# Measuring Dyskinesia in Parkinson's Clinical Trials

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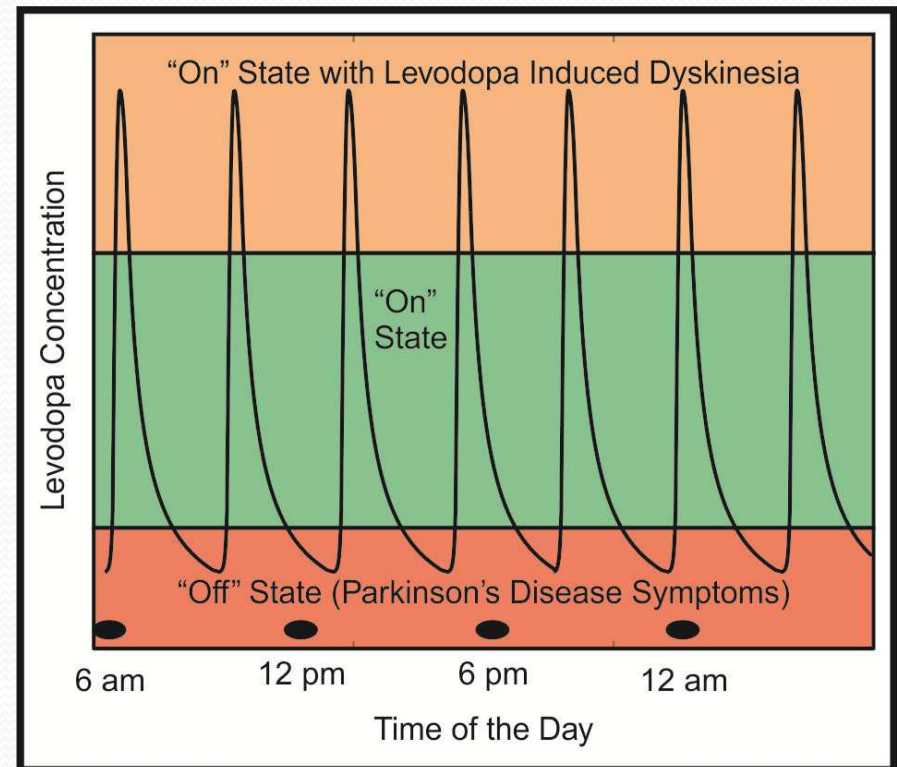Webinar Series

GREAT LAKES NEUROTECHNOLOGIES

# Question 1:

1. How are PD motor complications evaluated in clinical trials?

2. What are the challenges with clinical trial dyskinesia endpoints, and how can they be improved?

3. How can home-based motion sensor dyskinesia assessment improve your clinical trials?

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# Motor Complications of Chronic Levodopa Therapy

1. Motor fluctuations
   - Alternate between therapy "off" and "on" states over dose cycles

2. Levodopa-induced dyskinesia (LID)
   - Involuntary, episodic, and irregular movements
   - Peak-dose most common

**Advanced Stages**



Keijsers, N. L., M. W. Horstink, et al. (2003). "Automatic assessment of levodopa-induced dyskinesias in daily life by neural networks." Mov Disord **18**(1): 70-80.

# Question 2:

1. How are PD motor complications evaluated in clinical trials?

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# Clinical Trial Review

**ClinicalTrials.gov**
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**377 studies found for**:   "parkinson's disease" AND "dyskinesia"

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| Rank | Status | Study |
|------|--------|-------|
| 1 | Not yet recruiting | **Safety and Efficacy of AVP-923 in the Treatment of Levodopa-induced Dyskinesia in Parkinson's Disease Patients**<br>**Conditions:**  Dyskinesia;  Parkinson's Disease<br>**Interventions:**  Drug: AVP-923-45;  Drug: Placebo |
| 2 | Recruiting | **Open-label, Long-term Safety Extension Study of AFQ056 in Parkinson's Patients With L-dopa Induced Dyskinesias**<br>**Conditions:**  Dyskinesias;  Parkinson Disease;  Movement Disorders;  Parkinsonian Disorders;  Anti-Dyskinesia Agents |

# Clinical Trial Endpoints

- Clinical Assessments
  - UPDRS, UDysRS, mAIMS, PDYS-26
  - Patient retrospective recall

- Patient diaries
  - Self assessment at home
  - 0.5-1 hr interval diary entries

- Body-worn motion sensors
  - Shift in research
  - Unconstrained continuous assessment at home
    - Transition to clinical trial use not trivial
    - Importance of quality assurance (e.g. FDA, ISO, CE, TGA)



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# Challenges with Clinical Trial Endpoints

- Resolution of clinical rating scales
  - Severity: 0-4 integer scoring
  - Temporal: snapshot of dyskinesia response

- Compliance of home diaries
  - Correlation between reported and actual compliance
  - Patient awareness of, understanding, and recognizing therapy states

- Costs
  - Clinician and patient time in clinic
  - Accuracy may affect statistical power

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# Motion Sensor LID Assessment:
# Clinical Validation Study

- Collaborators
  - Michelle Burack, MD, PhD
  - NIH-funded SBIR Phase I

- Goals
  1. Capture peak-dose dyskinesia over a levodopa dose using hand-worn motion sensors
  2. Develop a scoring model to automatically rate dyskinesia
  3. Determine whether a single motion sensor unit could accurately assess global dyskinesia

# Methods: Study Preparation

- Off levodopa from previous night or end of dose

- A wireless motion sensor unit positioned on each hand

- Two discrete motor tasks:
  1. Arms resting
  2. Arms Extended

- Serial subtractions as distraction



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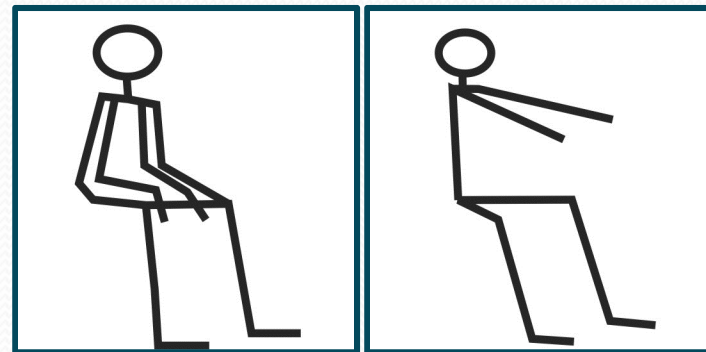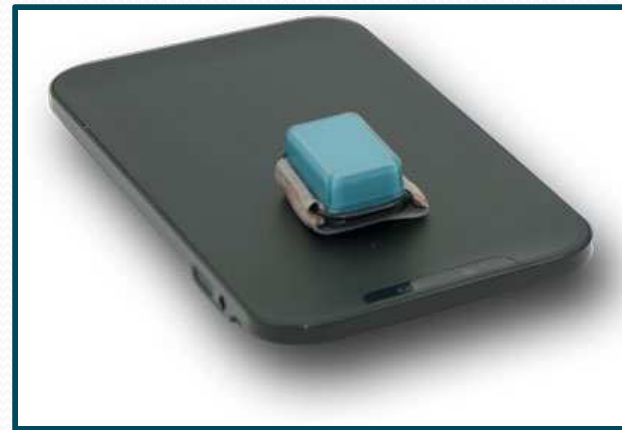
# Methods: Data Collection

- Two motor tasks at hours 0, 1, 2, and 3 after levodopa dose

- Motion sensor data were wirelessly streamed to a computer

- Video of task performance was recorded and later scored by two expert raters
  - modified-Abnormal Involuntary Movement Scale (m-AIMS)
  - 0 (none) to 4 (severe) global dyskinesia ratings

- Severity scoring models developed using sensor data and clinician global m-AIMS scores

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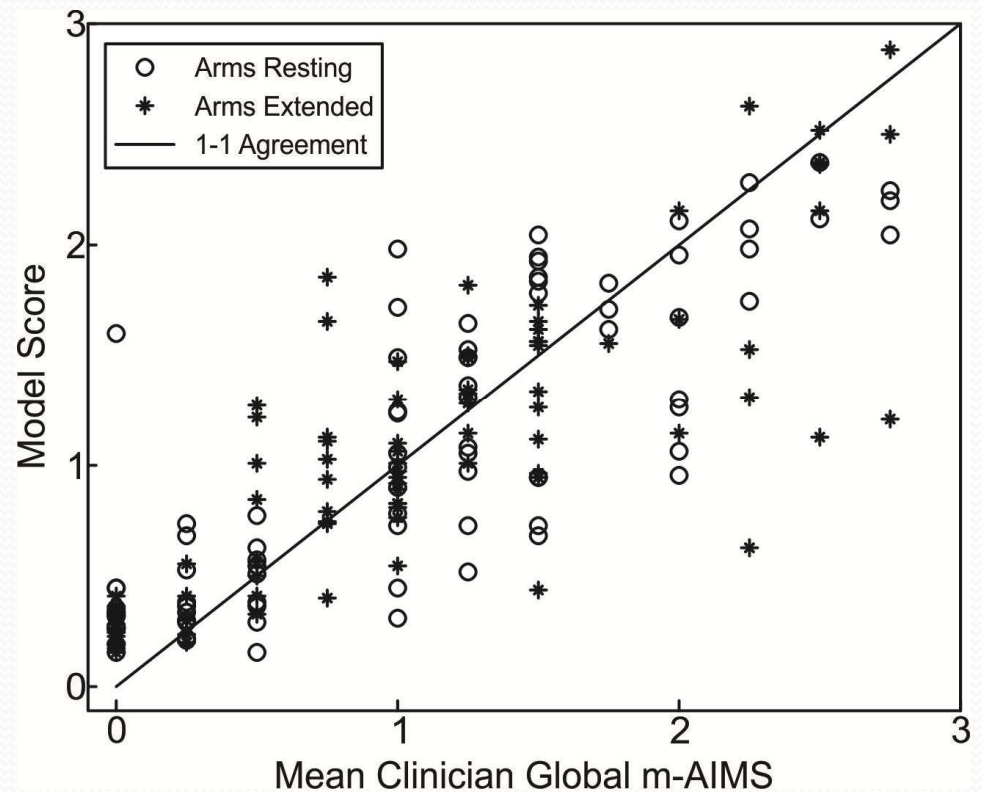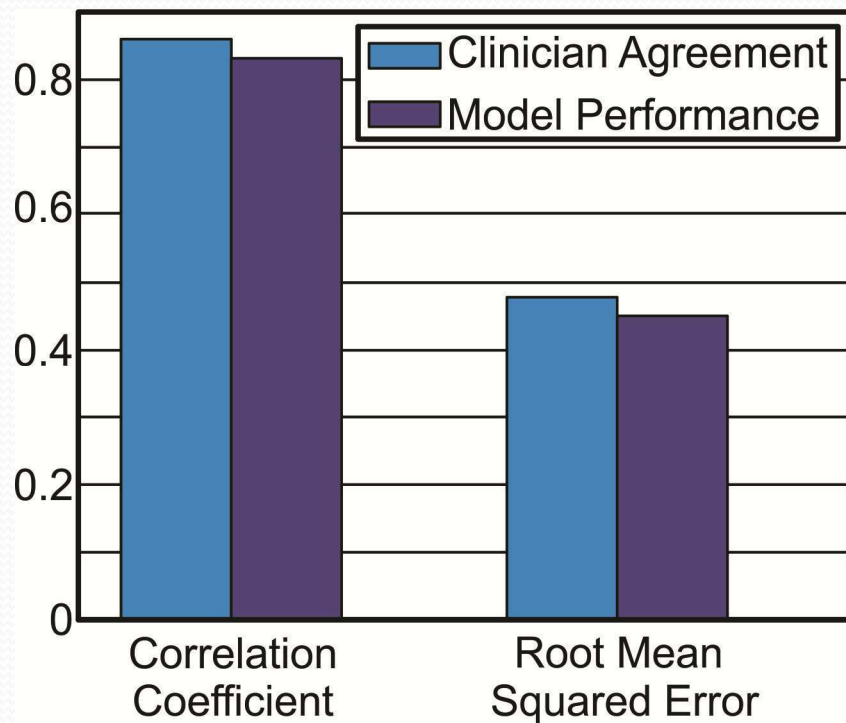# Clinical Assessment



Arms Extended Task
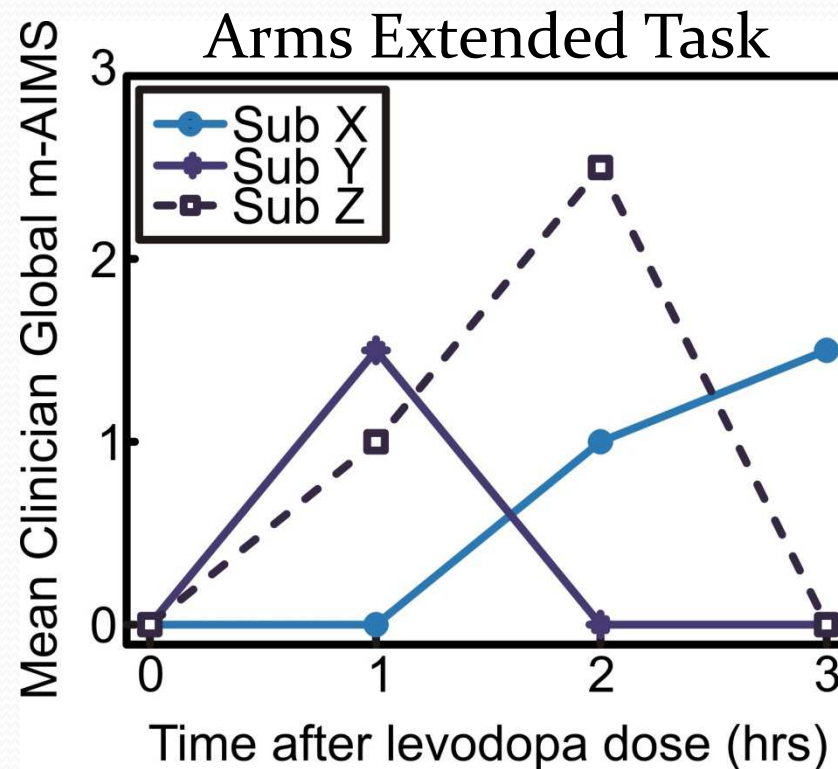
**The time to reach peak-dose dyskinesia varied by subject**

# Symptom Feature Extraction
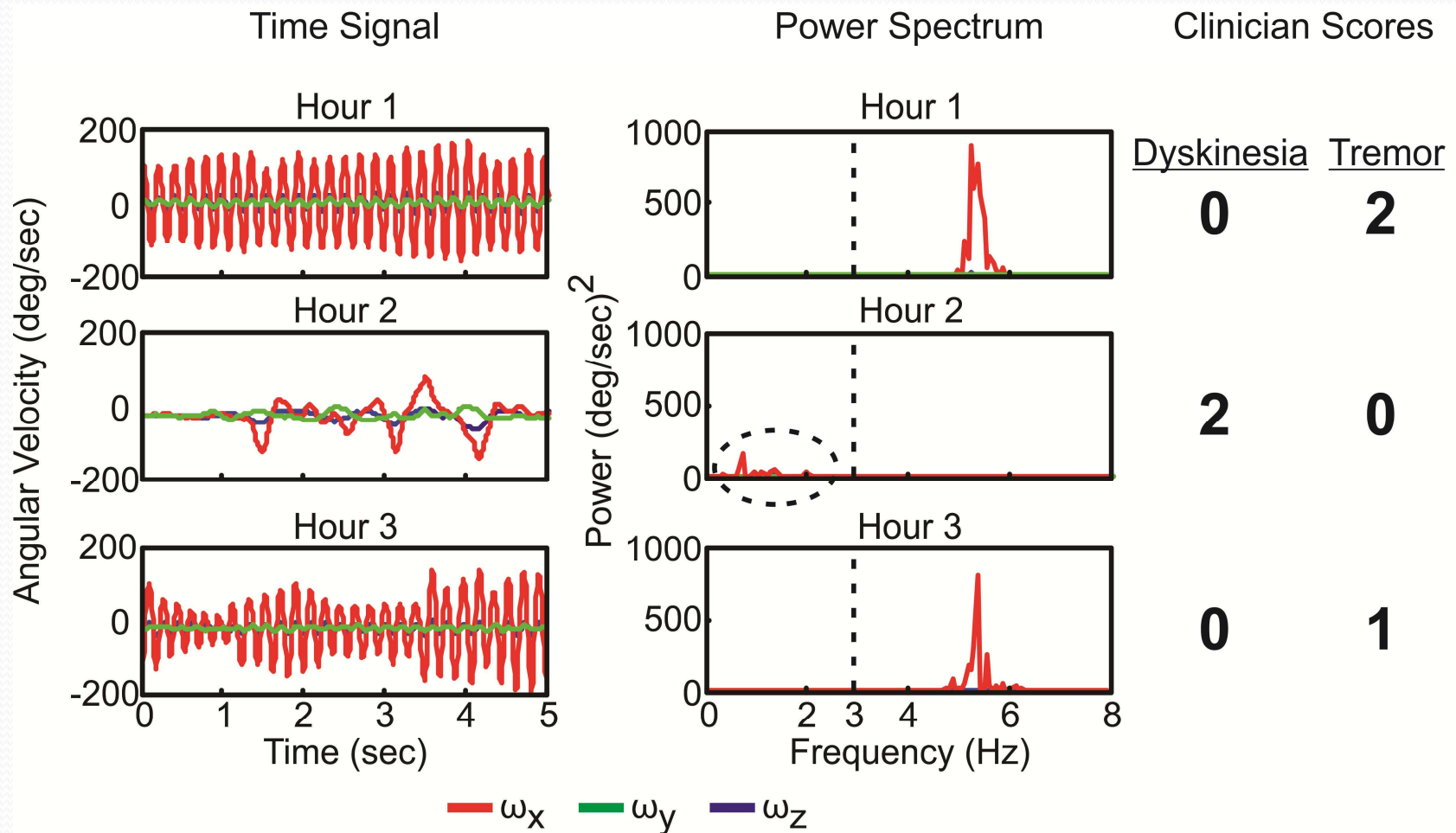
# Dyskinesia Severity Scoring Model

# Question 3:

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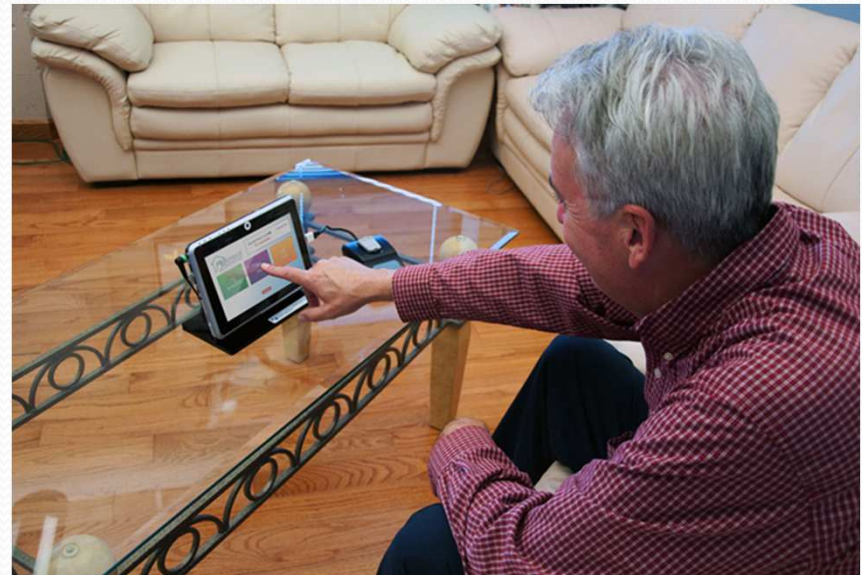
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# Clinical Trial Drug Comparison
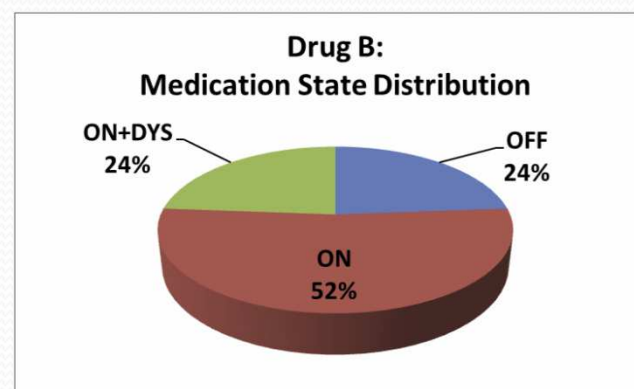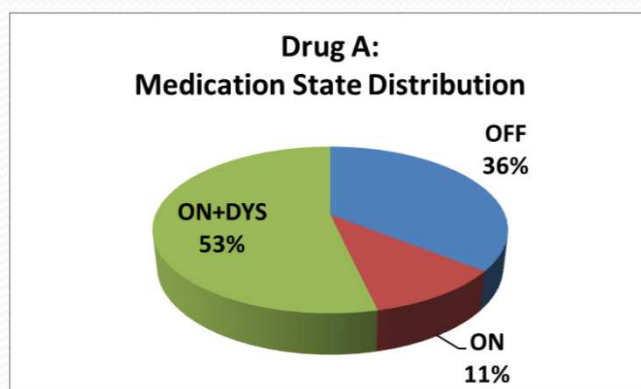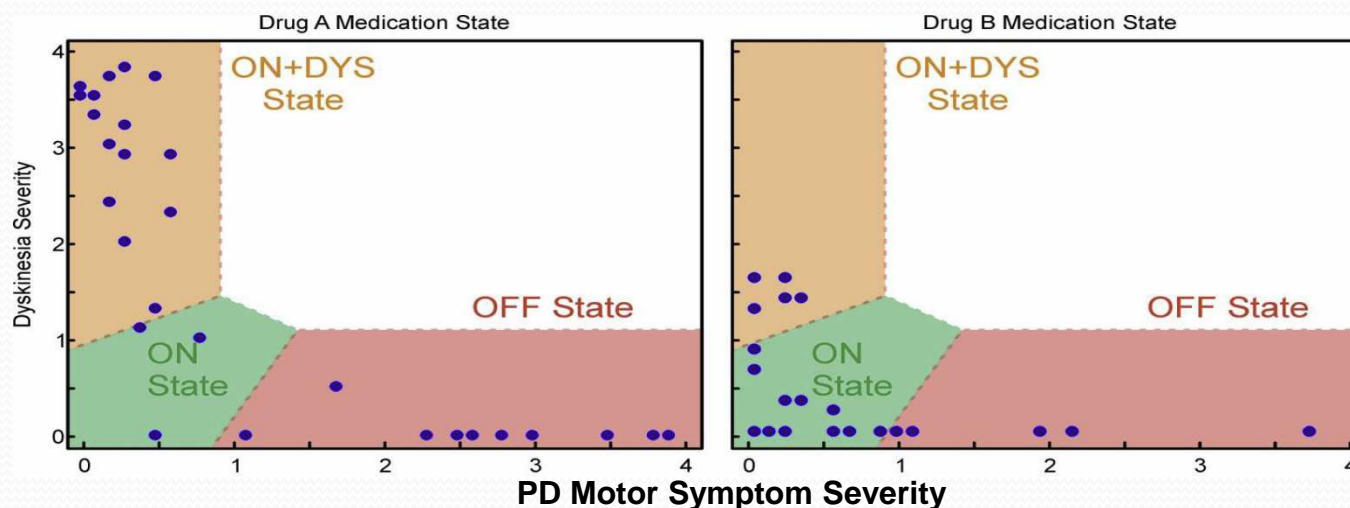
# Advantages For Your Clinical Trials

Motion sensor assessment
during discrete tasks

- Clinical validation and quality assurance

- Home assessment kit

- Single motion sensor to assess global dyskinesia fluctuations

- Electronic formatting

  - Instant access, reports

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| Time | Rest Tremor | Postural Tremor | Finger Taps Speed | Finger Taps Amplitude | Finger Taps Rhythm | Dyskinesia |
|------|------|------|------|------|------|------|
| 6:55 AM | 3.9 | 3.4 | 2.6 | 2.5 | 2.3 | 0.0 |
| 6:57 AM | Drug Dose A | | | | | |
| 7:28 AM | 2.5 | 3.0 | 1.7 | 1.4 | 1.0 | 0.0 |
| 7:59 AM | 0.5 | 1.9 | 1.8 | 1.5 | 1.2 | 1.3 |
| 8:30 AM | 0.3 | 0.9 | 0.3 | 0.5 | 1.0 | 2.9 |
| 9:05 AM | 0.1 | 0.5 | 0.2 | 0.2 | 1.2 | 3.5 |
| 9:33 AM | 0.3 | 0.4 | 0.0 | 0.0 | 1.0 | 3.8 |
| 10:02 AM | 0.5 | 0.1 | 0.5 | 0.3 | 1.0 | 3.7 |
| 10:31 AM | 0.6 | 2.0 | 1.0 | 0.5 | 1.5 | 2.9 |
| 10:58 AM | 3.0 | 3.1 | 2.3 | 2.2 | 2.0 | 0.0 |
| 11:35 AM | 3.5 | 3.4 | 2.0 | 2.0 | 1.8 | 0.0 |
| 11:50 PM | Drug Dose A | | | | | |

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# References

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# Questions?

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