importance of the liver-brain axis with the critical role of the liver in the neurodegeneration process.[1,2]
- Alpha-synuclein (α-syn) aggregation is the hallmark pathological lesion in the brains of patients with Parkinson's disease (PD). A recent study demonstrated that α-syn pathology also accumulates within the liver, the main organ responsible for substance clearance and detoxification.[3]
- Besides the proteostasis alterations oxidative stress, and neuroinflammation are believed to be involved in the pathology.
- In this study, we evaluated the basic levels of expression of genes in the brain and liver to reveal potential targets involved in the communication of both organs in rotenone-treated rats, a rodent model of PD[4], and as compared to control rats.
- Specifically the expression of genes related to α-syn production (***SNCA, LRP1***)[5,6] other PD-related genes (***DJ1, Atp13a2, PARK2, PINK1***)[6], oxidative stress (***NFe2l2***)[7], and inflammation (***NF-κB, INF-γ,*** and ***TNF-α***)[8] was assessed.

METHOD



RESULTS & DISCUSSION

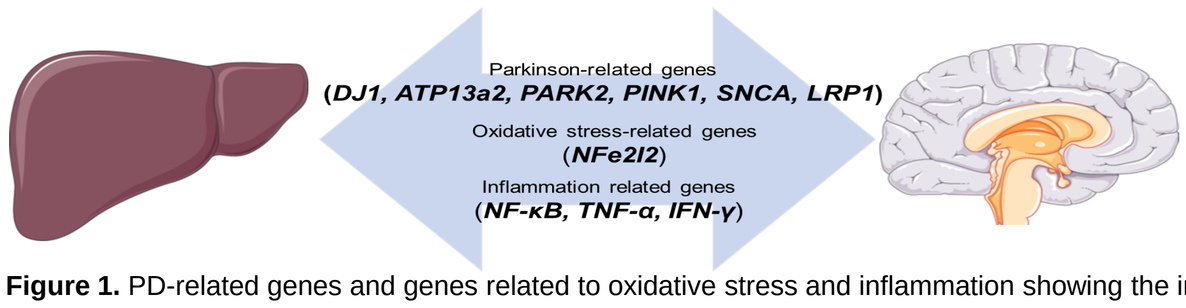
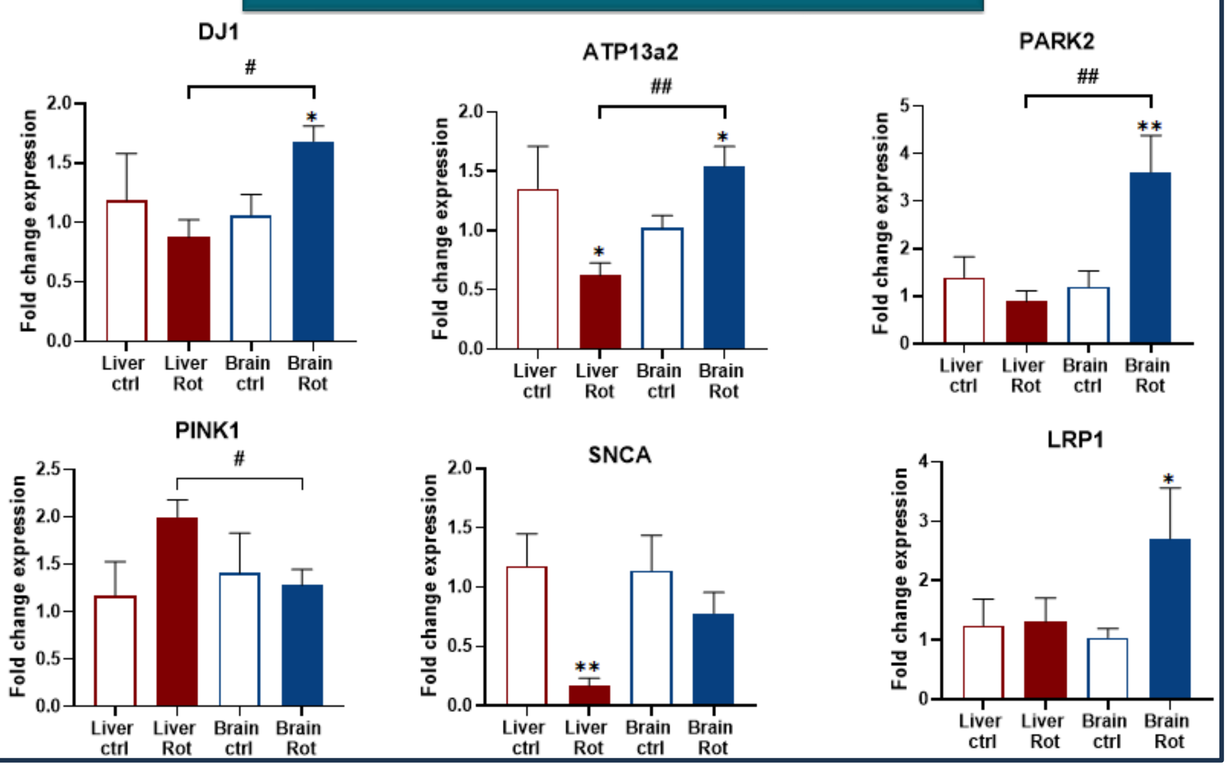
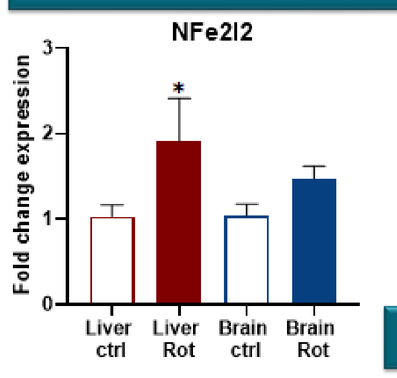


Figure 1. PD-related genes and genes related to oxidative stress and inflammation showing the importance of the liver-brain axis in the development and prognosis of PD

PARKINSON'S DISEASE



OXIDATIVE STRESS



INFLAMMATION

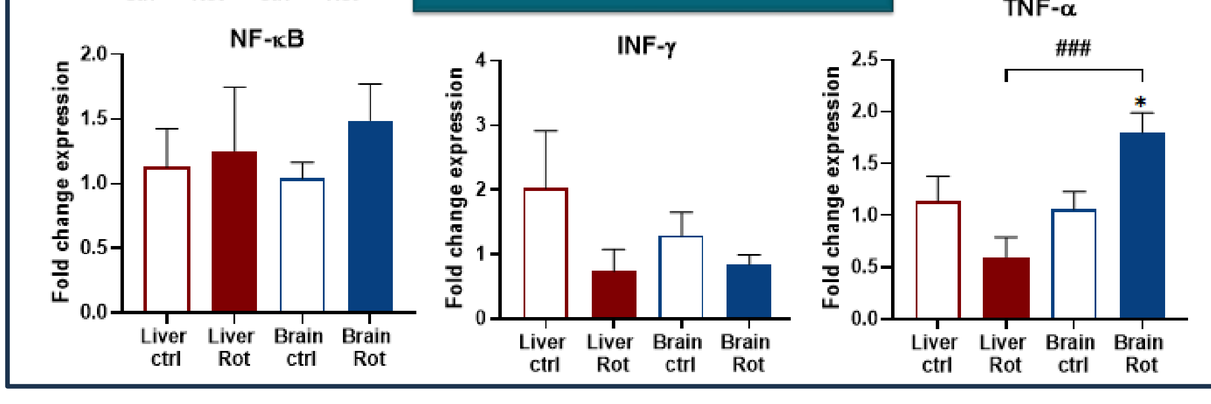


Figure 2. mRNA levels of ***DJ1, ATP13a2, PARK2, PINK1, SNCA, LRP1, NFe212, NF-κB, INF-γ*** and ***TNF-α*** in the brain and liver of control (ctrl) and rotenone (Rot) treatment groups. Expression levels were normalized to reference genes (Access number: NM_0311442 and NM_020071.2) and the relative expression levels of their mRNAs were determined using the ($2^{-\Delta\Delta ct}$) method. Data are expressed as mean ± SEM (n = 5) and analyzed by Unpaired t-test and two-way ANOVA with uncorrected Fisher's LSD test. ∗P < 0.05, ∗∗P < 0.01 vs. control rats # p < 0.05, ## p < 0.005 ### p < 0.001 vs. liver Rot or brain Rot.

SUMMARY OF RESULTS

Rot treated rats vs. controls show:

- **Hepatic down-regulation PD-related genes *ATP13a2*** and ***SNCA***
- **Hepatic up-regulation of Oxidative stress-related gene *NFe212***
- **Brain up-regulation of PD-related genes *DJ1, ATP13a2, LRP1*** and ***PARK2*****,** and **inflammatory gene *TNF-α***
- **Significant changes in the expression of PD-related genes *DJ1, ATP13a2, PARK2* and *PINK1*, and inflammatory gene *TNF-α* between the liver and the brain were only observed in Rot-treated rats**

CONCLUSION

- The study suggests that changes in the liver may be involved in pathological conditions linked to PD and supports research on peripheral markers related to the liver-brain axis in this disease.

PERSPECTIVES

- The liver-brain axis alterations observed in the rotenone-induced rat model of PD in our study can open new paths to understanding the systemic aspects of PD.
- Further research is underway to determine whether liver-brain axis alterations could correlate with a worse disease prognosis and to establish potential integrative system targets for PD treatment.

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