KINEMATIC ANALYSES OF MOVEMENT DISTURBANCES IN PARKINSON'S DISEASE, AIMING AT "PROBATIO CLINICA SINE PLACEBO"

S. Katayama
Neurological Institute, Southern Tohoku General Hospital, Fukushima, Japan

Background and Purpose: "You never really understand something until you can put numbers to it (Lord Kelvin, 1883)" and very often, insight can be gleaned merely from the act of calculating something.

The severity of akinesia and tremor in Parkinson's disease (PD) is conventionally assessed using UPDRS (Part III) or other scoring system, e.g. the Parkinson Activity Scale (PAS), based on neurological examination and observation, but these methods lack quantitative aspects.

They provide us a useful but brief and momentary observation, and limited time resolution of the UPDRS constrains the capture of symptom fluctuation patterns during the course of a day. Clinician ratings can often vary across raters and at different times.

Akinesia is characterized by 1) delayed start and response time in movement, 2) delayed involuntary movement, 3) increased time to carry out movements, 4) difficulty in continuous activity to attain a goal and 5) difficulty in carrying out complex activities simultaneously as well as maintaining repetition (Delwaide, 1993).

Since these forms of akinesia as well as tremor are accompanied by changes in acceleration, we conducted long-term continuous actigraphy to assess the efficacy on motor activity during the whole course of drug treatment.

Methods: Measurement of the amount of movement was performed using an actigraph with wide-frequency band-pass filter in patients of PD with Hoehn and Yahr disability of 2 to 4 after obtaining their consent. For tremor recording, Actiwatch-Neurologica (Cambridge Neurotechnology, UK) was used. The actigraph was attached to the patient's wrist, usually on the akinesia dominant side without tremor or dyskinesia. Actigraphic measurements were performed over an extended period of time to examine variation in MA values before and after treatment with L-dopa preparations and dopamine antagonists.

Results: By averaging daily data gathered every 24 hour over several weeks or months, it was possible to quantify the circadian patterns of akinesia and tremor and to evaluate pharmaco- dynamic features of anti-parkinsonian medication.

They also enable us to titrate the lowest doses of drugs needed to alleviate akinesia and tremor.

The following results were obtained in our 20-year practice in movement disorders clinic.

1. Long-term measurements of daily motor activity (MA) of the limb using accelerometry
 a. Longitudinal daily accelerometric analysis
  i. Short-term rhythmic variation of movement disturbances, e.g. "two-week period" cycles in Parkinsonian akinesia
  ii. The month/year-long dynamic aspects of movement disorders, such as seasonal or working pattern variations
  iii. Titration of the optimal doses of anti-Parkinsonian drugs
 b. Kinematic analysis of daily patterns by averaging the actigraphic data
  i. Circadian rhythms in limb movements
  ii. The response profiles following each drug administration, such as "Wearing-off" or "On-off patterns" in advanced PD
2. Long-term quantitative analysis of tremor
  i. The diurnal and nocturnal patterns of tremor
  ii. Titration of the optimal doses of anti-tremor drugs

Discussion and Conclusion:

SWOT analysis (strengths, weaknesses, opportunities and threats) of accelerometric measurements was carried out in this study.

<u>Strength;</u>

1. Most subjects found the device comfortable, lightweight, and unobtrusive, and they would wear it in public. It maximized cosmetic acceptability and subject safety, as well as allowed unimpeded motion capture.
2. No experts/raters are needed. Accelerometer systems offer simplified operation requiring less operator expertise, training and attention.

3. Long-term continuous monitoring for weeks or months, even years would facilitate the assessment of the overall severity and the evaluation of therapeutic efforts and would make it possible to calculate average responses to medication.

Weakness;

1. Actigraphy does not give any representation of the content of movements, only indicating the magnitude and acceleration of movement. Without description of medication times or behavioral records, it is difficult to determine the true nature of fluctuations in motor symptoms, tremor or dyskinesia.
2. Some patients feel uncomfortable and unpleasant.
3. Higher price compared with pedometer.
4. No compatibility with each other due to the different specifications.

Opportunities;

1. Over 700 trials for PD have been found in the Clinical Trials.gov registry and the increasing numbers of application of kinematic analysis might be expected in future.
2. Combined use of kinematic analysis with “the ParkinsonNet Trial”.
3. Low cost actigraphs now available, but studies on their reliability and interchangeability for assessing a standardized bout of physical activity are needed.

Threats:

1. Under the present clinical trial system, ironically speaking, refrain from kinematic analysis that might unlock the key of the double blind trials.

“Probatio Clinica sine Placebo” is expected to become standard practice.