Test-Retest Reliability of a Parkinson's Disease Monitoring System

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GREAT LAKES NEUROTECHNOLOGIES

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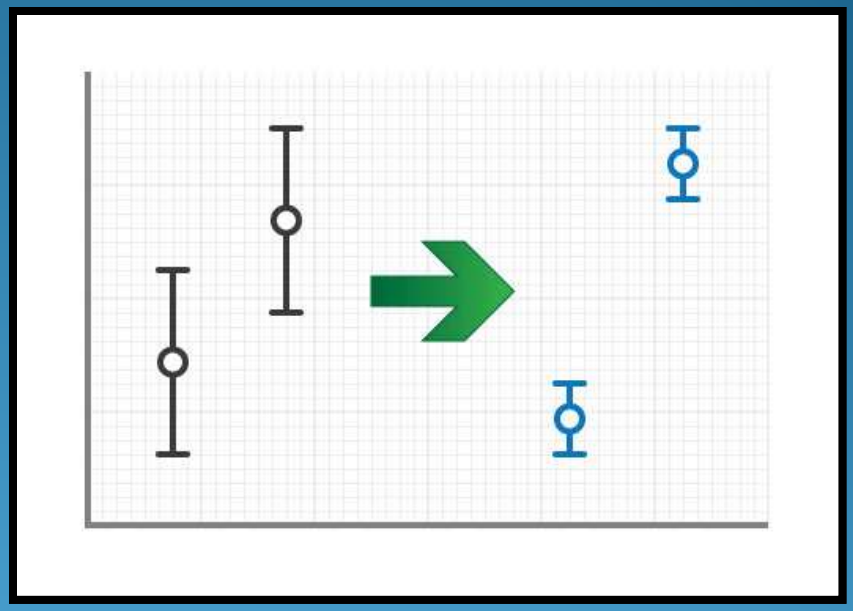
- Dr. LeWitt has served on scientific advisory boards for Civitas, Depomed, IMPAX, Intec, Ipsen, Knopp Biosciences, Merck, Merz, NeuroDerm, Noven, ProStrakan, Teva, and XenoPort, and has received speaker honoraria from Ipsen and Teva. He serves as Editor-in-Chief of *Clinical Neuropharmacology*, which is a compensated position. He also serves on the editorial board of *Journal of Neural Transmission*, *Translational Neurodegeneration, and Journal of Parkinson's Disease* without compensation. The Parkinson's Disease and Movement Disorders Program that Dr LeWitt directs has received clinical research grant support (for conducting clinical trial and other research) from Adamas, Allergan, Biotie, Great Lakes NeuroTechnologies, The Michael J. Fox Foundation, Merz, UCB, and XenoPort.
- Dr. Giuffrida received support from NIH/NINDS 1R43NS074627-01A1 and compensation from Great Lakes NeuroTechnologies for employment.

Outcomes in Clinical Trials

- Clinical Assessments (UPDRS)
- Patient Diaries
- Motion Sensors

- Sources of error
  - Patient physical/mental condition
  - Variations in testing procedure/interpretation
  - Tester error
  - Learning effects

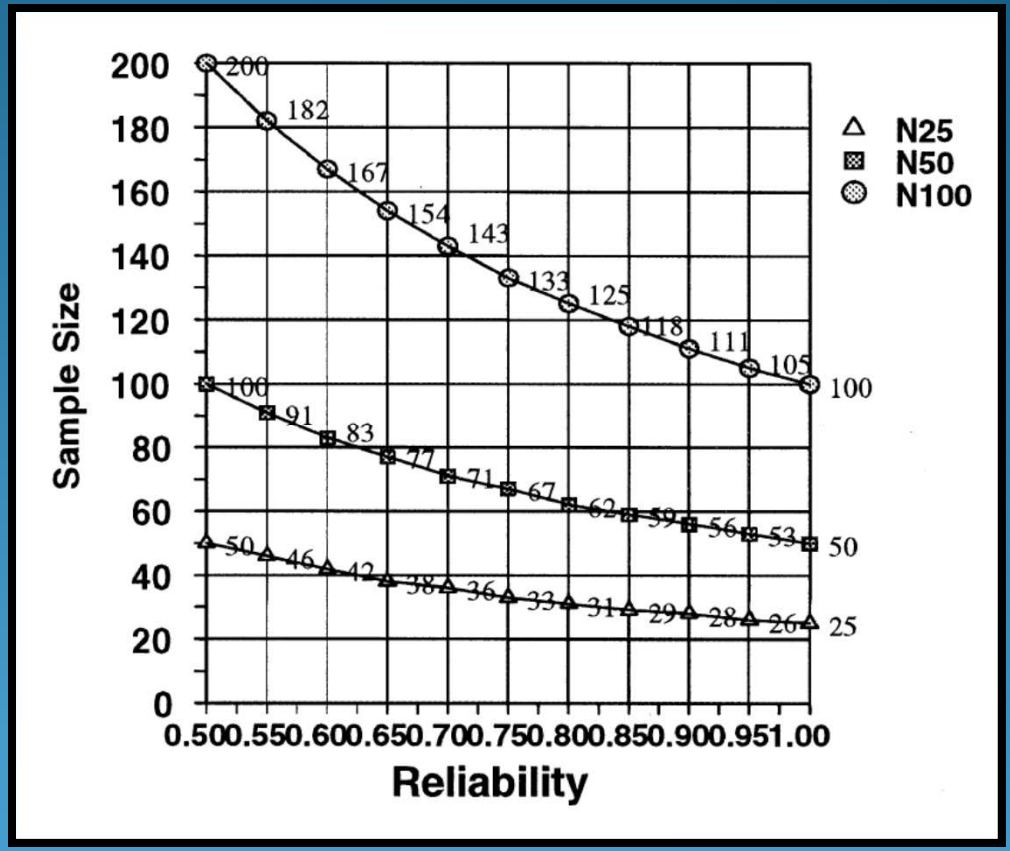


Problems with Clinical Trials

- Clinical Assessments
  - Bias
  - Placebo effects
  - Limited Resolution
  - Poor intra- and inter-rater reliability
- Patient Diaries
  - Compliance
  - Recall bias
  - Poor self-assessment
- Motion Sensor Monitoring
  - Extraneous patient movements
  - Dyskinesias
  - Gravitational artifacts
  - Sensor noise

Clinical Trial Sample Size Considerations

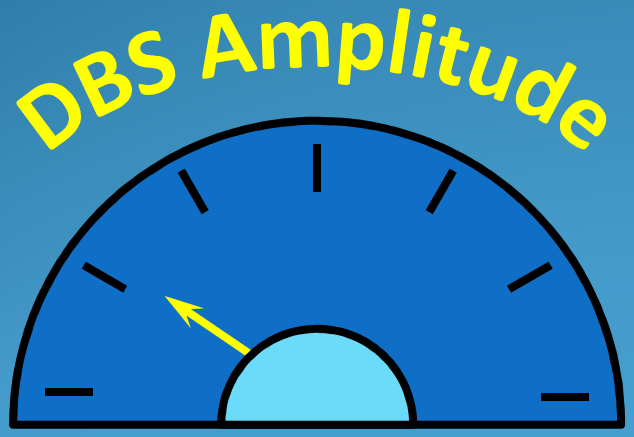
- The required sample size changes as a function of the reliability of the outcome measure.
- Sample size decreases as reliability increases.

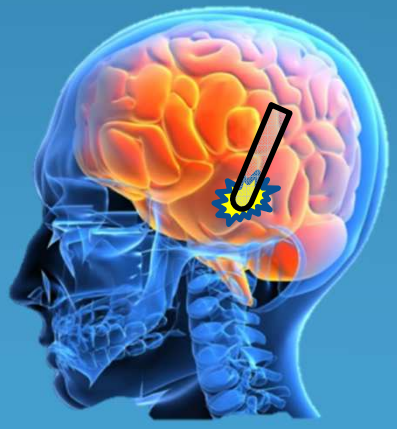


Perkins DO, Wyatt RJ, Bartko JJ. Penny-wise and pound-foolish: the impact of measurement error on sample size requirements in clinical trials. Biological Psychiatry. 2000 Apr 15;47(8):762–766.

Deep Brain Stimulation Tool

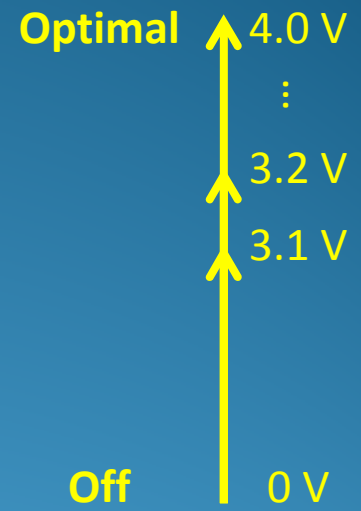
- Slowly modulate symptoms to simulate multiple disease states with relatively few subjects





Protocol

- 18 subjects
  - 13 male, 5 female
  - Age 44-76 years
- Tasks were performed three times each at eleven DBS stimulation amplitudes
- Videotaped for subsequent clinical rating



Rest Tremor

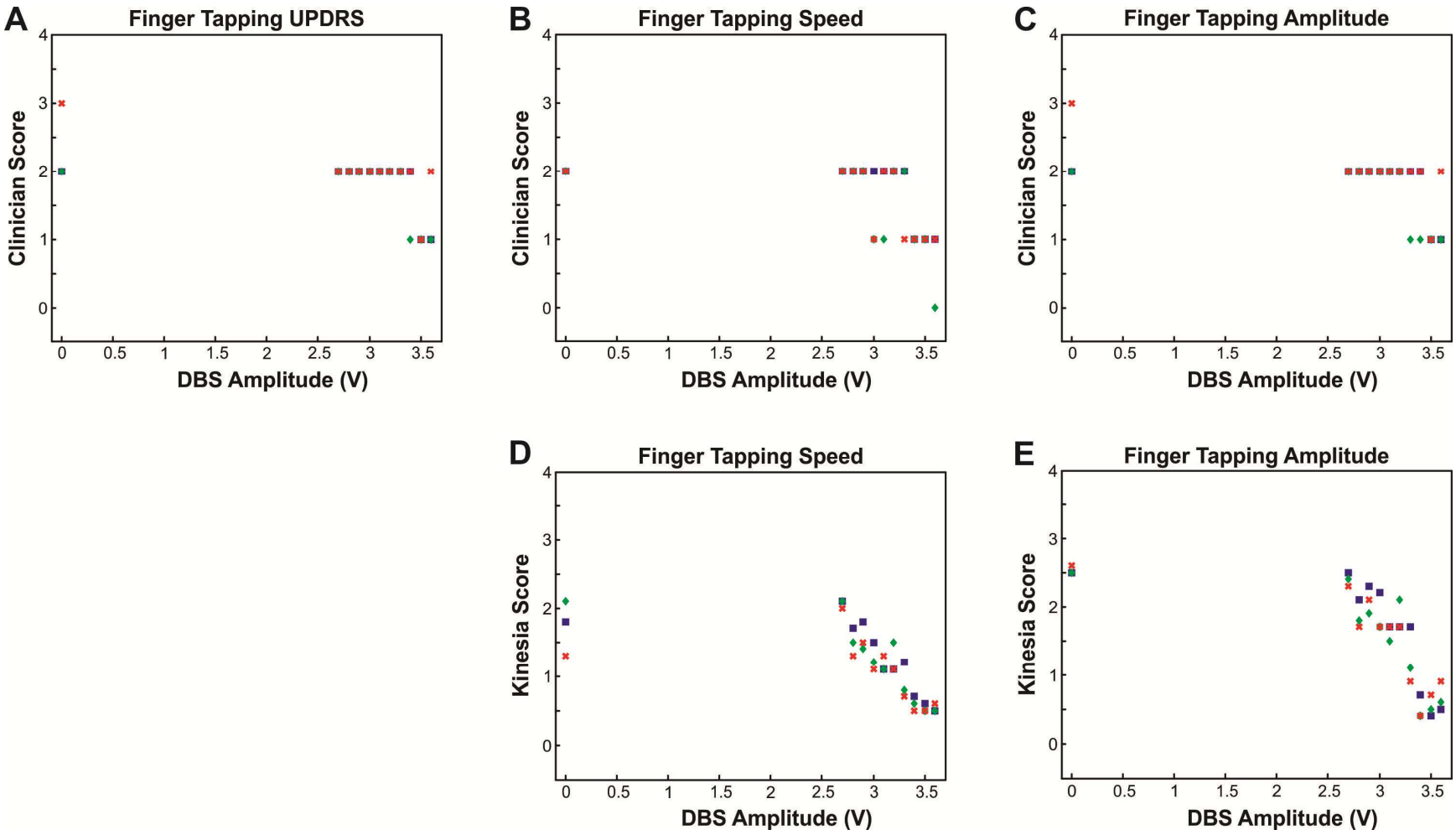
Postural Tremor

Finger taps

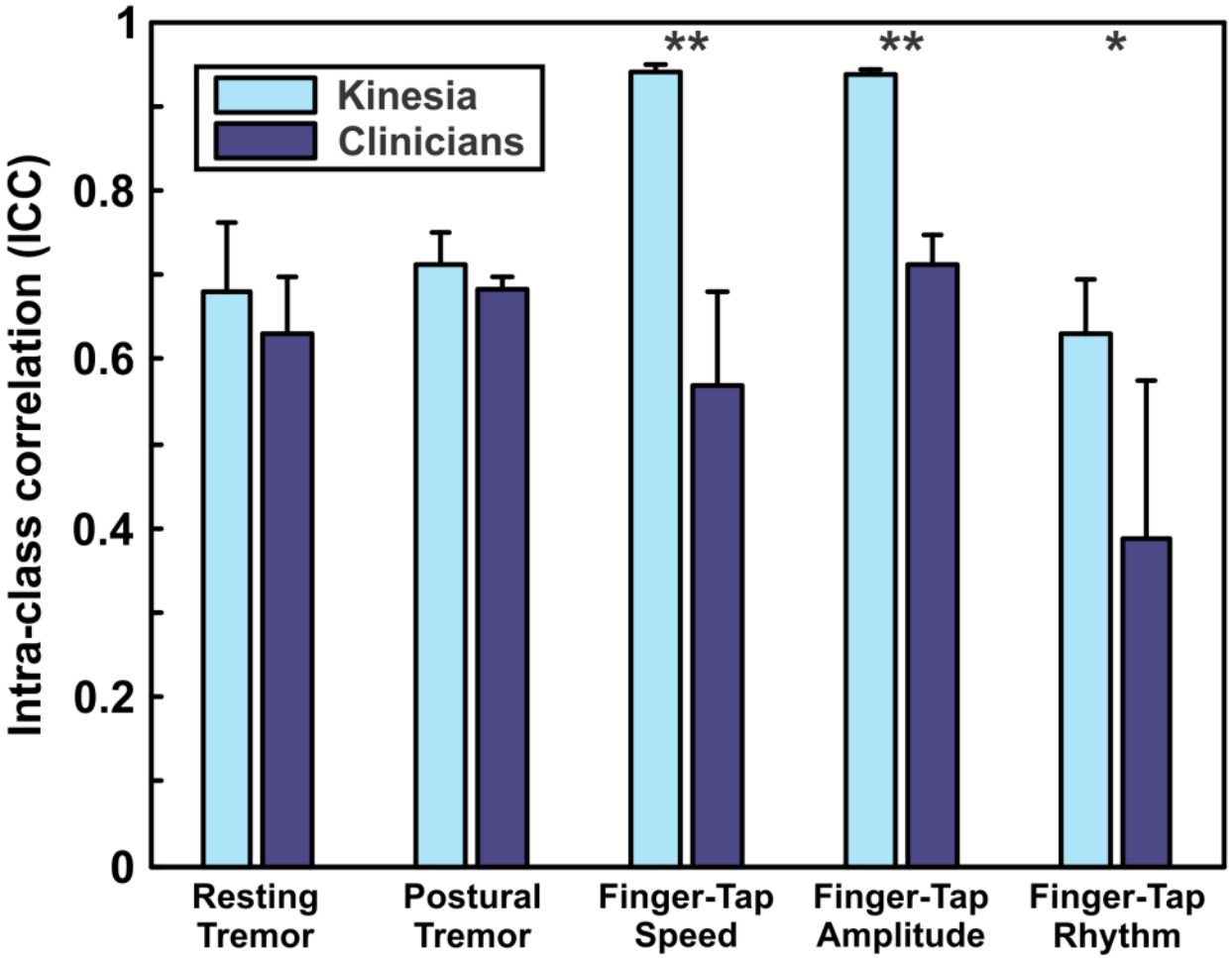
Assessment

- Unified Parkinson's Disease Rating Scale (UPDRS)
  - Resting Tremor
  - Postural Tremor
  - Finger Tapping (Bradykinesia)
- Modified Bradykinesia Rating Scale (MBRS)
  - Finger Tapping Speed (Bradykinesia)
  - Finger Tapping Amplitude (Hypokinesia)
  - Finger Tapping Rhythm (Dysrhythmia)
- Kinesia six degree-of-freedom motion sensor
  - 0 – 4 score based on motion data

DBS Modulation



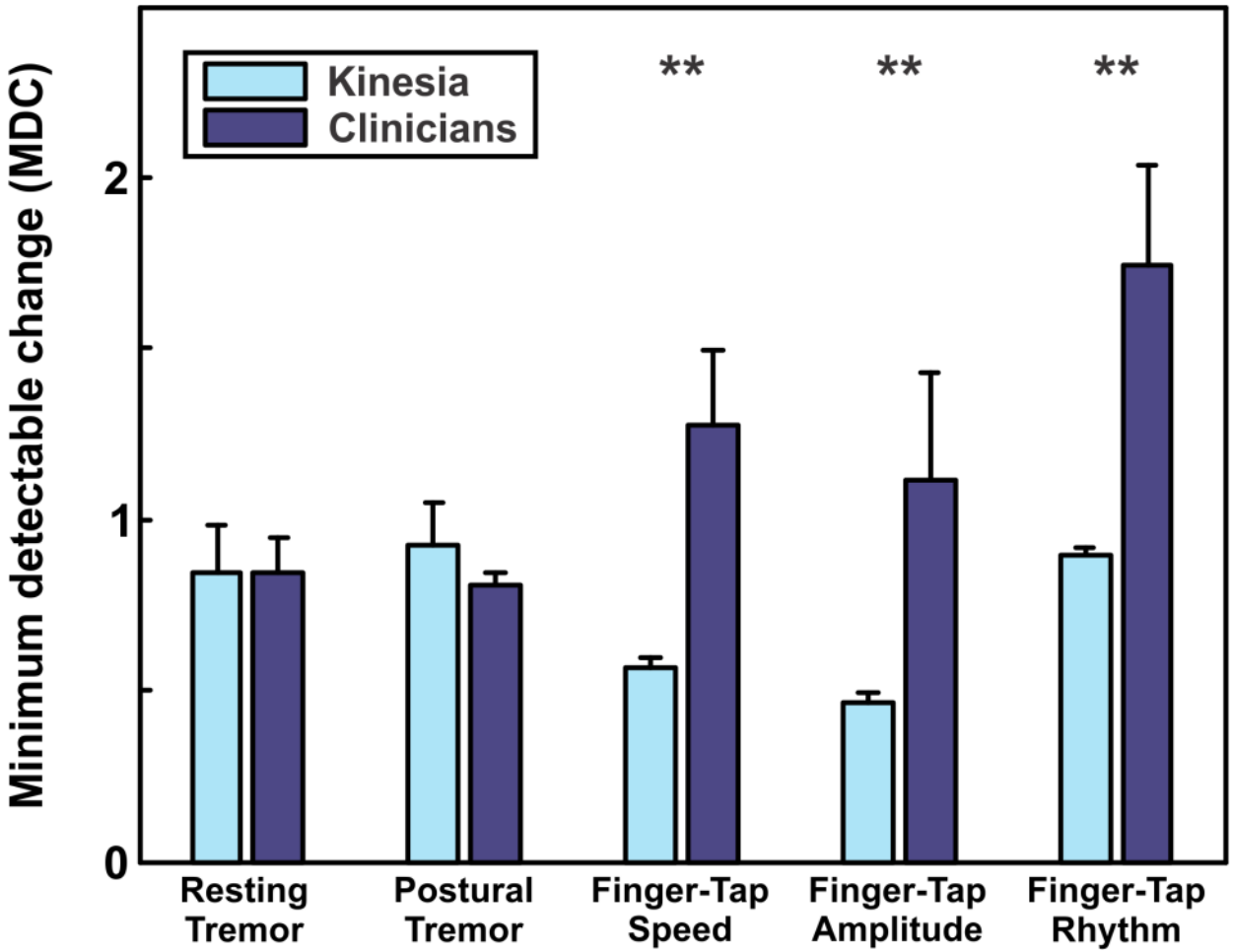
Intraclass Correlation (ICC)



* p<0.01

** p<0.001

Minimal Detectable Change (MDC)



** p<0.001

Sample Size Implications

	Clinician ICC	Kinesia ICC	Percent fewer subjects	Number of subjects based on Clinician	Number of subjects based on Kinesia
Rest Tremor	0.63	0.68	7.3	100	93
Postural Tremor	0.68	0.71	4.2	100	96
Speed	0.58	0.94	38.3	100	62
Amplitude	0.69	0.94	26.6	100	74
Rhythm	0.48	0.63	23.8	100	77

Conclusions

- Motion sensors can provide increased sensitivity and test-retest reliability over clinical assessments.
- The increased sensitivity and reliability afforded by motion sensors over clinical assessments **can decrease the number of subjects, shorten the duration, and lower the costs** required detect significant outcomes in clinical trials.
- Home-based motion sensor monitoring can improve temporal resolution in addition to score resolution.

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