SEX DIFFERENCES IN 6-OHDA LESIONED RATS IN PRECLINICAL MODEL FOR PARKINSON'S DISEASE

Raquel de Souza Lima[1], Jaime Fornaguera Trías[2]

1. *Neuroscience Research Center, University of Costa Rica, Costa Rica*
2. *Biochemistry department, School of Medicine, University of Costa Rica, Costa Rica*

INTRODUCTION

Although Parkinson's disease (PD) was described since 1817 its etiology is still unclear. The main neurotransmitter system affected, is the nigrostriatal dopaminergic system. PD is diagnosed mainly by its motor symptoms, which appear when there is a massive destruction of the dopaminergic system (80%). Although it is well known that PD is a progressive disease, most studies have focused on late stages when the destruction of the dopaminergic system is severe and there is little chance to recover or to stop it. Additionally PD affects men to a greater degree than women, but most studies have been done in men (or male animals).

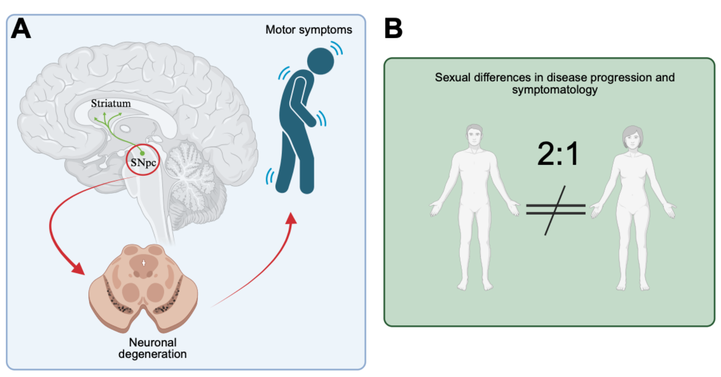

Figure 1: A. Neurodegeneration of the nigrostriatal dopaminergic pathway. **B.** Sex differences in PD.

OBJECTIVE

To better understand the early stages of Parkinson's disease using moderate lesions of the nigrostriatal dopaminergic system in both sexes.

METHODOLOGY

16 male rats and 16 female Wistar rats, 90 days old at the beginning of the experiment, were kept in group in polycarbonate cages. On days -1, 1, 7, and 14, spontaneous behaviors turning, scanning, rearing and locomotion were analyzed and video recorded, while on days 14 and 21 they were analyzed before and after pharmacological challenge (AMPH (1mg/kg i.p)= and APO (0.5mg/kg s.c) respectively). On day 0 stereotactic surgery was performed in which animals were injected with 6-OHDA (4µg/µl) or vehicle in the right substancia nigra pars compacta.

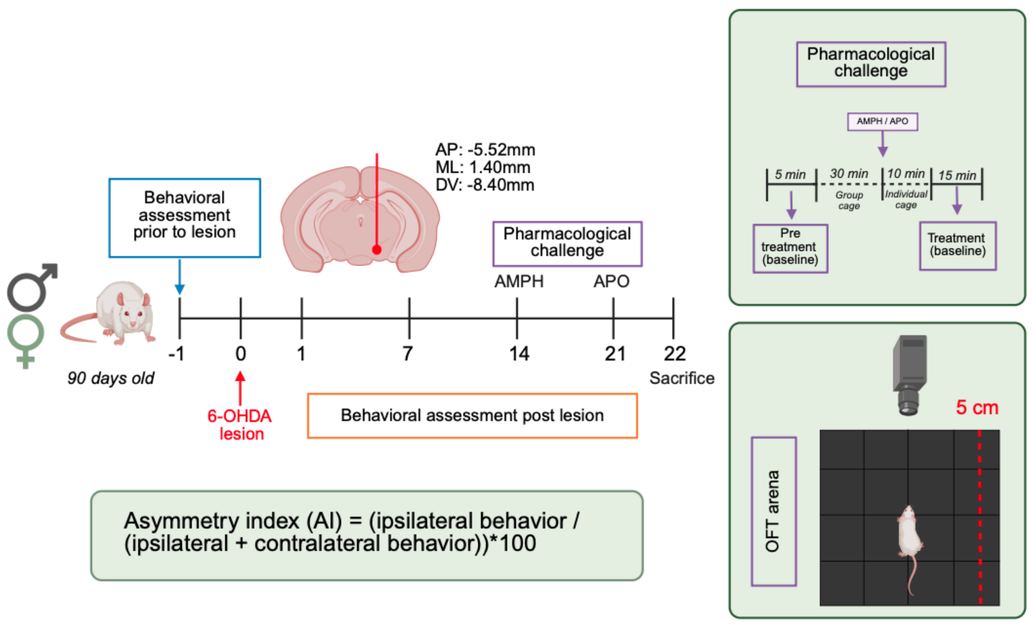

Figure 2: Experimental design.

RESULTS

According to the degree of injury obtained, the 6-OHDA subjects were separated into two subgroups: resistant, (DA depletion <15%) and and vulnerable (DA depletion >15%).

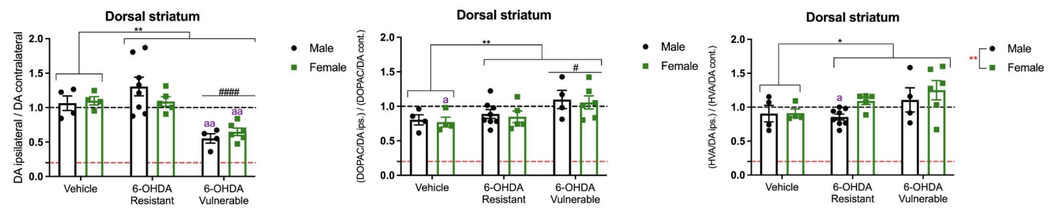

Figure 3: Neurochemical parameters in the dorsal striatum after injection (vehicle or 6-OHDA) in the substantia nigra pars compacta in male and female rats. Data are presented as mean ± SEM. ANOVA two-way test, followed by planned contrast analysis. Sex principal effect: *p<0.05; **p<0.01 compared with the vehicle group. #p<0.05, ####p<0.000 compared with the resistant group. ap<0.05; aap<0.01 compared to the reference value of 1.0 (One-sample t-test).

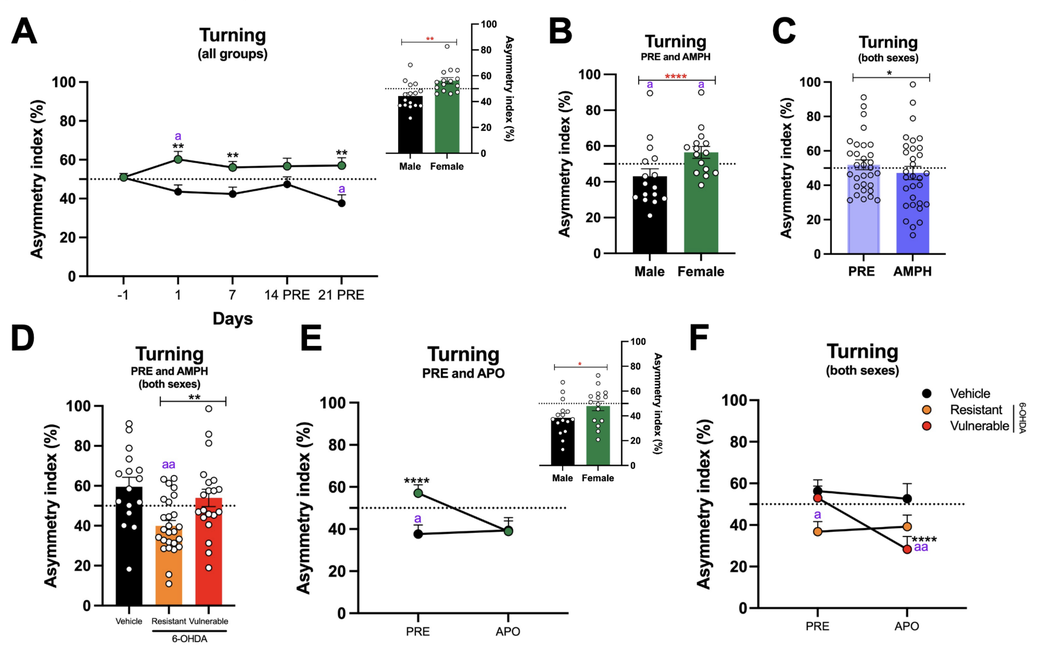

Figure 4: Turning behavior response in female and male rats injected with 6-OHDA or vehicle. Asymmetry index (AI) for turning behavior in both sexes on spontaneous days -1, 1, 7, 14PRE, and 21PRE, measured using the OFT.

CONCLUSION

Comparing sexes is essential to understand differences in susceptibility and help tailor treatments by sex. Multilevel analysis, along with genes and proteins involved in inflammation and plasticity processes should be included in the studies to better understand the mechanisms underlying these differences.

ACKNOWLEDGEMENTS

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