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The Effects of Vilazodone, YL-0919, and Vortioxetine in L-DOPA Treated Hemiparkinsonian Rats

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INTRODUCTION

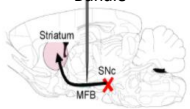
- Parkinson's Disease (PD) is a movement disorder cause by dopamine (DA) cell loss, leading to ***hypokinesia***, tremor, and rigidity[1,2].
- While L-DOPA replacement therapy reduces symptoms, it can also lead to ***hyperkinetic***, abnormal involuntary movements (AIMs) called L-DOPA Induced Dyskinesia (LID)[2].
- LID is associated with unregulated DA release from raphe-striatal 5-HT neurons[3].
- Drugs acting as 5-HT_{1A} receptor agonists and 5-HT transporter (SERT) blockers may reduce 5-HT cell-mediated DA release and reduce LID thus optimizing PD treatment.[7]

The current study evaluated the pharmacological effects of three 5-HT_{1A} agonist/SERT blockers, Vilazodone, YL-0919, and Vortioxetine on LID

METHODS

Female SD Rats N=36

Medial Forebrain Bundle



Forepaw Adjusting Steps (FAS)

Abnormal Involuntary Movements (AIMs)

Rat LID

FIG 1. EXPERIMENTAL DESIGN

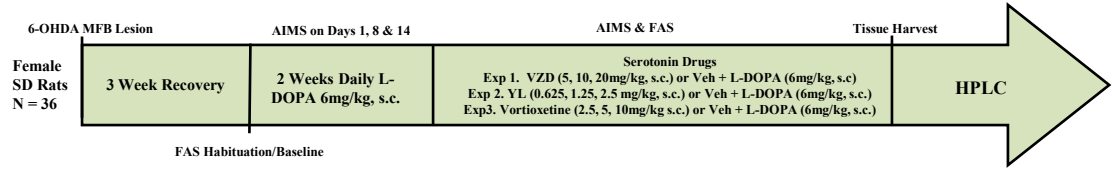
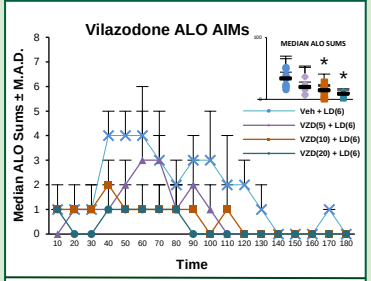


Fig 2. The effects of Vilazodone on ALO AIMs & FAS



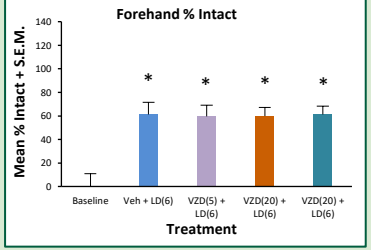
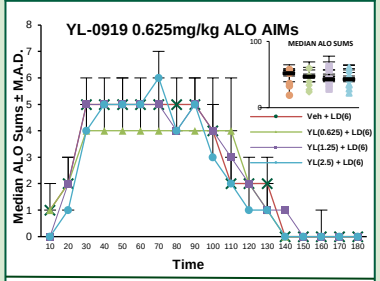


Fig 3. The effects of YL-0919 on ALO AIMs & FAS



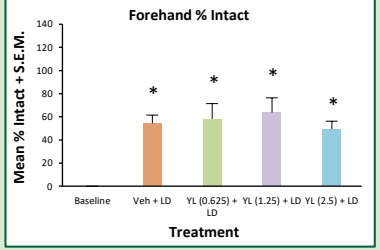
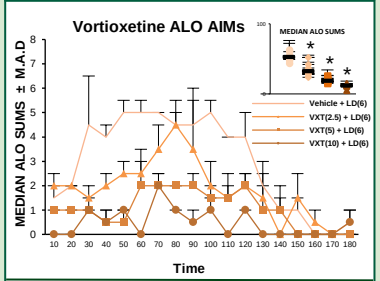
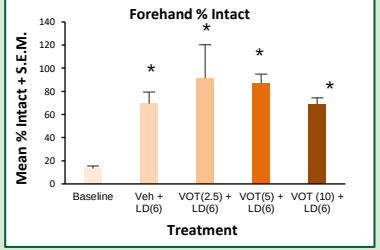


Fig 4. The effects of Vilazodone on ALO AIMs & FAS





Vilazodone and Vortioxetine significantly reduced AIMs and maintained L-DOPA beneficial prokinetic effects. YL had no effect on LID though it did maintain L-DOPA motor performance.

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DISCUSSION

- Vilazodone and Vortioxetine reduced dyskinesia while maintaining L-DOPA efficacy.
- No effect of YL-0919 on AIMs at any dose.
- Pharmacological differences may account for variation in antidyskinetic effects.[4,5,7]
- Vortioxetine while less selective for 5-HT_{1A}R, also has 5-HT_{1B}R agonist effects, previously shown to be antidyskinetic[5].
- Conversely, YL also acts on 5-HT_6R shown to increase 5-HT neuron firing[4], which may counteract its 5-HT_{1A}R and SERT effects.

FUTURE DIRECTIONS

- Investigate the differential pharmacological effects between Vilazodone/Vortioxetine and YL-0919.
- Use of microdialysis to observe DA and 5-HT release during Vilazodone and Vortioxetine treatment with L-DOPA.
- Research the 5-HT system to understand the mechanisms that lead to 5-HT neuroplasticity-driven LID.

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