# How Does Levodopa Affect Balance in Parkinson's disease? Insight from Machine Learning Analysis

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## Introduction

- **Dopa-resistant paradox**
  - Although **Levodopa is the gold-standard treatment for Parkinson's disease**, its effect on axial symptoms is limited; **patients on Levodopa often move faster but remain prone to falls**.
- **Two possible explanations of paradox**
  - **Sway area** (traditional metric) **reflect performance outcome**, whereas **sway velocity reflects neural control strategy** (rigid vs. dynamic control)
  - **Parkinson's disease is highly heterogeneous**, and **group-average statistics may mask responder and non-responder subgroups**; machine learning can identify these phenotypes.
- This study investigated whether Levodopa alters sway area or sway velocity and used machine learning to identify responder and non-responder phenotypes.

## Methods

- **Participants information (N=32)**

| Characteristic | Value |
|---|---|
| Age | 65.6 ± 10.4 years |
| Sex | Male 24<br>Female 8 |
| Hoehn & Yahr stage | 2.3 ± 0.6 |
| Medication states | OFF (12hr withdrawal),<br>ON (1hr after medication) |

- **Four experimental conditions**

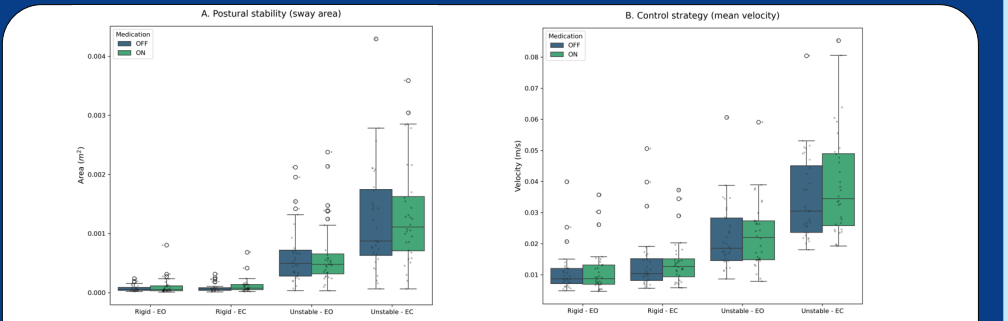
| | Eye open | Eye close |
|---|---|---|
| **Rigid surface** | RS-EO | RS-EC |
| **Unstable surface** | US-EO | US-EC |

- **Data characteristics and analysis**

| Data | Features | Statistics | Machine Learning |
|---|---|---|---|
| COP | Sway area | ANOVA | Random Forest |
| 100Hz | Sway velocity | Correlation | LOSO-CV |
| 3 trials avg | Strategy | | K-means |
| | ML/AP ratio | | Responder vs Non-responder |

## Results

- **Levodopa Increases Sway Velocity but Not Sway Area**



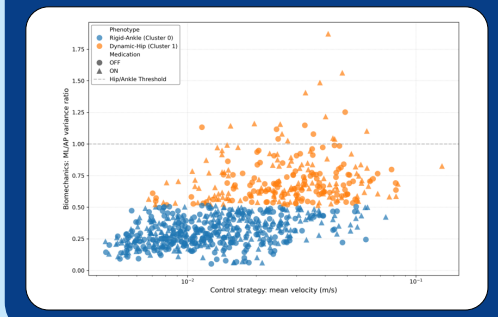

- **Repeated measures ANOVA**

| | | Sway area (static stability) | | | Sway velocity (control strategy) | | |
|---|---|---|---|---|---|---|---|
| Effect | Source of variation | df | F-value | p-value | df | F-value | p-value |
| Main Effect | Medication (ON vs OFF) | 1, 31 | 1.27 | 0.27 | 1, 31 | 1.68 | 0.21 |
| | Surface (Rigid vs Unstable) | 1, 31 | 60.80 | < 0.001* | 1, 31 | 109.56 | < 0.001* |
| | Vision (Open vs Closed) | 1, 31 | 81.65 | < 0.001* | 1, 31 | 157.09 | < 0.001* |
| Interaction Effect | Medication x Surface | 1, 31 | 0.27 | 0.61 | 1, 31 | 3.86 | 0.06 |
| | Medication x Vision | 1, 31 | 0.79 | 0.38 | 1, 31 | 3.32 | 0.08 |
| | Surface x Vision | 1, 31 | 83.69 | < 0.001* | 1, 31 | 89.26 | < 0.001* |
| | **Medication x Surface x Vision** | 1, 31 | 1.26 | 0.27 | 1, 31 | 5.37 | 0.03* |

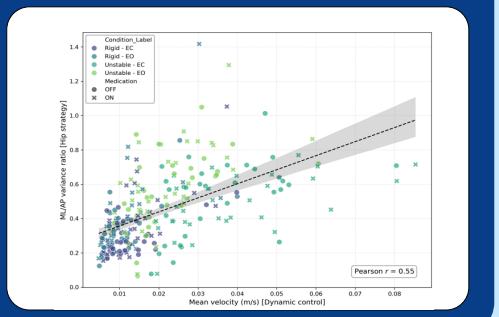
- **Bonferroni correction (sway velocity)**

| Condition | Mean difference (m/s) | t-statistics | p-value |
|---|---|---|---|
| Rigid surface - eyes open (RS-EO) | 0.0003 | 0.31 | 1.00 |
| Rigid surface - eyes closed (RS-EC) | 0.0003 | 0.23 | 1.00 |
| Unstable surface - eyes open (US-EO) | 0.0008 | 0.82 | 1.00 |
| Unstable surface - eyes closed (US-EC) | 0.0048 | 2.02 | 0.21 |

- **Clustering Reveals Distinct Rigid and Dynamic Postural Control Phenotypes**




- **Increased Sway Velocity Is Associated with Transition to Hip Strategy**




## Discussion

- **Levodopa didn't reduce sway area but increased sway velocity**, indicating that **medication changes neural control strategy rather than stabilizing posture.**
- Increased sway velocity was associated with a **transition from ankle strategy to hip strategy, suggesting restoration of sensory reweighting**.
- Machine learning identified a 31% non-responder subgroup that remained in a rigid control strategy despite medication
- This **heterogeneity** explains why traditional group statistics often conclude that Levodopa has limited effects on postural instability.

## Clinical Implications

- Traditional posturography using sway area on rigid surface may underestimate Levodopa effects.
- Sway velocity and adaptive response to sensory conflict are more sensitive biomarkers of dopaminergic response.
- Non-responders may have non-dopaminergic pathology and may benefit more from rehabilitation and sensory-based interventions rather than increased Levodopa dosage.

## Conclusion

- **Levodopa changes how patients control posture, not how much they sway.**
- Levodopa promotes a **rigid → dynamic strategy transition.**
- 31% non-responders remain resistant to medication.
- Dynamic sensory conflict testing is more sensitive than static balance tests.

## References


- Leroy et al. (2022) Effects of oral levodopa on balance in people with idiopathic Parkinson's disease. *Journal of Parkinson's disease*
- Mancini et al. (2008) Effects of Parkinson's disease and levodopa on functional limits of stability. *Clinical Biomechanics*
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